(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
06 June 2019 (06.06.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/108900 A1

(51) International Patent Classification:
G01N 33/50 (2006.01) *G01N 33/574* (2006.01)

(21) International Application Number:
PCT/US2018/063255

(22) International Filing Date:
30 November 2018 (30.11.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/593,043 30 November 2017 (30.11.2017) US
62/752,010 29 October 2018 (29.10.2018) US

(71) Applicants: **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, 4056 Basel (CH). **THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA** [US/US]; 3160 Chestnut Street, Suite 200, Philadelphia, PA 19104 (US).

(72) Inventors: **PRUTEANU-MALINICI, Iulian**; 250 Massachusetts Avenue, Cambridge, MA 02139 (US). **MANSFIELD, Keith**; 250 Massachusetts Avenue, Cambridge, MA 02139 (US). **ENGELS, Boris**; 250 Massachusetts Avenue, Cambridge, MA 02139 (US). **MELENHORST, Jan, J.**; 11 Exton Circle, Cherry Hill, NJ 08003 (US). **COHEN, Adam, David**; 211 Clwyd Rd., Bala Cynwyd, PA 19004 (US). **STADTMAUER, Edward, A.**; 1019 Great Springs Rd, Bryn Mawr, PA 19010 (US). **GARFALL, Alfred**; 410 W Rose Valley Rd, Wallingford, PA 19086 (US). **MILONE, Michael, C.**; 314 Surrey Road, Cherry Hill, NJ 08002 (US). **FRAIETTA, Joseph, A.**; 312 Raphael Ct, Williamstown, NJ 08094 (US).

(74) Agent: **COLLAZO, Diana, M.** et al.; Lando & Anastasi, LLP, Riverfront Office Park, One Main Street, Suite 1100, Cambridge, MA 02142 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,

(54) Title: BCMA-TARGETING CHIMERIC ANTIGEN RECEPTOR, AND USES THEREOF

(57) Abstract: The invention provides compositions and methods for treating diseases associated with expression of BCMA. The invention also relates to a method of administering a BCMA-targeting chimeric antigen receptor (CAR) therapy and an additional therapeutic agent.

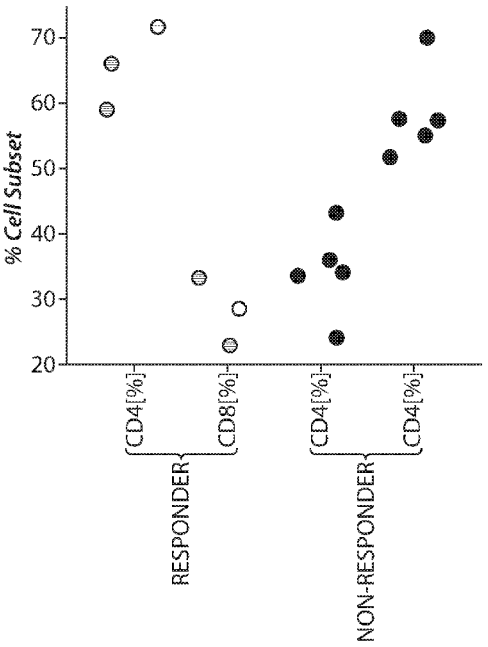


FIG. 1A

WO 2019/108900 A1

[Continued on next page]

TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

BCMA-TARGETING CHIMERIC ANTIGEN RECEPTOR, AND USES THEREOF

RELATED APPLICATIONS

This application claims priority to U.S. Serial No. 62/593,043 filed November 30, 2017, and U.S. Serial No. 62/752,010 filed October 29, 2018, the contents of each of which are incorporated herein by reference in their entirety.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on November 28, 2018, is named N2067-7137WO_SL.txt and is 1,411,518 bytes in size.

FIELD OF THE INVENTION

The present invention relates generally to the use of cells engineered to express a chimeric antigen receptor targeting B-cell maturation antigen protein (BCMA), optionally in combination with an additional therapeutic agent, to treat a disease associated with the expression of BCMA. The invention further describes prognostic biomarkers for BCMA-targeted therapies.

BACKGROUND OF THE INVENTION

BCMA is a tumor necrosis family receptor (TNFR) member expressed on cells of the B-cell lineage. BCMA expression is the highest on terminally differentiated B cells that assume the long lived plasma cell fate, including plasma cells, plasmablasts and a subpopulation of activated B cells and memory B cells. BCMA is involved in mediating the survival of plasma cells for maintaining long-term humoral immunity. The expression of BCMA has been recently linked to a number of cancers, autoimmune disorders, and infectious diseases. Cancers with increased expression of BCMA include some hematological cancers, such as multiple myeloma (MM), Hodgkin's and non-Hodgkin's lymphoma, diffuse large B-cell lymphoma (DLBCL), various leukemias (e.g., chronic lymphocytic leukaemia (CLL)), and glioblastoma.

Given the ongoing need for improved strategies for targeting diseases such as cancer, new compositions and methods for improving therapeutic agents that target BCMA, e.g., anti-BCMA chimeric antigen receptor (CAR) therapies, are highly desirable.

SUMMARY OF THE INVENTION

The disclosure features, at least in part, a method of treating a disease or disorder associated with expression of B-cell maturation antigen (BCMA, also known as TNFRSF17, BCM, or CD269). In certain embodiments, the disorder is a cancer, e.g., a hematological cancer. In some embodiments, the disclosure features a BCMA CAR-expressing cell therapy, e.g., as a monotherapy or in a combination therapy with an additional therapeutic agent. In some embodiments, the BCMA CAR-expressing cell therapy is a cell (e.g., a population of cells) that expresses a CAR molecule that binds BCMA. In some embodiments, the combination therapy maintains or has better clinical effectiveness as compared to either therapy alone. In one embodiment, the BCMA CAR-expressing cell therapy and the additional therapeutic agent are present in a single dose form, or as two or more dose forms. In one embodiment, provided herein is a composition comprising a BCMA CAR-expressing cell therapy and an additional therapeutic agent for use as a medicament. In one embodiment, provided herein is a composition comprising a BCMA CAR-expressing cell therapy and an additional therapeutic agent for use in the treatment of a disease associated with expression of BCMA. In one aspect, provided herein is a kit comprising a BCMA CAR-expressing cell therapy and an additional therapeutic agent. In some embodiments, the disclosure additional features methods of evaluating or predicting a subject's responsiveness to a BCMA CAR-expressing cell therapy, or methods of evaluating or predicting the potency of a BCMA CAR-expressing cell therapy in a subject. In some embodiments, a BCMA-targeting CAR therapy is manufactured or administered based on the acquisition of a level of a biomarker from a patient sample.

In one aspect, this invention features methods of predicting *in vivo* expansion of BCMA CAR T cells in a subject. In another aspect, featured herein are methods of predicting a subject's responsiveness to BCMA CAR T cells. In some embodiments, a higher CD4+:CD8+ T cell ratio in a leukapheresis product isolated from the subject can be used to predict greater *in vivo* expansion of BCMA CAR T cells in the subject and/or greater clinical responses of the subject to the BCMA CAR T cells. In some embodiments, a lower CD4+:CD8+ T cell ratio in a leukapheresis product isolated from the subject can be used to predict weaker *in vivo* expansion of BCMA CAR T cells in the subject and/or weaker clinical responses of the subject to the BCMA CAR T cells. In some embodiments, a higher CD4+:CD8+ T cell ratio in a seed culture at the start of the manufacturing of the BCMA CAR T cells (e.g., in a leukapheresis product after monocytes are removed) can be used to predict greater *in vivo* expansion of BCMA CAR T cells in the subject and/or greater clinical responses of the subject to the BCMA CAR T cells. In some embodiments, a lower CD4+:CD8+ T cell ratio in a seed culture at the start of the manufacturing of the BCMA CAR T cells (e.g., in a leukapheresis product after monocytes are removed) can be used to predict weaker *in vivo* expansion of BCMA CAR T cells in the subject and/or weaker clinical responses of the subject to the BCMA CAR T cells. In some embodiments, a

higher CD4+:CD8+ T cell ratio in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR T cells can be used to predict greater *in vivo* expansion of BCMA CAR T cells in the subject. In some embodiments, a lower CD4+:CD8+ T cell ratio in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR T cells can be used to predict weaker *in vivo* expansion of BCMA CAR T cells in the subject.

In some embodiments, a higher frequency of CD8+ T cells with an "early-memory" phenotype (e.g., a higher frequency of CD45RO-CD27+CD8+ T cells) in a leukapheresis product isolated from the subject can be used to predict greater *in vivo* expansion of BCMA CAR T cells in the subject and/or greater clinical responses of the subject to the BCMA CAR T cells. In some embodiments, a lower frequency of CD8+ T cells with an "early-memory" phenotype (e.g., a lower frequency of CD45RO-CD27+CD8+ T cells) in a leukapheresis product isolated from the subject can be used to predict weaker *in vivo* expansion of BCMA CAR T cells in the subject and/or weaker clinical responses of the subject to the BCMA CAR T cells.

In some embodiments, greater *in vitro* expansion of seeded cells from the subject during manufacturing of the BCMA CAR T cells can be used to predict greater *in vivo* expansion of BCMA CAR T cells in the subject. In some embodiments, weaker *in vitro* expansion of seeded cells from the subject during manufacturing of the BCMA CAR T cells can be used to predict weaker *in vivo* expansion of BCMA CAR T cells in the subject.

In one aspect, provided herein is a method of evaluating or predicting a subject's responsiveness to a BCMA CAR-expressing cell therapy, wherein the subject has a disease associated with the expression of BCMA, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of

the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

(a) an increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased responsiveness of the subject to the BCMA CAR-expressing cell therapy; or

(b) a decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy,

thereby evaluating or predicting the subject's responsiveness to the BCMA CAR-expressing cell therapy.

In some embodiments, the method comprises acquiring a value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the method comprises acquiring a value for the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of

CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., population doublings by day 9 (PDL9).

In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased responsiveness of the subject to the BCMA CAR-expressing cell therapy. In some embodiments, the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy.

In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased responsiveness of the subject to the BCMA CAR-expressing cell therapy. In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of the subject as a responder of the BCMA CAR-expressing cell therapy. In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of the subject as suitable for the BCMA CAR-expressing cell therapy. In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of

increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy. In some embodiments, the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of the subject as a non-responder of the BCMA CAR-expressing cell therapy. In some embodiments, the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) comprises a ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells), e.g., as measured by an assay disclosed herein, e.g., flow cytometry. In some embodiments,

In some embodiments, the ratio being:

(1) greater than or equal to 1 (e.g., between 1 and 5, e.g., between 1 and 3.5); or

(2) greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5),

is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the ratio being less than 1 (e.g., between 0.001 and 1) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the value for the level or activity of CD8+ Tscm (stem cell memory T cells) comprises the percentage of CD8+ Tscm (stem cell memory T cells) among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the level or activity of HLADR-CD95+CD27+CD8+ cells comprises the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being greater than or equal to 25% (e.g., between 30% and 90%, e.g., between 35% and 85%, e.g., between 40% and 80%, e.g., between 45% and 75%, e.g., between 50% and 75%) is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being less than 25% (e.g., between 0.1% and 25%, e.g., between 0.1% and 22%, e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%)) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the value for the level or activity of CD45RO-CD27+CD8+ cells comprises the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 20% (e.g., between 20% and 90%, e.g., between 20% and 80%, e.g., between 20% and 70%, e.g., between 20% and 60%) is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 20% (e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells comprises the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 15% (e.g., between 15% and 90%, e.g., between 15% and 80%, e.g., between 15% and 70%, e.g., between 15% and 60%, e.g., between 15% and 50%) is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 15% (e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%, e.g., between 0.1% and 8%) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per μg DNA using qPCR.

In some embodiments, the value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy comprises the fold expansion of seeded cells from the subject during manufacturing (e.g., total cell counts at the end of manufacturing relative to at the start of manufacturing) of the BCMA CAR-expressing cell therapy, e.g., as measured by an assay disclosed herein, e.g., as measured by cell counting.

In some embodiments, the method further comprises performing:

manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, the BCMA CAR-expressing cell therapy to the subject, when:

(a) the subject was indicated or predicted to have increased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject was indicated or predicted as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject was indicated or predicted as suitable for the BCMA CAR-expressing cell therapy; or

(d) the BCMA CAR-expressing cell therapy was indicated or predicted to have increased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per μg DNA using qPCR.

In some embodiments, the method further comprises performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of the BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not the BCMA CAR-expressing cell therapy) to the subject;

administering the BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of the BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject, when:

(a) the subject was indicated or predicted to have decreased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject was indicated or predicted as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) the BCMA CAR-expressing cell therapy was indicated or predicted to have decreased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per μg DNA using qPCR.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising:

responsive to an increased value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of a BCMA CAR-expressing cell therapy,

as compared to a reference value, e.g., a non-responder reference value, performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject,

thereby treating the subject having the disease associated with the expression of BCMA.

In some embodiments, the method comprises: responsive to an increased value for one, two, three, four, five, or all of (i)-(vi), identifying or predicting one, two, three, or all of:

(a) the subject as having increased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) the BCMA CAR-expressing cell therapy as having increased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising:

responsive to a decreased value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of a BCMA CAR-expressing cell therapy,

as compared to a reference value, e.g., a responder reference value, performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject,

thereby treating the subject having the disease associated with the expression of BCMA.

In some embodiments, the method comprises: response to a decreased value for one, two, three, four, five, or all of (i)-(vi), identifying or predicting one, two, or all of:

(a) the subject as having decreased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) the BCMA CAR-expressing cell therapy as having decreased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) comprises a ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells), e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the method comprises:

responsive to the ratio being:

(1) greater than or equal to 1 (e.g., between 1 and 5, e.g., between 1 and 3.5); or

(2) greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the method comprises:

responsive to the ratio being less than 1 (e.g., between 0.001 and 1), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or

CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the value for the level or activity of CD8+ Tscm (stem cell memory T cells) comprises the percentage of CD8+ Tscm (stem cell memory T cells) among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the level or activity of HLADR-CD95+CD27+CD8+ cells comprises the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the method comprises:

responsive to the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being greater than or equal to 25% (e.g., between 30% and 90%, e.g., between 35% and 85%, e.g., between 40% and 80%, e.g., between 45% and 75%, e.g., between 50% and 75%), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the method comprises:

responsive to the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being less than 25% (e.g., between 0.1% and 25%, e.g., between 0.1% and 22%, e.g., between 0.1% and 20%,

e.g., between 0.1% and 18%, e.g., between 0.1% and 15%), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the value for the level or activity of CD45RO-CD27+CD8+ cells comprises the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the method comprises:

responsive to the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 20% (e.g., between 20% and 90%, e.g., between 20% and 80%, e.g., between 20% and 70%, e.g., between 20% and 60%), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the method comprises:

responsive to the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 20% (e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-

expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells comprises the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the method comprises:

responsive to the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 15% (e.g., between 15% and 90%, e.g., between 15% and 80%, e.g., between 15% and 70%, e.g., between 15% and 60%, e.g., between 15% and 50%), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the method comprises:

responsive to the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 15% (e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%, e.g., between 0.1% and 8%), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

In some embodiments, the value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy comprises the fold expansion of seeded cells from the subject during manufacturing (e.g., total cell counts at the end of manufacturing relative to at the start of manufacturing) of the BCMA CAR-expressing cell therapy, e.g., as measured by an assay disclosed herein, e.g., as measured by cell counting.

In one aspect, provided herein is a method of evaluating or predicting the potency of a BCMA CAR-expressing cell therapy in a subject, wherein the subject has a disease associated with the expression of BCMA and wherein the BCMA CAR-expressing cell therapy is manufactured using cells (e.g., T cells) from the subject, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

(a) an increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased potency of the BCMA CAR-expressing cell therapy in the subject; or

(b) a decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased potency of the BCMA CAR-expressing cell therapy in the subject,

thereby evaluating or predicting the potency of the BCMA CAR-expressing cell therapy.

In some embodiments, the method comprises acquiring a value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-

expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the method comprises acquiring a value for the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., population doublings by day 9 (PDL9).

In some embodiments, the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In some embodiments, the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

In one aspect, disclosed herein is a method of manufacturing a BCMA CAR-expressing cell therapy, wherein the BCMA CAR-expressing cell therapy is manufactured using cells (e.g., T cells) from a subject, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

responsive to an increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, manufacturing the BCMA CAR-expressing cell therapy using cells from the subject.

In some embodiments, the method comprises acquiring a value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the method comprises acquiring a value for the level or

activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., population doublings by day 9 (PDL9).

In one aspect, provided herein is a method of manufacturing a BCMA CAR-expressing cell therapy, wherein the BCMA CAR-expressing cell therapy is manufactured using cells (e.g., T cells) from a subject, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of

the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

responsive to a decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, performing one, two, three, or all of:

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), and manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject.

In some embodiments, the method comprises acquiring a value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample

(e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the method comprises acquiring a value for the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)). In some embodiments, the method comprises acquiring a value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., population doublings by day 9 (PDL9).

In some embodiments, the value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) comprises a ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells), e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the level or activity of CD8+ Tscm (stem cell memory T cells) comprises the percentage of CD8+ Tscm (stem cell memory T cells) among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the level or activity of HLADR-CD95+CD27+CD8+ cells comprises the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the level or activity of CD45RO-CD27+CD8+ cells comprises the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells comprises the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

In some embodiments, the value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy comprises the fold expansion of seeded cells from the subject during manufacturing (e.g., total cell counts at the end of manufacturing relative to at the start of manufacturing) of the BCMA CAR-expressing cell therapy, e.g., as measured by an assay disclosed herein, e.g., as measured by cell counting.

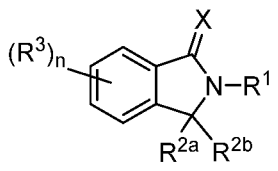
In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with one, two, or all of:

(1) an agent that increases the efficacy of the cell comprising the CAR nucleic acid or CAR polypeptide;

(2) an agent that ameliorates one or more side effects associated with administration of the cell comprising the CAR nucleic acid or CAR polypeptide;

(3) an agent that treats the disease associated with the expression of BCMA.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a compound of Formula (I) (COF1), wherein the COF1 is:



(I)

or a pharmaceutically acceptable salt, ester, hydrate, solvate, or tautomer thereof, wherein:

X is O or S;

R^1 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl, each of which is optionally substituted by one or more R^4;

each of R^{2a} and R^{2b} is independently hydrogen or C_1-C_6 alkyl; or R^{2a} and R^{2b} together with the carbon atom to which they are attached form a carbonyl group or a thiocarbonyl group;

each of R^3 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, $-C(O)R^A$, $-C(O)OR^B$, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, $-S(O)_xR^E$, -

$S(O)_xN(R^C)(R^D)$, or $-N(R^C)S(O)_xR^E$, wherein each alkyl, alkenyl, alkynyl, and heteroalkyl is independently and optionally substituted with one or more R^6;

each R^4 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, oxo, $-C(O)R^A$, $-C(O)OR^B$, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, $-S(O)_xR^E$, $-S(O)_xN(R^C)(R^D)$, $-N(R^C)S(O)_xR^E$, carbocyclyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, heteroalkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently and optionally substituted with one or more R^7;

each of R^A, R^B, R^C, R^D, and R^E is independently hydrogen or C_1-C_6 alkyl;

each R^6 is independently C_1-C_6 alkyl, oxo, cyano, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, aryl, or heteroaryl, wherein each aryl and heteroaryl is independently and optionally substituted with one or more R^8;

each R^7 is independently halo, oxo, cyano, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, or $-N(R^C)C(O)R^A$;

each R^8 is independently C_1-C_6 alkyl, cyano, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, or $-N(R^C)C(O)R^A$;

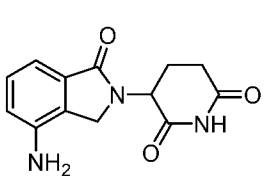
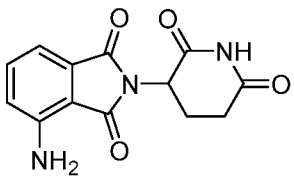
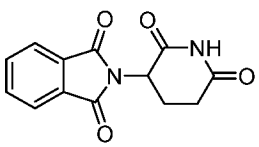
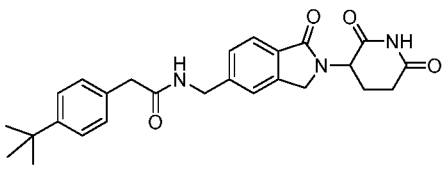
n is 0, 1, 2, 3 or 4; and

x is 0, 1, or 2, optionally wherein:

(1) the COF1 is an immunomodulatory imide drug (IMiD), or a pharmaceutically acceptable salt thereof;

(2) the COF1 is selected from the group consisting of lenalidomide, pomalidomide, thalidomide, and 2-(4-(tert-butyl)phenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)acetamide, or a pharmaceutically acceptable salt thereof;

(3) the COF1 is selected from the group consisting of:


,

,

, and

, or a pharmaceutically acceptable salt thereof; or

(4) the COF1 is lenalidomide, or a pharmaceutically acceptable salt thereof.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a kinase inhibitor, e.g., a BTK inhibitor, e.g., ibrutinib.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a second CAR-expressing cell therapy.

In some embodiments, the second CAR-expressing cell therapy is a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019. In some embodiments, the CD19 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the CD19 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD19 CAR. In some embodiments, the CD19 CAR comprises an amino acid sequence disclosed in Table 8, 9, or 10 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 8, 9, or 10), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second CAR-expressing cell therapy is a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein. In some embodiments, the CD20 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the CD20 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD20 CAR. In some embodiments, the CD20 CAR comprises an amino acid sequence disclosed in Table 11, 12, or 13 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 11, 12, or 13), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second CAR-expressing cell therapy is a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein. In some embodiments, the CD22 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the CD22 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD22 CAR. In some embodiments, the CD22 CAR comprises an amino acid sequence disclosed in Table 14 or 15 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 14 or 15), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second CAR-expressing cell therapy is a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA

CAR (e.g., a BCMA CAR disclosed herein). In some embodiments, the second CAR is selected from the group consisting of a CD19 CAR (e.g., a CD19 CAR disclosed herein), a CD20 CAR (e.g., a CD20 CAR disclosed herein), and a CD22 CAR (e.g., a CD22 CAR disclosed herein). In some embodiments, the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein). In some embodiments, the CD19 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD19 CAR. In some embodiments, the CD19 CAR comprises an amino acid sequence disclosed in Table 8, 9, or 10 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 8, 9, or 10), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions. In some embodiments, the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein). In some embodiments, the CD20 CAR comprises an amino acid sequence disclosed in Table 11, 12, or 13 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 11, 12, or 13), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions. In some embodiments, the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein). In some embodiments, the CD22 CAR comprises an amino acid sequence disclosed in Table 14 or 15 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 14 or 15), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second CAR-expressing cell therapy is a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to a first antigen and a second antigen, wherein the first antigen is BCMA. In some embodiments, the second antigen is selected from the group consisting of CD19, CD20, and CD22. In some embodiments, the second antigen is CD19. In some embodiments, the second antigen is CD20. In some embodiments, the second antigen is CD22.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a CD19 inhibitor, e.g., a CD19 inhibitor disclosed herein. In some embodiments, the CD19 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a CD20 inhibitor, e.g., a CD20 inhibitor disclosed herein. In some embodiments, the CD20 inhibitor is a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338. In some embodiments, the CD20 inhibitor is administered after the administration of the BCMA CAR-

expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a CD22 inhibitor, e.g., a CD22 inhibitor disclosed herein. In some embodiments, the CD22 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a molecule that binds to Fc receptor like 2 (FCRL2) or Fc receptor like 5 (FCRL5). In some embodiments, the molecule is a CAR-expressing cell therapy comprising a cell expressing a CAR that binds to FCRL2 or FCRL5. In some embodiments, the molecule is a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to a first antigen and a second antigen, wherein the first antigen is FCRL2 or FCRL5, optionally wherein the second antigen is CD3.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an interleukin-15 (IL-15) polypeptide, an interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both an IL-15 polypeptide and an IL-15Ra polypeptide, e.g., hetIL-15.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an inhibitor of TGF beta.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an EGFR inhibitor, e.g., an $EGFR^{mut}$-tyrosine kinase inhibitor (TKI). In some embodiments, the EGFR inhibitor is EGF816. In some embodiments, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide. In some embodiments, the EGFR inhibitor is compound A40 disclosed in Table 27.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an adenosine A2AR antagonist. In some embodiments, the adenosine A2AR antagonist is selected from the group consisting of PBF509, CPI444, AZD4635, Vipadenant, GBV-2034, and AB928. In some embodiments, the adenosine A2AR antagonist is selected from the group consisting of 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-

[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an anti-CD73 antibody molecule, e.g., an anti-CD73 antibody molecule disclosed herein.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with a check point inhibitor. In some embodiments, the check point inhibitor is a PD-1 inhibitor. In some embodiments, the PD-1 inhibitor is selected from the group consisting of PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, and AMP-224. In some embodiments, the PD-1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject, e.g. for at least 1, 2, 3, 4, or 5 weeks, e.g., for at least, 1, 2, 3, 4, 5, 10, 15, 20, 25, or 30-fold. In some embodiments, the BCMA CAR-expressing cells are administered to the subject prior to the administration of the PD-1 inhibitor. In some embodiments, the BCMA CAR-expressing cells do not expand or have minimal expansion (e.g., no more than 1, 2, 3, 4, 5, or 10-fold expansion) in the subject at the time the PD-1 inhibitor is administered. In some embodiments, the check point inhibitor is a PD-L1 inhibitor. In some embodiments, the PD-L1 inhibitor is selected from the group consisting of FAZ053, Atezolizumab, Avelumab, Durvalumab, and BMS-936559. In some embodiments, the PD-L1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject, e.g. for at least 1, 2, 3, 4, or 5 weeks, e.g., for at least, 1, 2, 3, 4, 5, 10, 15, 20, 25, or 30-fold. In some embodiments, the BCMA CAR-expressing cells are administered to the subject prior to the administration of the PD-L1 inhibitor. In some embodiments, the BCMA CAR-expressing cells do not expand or have minimal expansion (e.g., no more than 1, 2, 3, 4, 5, or 10-fold expansion) in the subject at the time the PD-L1 inhibitor is administered. In some embodiments, the check point inhibitor is a LAG-3 inhibitor. In some embodiments, the LAG-3 inhibitor is selected from the group consisting of LAG525, BMS-986016, TSR-033, MK-4280 and REGN3767. In some embodiments, the check point inhibitor is a TIM-3 inhibitor. In some embodiments, the TIM-3 inhibitor is selected from the group consisting of MGB453, TSR-022, and LY3321367.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an antibody molecule that binds to CD32B.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an antibody molecule that binds to IL-17, e.g., an antagonistic antibody molecule that binds to IL-17, e.g., CJM112.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an antibody molecule that binds to IL-1 beta.

In certain embodiments of the foregoing aspects, the method comprises administering the BCMA CAR-expressing cell therapy to the subject in combination with an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO), e.g., an IDO1 inhibitor. In some embodiments, the inhibitor of IDO and/or TDO is INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287. In some embodiments, the inhibitor of IDO and/or TDO is (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject. In some embodiments, the second therapy is a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019. In some embodiments, the CD19 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the CD19 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD19 CAR. In some embodiments, the CD19 CAR comprises an amino acid sequence disclosed in Table 8, 9, or 10 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 8, 9, or 10), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second therapy is a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein. In some embodiments, the CD20 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the CD20 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD20 CAR. In some embodiments, the CD20 CAR comprises an amino acid sequence disclosed in Table 11, 12, or 13 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 11, 12, or 13), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second therapy is a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein. In some embodiments, the CD22 CAR-expressing cell

therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the CD22 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD22 CAR. In some embodiments, the CD22 CAR comprises an amino acid sequence disclosed in Table 14 or 15 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 14 or 15), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second therapy is a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein). In some embodiments, the second CAR is selected from the group consisting of a CD19 CAR (e.g., a CD19 CAR disclosed herein), a CD20 CAR (e.g., a CD20 CAR disclosed herein), and a CD22 CAR (e.g., a CD22 CAR disclosed herein). In some embodiments, the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein). In some embodiments, the CD19 CAR-expressing cell therapy comprises a cell (e.g., a population of cells) expressing a CD19 CAR. In some embodiments, the CD19 CAR comprises an amino acid sequence disclosed in Table 8, 9, or 10 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 8, 9, or 10), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions. In some embodiments, the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein). In some embodiments, the CD20 CAR comprises an amino acid sequence disclosed in Table 11, 12, or 13 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 11, 12, or 13), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions. In some embodiments, the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein). In some embodiments, the CD22 CAR comprises an amino acid sequence disclosed in Table 14 or 15 (e.g., a CDR, scFv, or full-length amino acid sequence disclosed in Table 14 or 15), or a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, e.g., conserved substitutions.

In some embodiments, the second therapy is a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR that binds to a first antigen and a second antigen, wherein the first antigen is BCMA. In some embodiments, the second antigen is selected from the group consisting of CD19, CD20, and CD22. In some embodiments, the second antigen is CD19. In some embodiments, the second antigen is CD20. In some embodiments, the second antigen is CD22.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a

second therapy to the subject. In some embodiments, the second therapy is a CD19 inhibitor, e.g., a CD19 inhibitor disclosed herein. In some embodiments, the CD19 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In some embodiments, the second therapy is a CD20 inhibitor, e.g., a CD20 inhibitor disclosed herein. In some embodiments, the CD20 inhibitor is a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338. In some embodiments, the CD20 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In some embodiments, the second therapy is a CD22 inhibitor, e.g., a CD22 inhibitor disclosed herein. In some embodiments, the CD22 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is a molecule that binds to Fc receptor like 2 (FCRL2) or Fc receptor like 5 (FCRL5). In some embodiments, the molecule is a CAR-expressing cell therapy comprising a cell expressing a CAR that binds to FCRL2 or FCRL5. In some embodiments, the molecule is a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to a first antigen and a second antigen, wherein the first antigen is FCRL2 or FCRL5, optionally wherein the second antigen is CD3.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an inhibitor of TGF beta.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an EGFR inhibitor, e.g., an $EGFR^{mut}$-tyrosine kinase inhibitor (TKI). In some embodiments, the EGFR inhibitor is EGF816. In some embodiments, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide. In some embodiments, the EGFR inhibitor is compound A40 disclosed in Table 27.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an adenosine A2AR antagonist. In some

embodiments, the adenosine A2AR antagonist is selected from the group consisting of PBF509, CPI444, AZD4635, Vipadenant, GBV-2034, and AB928. In some embodiments, the adenosine A2AR antagonist is selected from the group consisting of 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an anti-CD73 antibody molecule, e.g., an anti-CD73 antibody molecule disclosed herein.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is a check point inhibitor. In some embodiments, the check point inhibitor is a PD-1 inhibitor. In some embodiments, the PD-1 inhibitor is selected from the group consisting of PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, and AMP-224. In some embodiments, the PD-1 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of PD-1 or PD-L1 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the PD-1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject, e.g. for at least 1, 2, 3, 4, or 5 weeks, e.g., for at least, 1, 2, 3, 4, 5, 10, 15, 20, 25, or 30-fold. In some embodiments, the BCMA CAR-expressing cells are administered to the subject prior to the administration of the PD-1 inhibitor. In some embodiments, the BCMA CAR-expressing cells do not expand or have minimal expansion (e.g., no more than 1, 2, 3, 4, 5, or 10-fold expansion) in the subject at the time the PD-1 inhibitor is administered. In some embodiments, the check point inhibitor is a PD-L1 inhibitor. In some embodiments, the PD-L1 inhibitor is selected from the group consisting of FAZ053, Atezolizumab, Avelumab, Durvalumab, and BMS-936559. In some embodiments, the PD-L1 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of PD-1 or PD-L1 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the PD-L1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject, e.g. for at least 1, 2, 3, 4, or 5 weeks, e.g., for at least, 1, 2, 3, 4, 5, 10, 15, 20, 25, or 30-fold. In some embodiments, the BCMA CAR-expressing cells are administered to the subject prior to the administration of the PD-L1 inhibitor.

In some embodiments, the BCMA CAR-expressing cells do not expand or have minimal expansion (e.g., no more than 1, 2, 3, 4, 5, or 10-fold expansion) in the subject at the time the PD-L1 inhibitor is administered. In some embodiments, the check point inhibitor is a LAG-3 inhibitor. In some embodiments, the LAG-3 inhibitor is selected from the group consisting of LAG525, BMS-986016, TSR-033, MK-4280 and REGN3767. In some embodiments, the LAG-3 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of LAG-3 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy. In some embodiments, the check point inhibitor is a TIM-3 inhibitor. In some embodiments, the TIM-3 inhibitor is selected from the group consisting of MGB453, TSR-022, and LY3321367. In some embodiments, the TIM-3 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of TIM-3 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an antibody molecule that binds to CD32B.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an antibody molecule that binds to IL-17, e.g., an antagonistic antibody molecule that binds to IL-17, e.g., CJM112.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an antibody molecule that binds to IL-1 beta.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO), e.g., an IDO1 inhibitor. In some embodiments, the inhibitor of IDO and/or TDO is INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287. In some embodiments, the inhibitor of IDO and/or TDO is (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan. In some embodiments, the inhibitor of IDO and/or TDO is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after IDO and/or TDO expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

In certain embodiments for the foregoing aspects, the second therapy is administered prior to, concurrently with, or subsequent to the administration of the BCMA CAR-expressing cell therapy.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, wherein the subject has received or is receiving a BCMA CAR-expressing cell therapy, comprising:

responsive to an increase in a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy, relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, wherein the subject has received or is receiving a BCMA CAR-expressing cell therapy, comprising:

acquiring a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy,

responsive to an increase in the value relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

In one aspect, disclosed herein is a method of treating a subject having a disease associated with the expression of BCMA, comprising:

administering a BCMA CAR-expressing cell therapy to the subject,

responsive to an increase in a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy, relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

In one aspect, disclosed herein is method of treating a subject having a disease associated with the expression of BCMA, comprising:

administering a BCMA CAR-expressing cell therapy to the subject,

acquiring a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy,

responsive to an increase in the value relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

In certain embodiments of the foregoing aspects, the value of the level or activity of the antigen comprises the expression level of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), as measured by an assay described herein, e.g., immunohistochemistry.

In some embodiments, the at least one time point is 5, 10, 15, 20, 25, 28, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, or 90 days after the subject began receiving the BCMA CAR-expressing cell therapy.

In some embodiments, the subject experiences a decrease in BCMA expression after the subject began receiving the BCMA CAR-expressing cell therapy.

In certain embodiments of the foregoing aspects, the BCMA CAR-expressing cell therapy comprises a cell expressing a BCAM CAR. In some embodiments, the BCMA CAR comprises one or more of (e.g., all three of) heavy chain complementary determining region 1 (HCDR1), HCDR2, and HCDR3 listed in Table 3 or 5 and/or one or more of (e.g., all three of) light chain complementary determining region 1 (LCDR1), LCDR2, and LCDR3 listed in Table 4 or 5, or a sequence with 95-99% identify thereof. In some embodiments, the BCMA CAR comprises a heavy chain variable region (VH) listed in Table 2 or 5 and/or a light chain variable region (VL) listed in Table 2 or 5, or a sequence with 95-99% identify thereof. In some embodiments, the BCMA CAR comprises a BCMA scFv domain amino acid sequence listed in Table 2 or 5 (e.g., SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, and SEQ ID NO: 149), or a sequence with 95-99% identify thereof. In some embodiments, the BCMA CAR comprises a full-length BCMA CAR amino acid sequence listed in Table 2 or 5 (e.g., residues 22-483 of SEQ ID NO: 109, residues 22-490 of SEQ ID NO: 99, residues 22-488 of SEQ ID NO: 100, residues 22-487 of SEQ ID NO: 101, residues 22-493 of SEQ ID NO: 102, residues 22-490 of SEQ ID NO: 103, residues 22-491 of SEQ ID NO: 104, residues 22-482 of SEQ ID NO: 105, residues 22-483 of SEQ ID NO: 106, residues 22-485 of SEQ ID NO: 107, residues 22-483 of SEQ ID NO: 108, residues 22-490 of SEQ ID NO: 110,

residues 22-483 of SEQ ID NO: 111, residues 22-484 of SEQ ID NO: 112, residues 22-485 of SEQ ID NO: 113, residues 22-487 of SEQ ID NO: 213, residues 23-489 of SEQ ID NO: 214, residues 22-490 of SEQ ID NO: 215, residues 22-484 of SEQ ID NO: 216, residues 22-485 of SEQ ID NO: 217, residues 22-489 of SEQ ID NO: 218, residues 22-497 of SEQ ID NO: 219, residues 22-492 of SEQ ID NO: 220, residues 22-490 of SEQ ID NO: 221, residues 22-485 of SEQ ID NO: 222, residues 22-492 of SEQ ID NO: 223, residues 22-492 of SEQ ID NO: 224, residues 22-483 of SEQ ID NO: 225, residues 22-490 of SEQ ID NO: 226, residues 22-485 of SEQ ID NO: 227, residues 22-486 of SEQ ID NO: 228, residues 22-492 of SEQ ID NO: 229, residues 22-488 of SEQ ID NO: 230, residues 22-488 of SEQ ID NO: 231, residues 22-495 of SEQ ID NO: 232, residues 22-490 of SEQ ID NO: 233), or a sequence with 95-99% identify thereof. In some embodiments, the BCMA CAR is encoded by a nucleic acid sequence listed in Table 2 or 5 (e.g., SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, SEQ ID NO: 169, SEQ ID NO: 170), or a sequence with 95-99% identify thereof.

In certain embodiments of the foregoing aspects, the disease associated with the expression of BCMA is cancer, optionally wherein the cancer is a hematological cancer. In some embodiments, the disease associated with the expression of BCMA is an acute leukemia chosen from one or more of B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia; a prostate cancer (e.g., castrate-resistant or therapy-resistant prostate cancer, or metastatic prostate cancer), pancreatic cancer, lung cancer; or a plasma cell proliferative disorder (e.g., asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammapathy of undetermined significance (MGUS), Waldenstrom's macroglobulinemia, plasmacytomas (e.g., plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, and POEMS syndrome (also known

as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome)), or a combination thereof. In some embodiments, the disease associated with the expression of BCMA is ALL, CLL, DLBCL, or multiple myeloma. In some embodiments, the subject is a human patient.

The materials, methods, and examples are illustrative only and not intended to be limiting.

Headings, sub-headings or numbered or lettered elements, e.g., (a), (b), (i) etc, are presented merely for ease of reading. The use of headings or numbered or lettered elements in this document does not require the steps or elements be performed in alphabetical order or that the steps or elements are necessarily discrete from one another.

All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety.

Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

FIGs.1A and 1B are a pair of graphs showing the percentage of CD4+ or CD8+ T cells among CD3+ T cells (FIG. 1A) and the CD4:CD8 T cell ratio (FIG. 1B) in apheresis samples acquired from multiple myeloma patients who were later determined to be Responders (R, $N_R = 3$) or Non-Responders (NR, $N_{NR} = 5$) to treatment with an infusion of CART-BCMA. These data demonstrate that Responders had a higher percentage of CD4+ T cells and a lower percentage of CD8+ T cells (and thus a higher CD4:CD8 ratio) in their apheresis sample than Non-Responders did. A CD4:CD8 ratio greater than about 1.6 was found to be predictive of response to CART-BCMA.

FIGs. 2A, 2B, and 2C are graphs showing that the percentage of HLADR-CD95+CD27+CD8+ T cells (FIG. 2A), CD45RO-CD27+CD8+ T cells (FIG. 2B), or CCR7+CD45RO-CD27+CD8+ T cells (FIG. 2C) among CD8+ T cells is higher in apheresis samples acquired from multiple myeloma patients who were later determined to be Responders (R, $N_R = 3$) to CART-BCMA as compared to Non-Responders (NR, $N_{NR} = 5$). P-values are shown for each graph.

FIG. 3 is a series of images showing CD138+ cell localization as determined by immunohistochemistry (IHC) in bone marrow core biopsies acquired prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17. Patient outcomes to treatment with CART-BCMA are provided

in the Examples and are referred to herein as follows: Progressive disease (PD); Stable disease (SD); Minor response (MR); Partial regression (PR); and Very good partial regression (VGPR). Pretreatment, Day 28, and Day 90 samples acquired from Patient 13 had 1%, 0%, and 0% CD138+ MM cell infiltration, respectively. Pretreatment and Day 28 samples acquired from Patient 14 had 80% and 90% CD138+ MM cell infiltration, respectively. Pretreatment, Day 28, and Day 90 samples acquired from Patient 15 had 95%, 5%, and 10% CD138+ MM cell infiltration, respectively. Pretreatment, Day 28, and Day 90 samples acquired from Patient 16 had 50%, 5%, and 75% CD138+ MM cell infiltration, respectively. Pretreatment, Day 28, and Day 90 samples acquired from Patient 17 had 50%, 5%, and 75% CD138+ MM cell infiltration, respectively.

FIG. 4 is a series of images showing BCMA protein expression as determined by IHC in bone marrow core biopsies acquired prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17.

FIG. 5 is a series of images showing a comparison between BCMA protein expression as determined by IHC to BCMA mRNA levels as determined by in situ hybridization (ISH) in bone marrow core biopsies acquired prior to administration of CART-BCMA from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17.

FIGs. 6A, 6B, and 6C are a series of images showing BCMA protein expression as determined by IHC, BCMA mRNA levels as determined by ISH, and CART-BCMA mRNA levels as determined by ISH in bone marrow core biopsies acquired from Patient 15 (FIG. 6A), Patient 16 (FIG. 6B), and Patient 17 (FIG. 6C), prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA.

FIGs. 7A, 7B, and 7C are a series of images showing IDO1, IFN-γ, and TGFβ mRNA levels as determined by ISH in bone marrow core biopsies acquired from Patient 15 (FIG. 7A), Patient 16 (FIG. 7B), and Patient 17 (FIG. 7C), prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA. FIGs. 7D and 7E are a series of images showing CAR, IFN-γ, and IDO1 mRNA levels as determined by ISH in biopsies acquired from Patient 19 (FIG. 7D) and Patient 20 (FIG. 7E), prior to administration ("Pre"), and on Day 10 and Day 28 post-infusion of CART-BCMA.

FIGs. 8A, 8B, and 8C are a series of images showing PD-L1, PD1, CD3, and FoxP3 protein expression as determined by IHC in bone marrow core biopsies acquired from Patient 15 (FIG. 8A), Patient 16 (FIG. 8B), and Patient 17 (FIG. 8C), prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA. FIGs. 8D and 8E are a series of images showing PD1, PD-L1, and FoxP3 protein expression as determined by IHC in biopsies acquired from Patient 19 (FIG. 8D) and Patient 20 (FIG. 8E), prior to administration ("Pre"), and on Day 10 and Day 28 post-infusion of CART-BCMA.

FIG. 9 is a series of images showing CD19 protein expression as determined by IHC in bone marrow core biopsies acquired prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17.

FIG. 10 is a series of images showing CD20 protein expression as determined by IHC in bone marrow core biopsies acquired prior to administration ("Pre"), and on Day 28 and Day 90 ("3 month") post-infusion of CART-BCMA from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17.

FIGs. 11A and 11B are a series of spectrally unmixed pseudo fluorescent microscopy images showing that BCMA positive cells and CD19 positive cells are separate populations in bone marrow core biopsies acquired from Patient 15 prior to administration ("pre") and on Day 90 ("3M") post-infusion of CAR-BCMA.

FIGs. 12A and 12B are a series of spectrally unmixed pseudo fluorescent microscopy images showing that CD19+ $CD34^{dim}$ cell population was present in the pretreatment bone marrow core biopsies acquired from Patient 15 and Patient 17, respectively.

FIG. 13 is a series of spectrally unmixed pseudo fluorescent microscopy images showing that the CD19 population was variably CD138+ and CD138- in the pretreatment bone marrow core biopsies acquired from Patient 15.

FIG. 14 is a graph comparing the level of tumor burden in a KMS11 tumor model following implant and administration of PBS, untransduced T cells ("UTD"), or T cells transduced with either a tool CAR ("J6MO"), BCMA-4, BCMA-9, BCMA-10 ("MCM998"), BCMA-13, or BCMA-15. BCMA-10 demonstrated the most potent anti-tumor activity.

FIG. 15 is a diagram showing the design of a clinical trial (NCT Number: NCT02546167; UPCC 14415) to assess the safety and feasibility of infusion of autologous T cells expressing CART-BCMA in adult patients with multiple myeloma.

FIG. 16A is a table showing MM patient disease characteristics. FIG. 16B is a table showing the presence of baseline lymphopenia due to disease and prior therapies in MM patients.

FIGs. 17A, 17B, and 17C are graphs showing patient response for Cohort 1, Cohort 2, and Cohort 3, respectively.

FIGs. 18A and 18B are a series of graphs showing expansion of CART-BCMA evaluated by flow cytometry in Cohort 1 patients and Cohort 2/3 patients, respectively.

FIGs. 19A and 19B are a series of graphs showing expansion of CART-BCMA evaluated by PCR in Cohort 1 patients and Cohort 2/3 patients, respectively. The plots show the number of detected CART genes per µg of DNA isolated from patient's blood (y-axis) at the respective day post CART infusion (x-axis).

FIGs. 20A and 20B are graphs showing that BCMA expansion may correlate with clinical outcomes.

FIG. 21A, 21B, 21C, and 21D are graphs showing the fraction of CAR-positive (CAR+) CD4/CD8 cells at various time points post-infusion in Responders compared to Non-Responders.

FIG. 22 is a series of graphs showing the changes in level of cytokine expression at various time points post infusion of CART-BCMA. The y-axis in each graph shows fold change from Day 0. The x-axis in each graph shows days post-infusion of CART-BCMA.

FIGs. 23A and 23B are graphs showing the change in IL-6 expression at various time points post infusion of CART-BCMA. The y-axis in each graph shows fold change from Day 0. The x-axis in each graph shows days post-infusion of CART-BCMA.

FIGs. 24A and 24B are graphs showing the change in IFN-γ expression at various time points post infusion of CART-BCMA. The y-axis in each graph shows fold change from Day 0. The x-axis in each graph shows days post-infusion of CART-BCMA.

FIGs. 25A and 25B are graphs showing the serum level of BCMA in 14 normal donors (FIG. 25A) and 12 myeloma patients (FIG. 25B).

FIGs. 26A, 26B, 26C, and 26D are graphs showing serum BCMA level at various time points post infusion of CART-BCMA. The y-axis in FIGs. 26A and 26B shows peripheral blood (PB) serum BCMA levels. The y-axis in FIGs. 26C and 26D shows PB serum BCMA level fold change from baseline. The x-axis in each graph shows days post-infusion of CART-BCMA.

FIGs. 27A, 27B, and 27C are graphs showing data collected from three multiple myeloma patients who received CART-BCMA treatment. The y-axis on the left shows the percentage of CD4+ or CD8+ CART cells. The y-axis on the right shows the level of serum BCMA (ng/mL) or the number of CART copies (BBz) per μg DNA, as evaluated by qPCR.

FIGs. 28A and 28B are graphs showing CD4+ T cell subsets of normal donors (FIG. 28A) and multiple myeloma (MM) patients (FIG. 28B). FIGs. 28C and 28D are graphs showing CD8+ T cell subsets of normal donors (FIG. 28C) and MM patients (FIG. 28D). FIGs. 28E and 28F are graphs showing CD4+ and CD8+ T cell subsets, respectively, in apheresis samples acquired from MM patients (dots with slashes represent non-responders and white dots represent responders).

FIG. 29 is a series of graphs showing T cell differentiation in apheresis samples acquired from MM patients. The x-axis shows CD45RO expression and the y-axis shows CCR7 expression. Signal in the top left quadrant indicates naïve cell phenotype; signal in top right quadrant indicates central memory (T_{CM}) phenotype; signal in bottom right quadrant indicates effector memory (T_{EM}) phenotype; and signal in bottom left quadrant indicates T_{EMRA}. CR stands for complete response. PD stands for progressive disease. VGPR stands for very good partial response.

FIGs. 30A and 30B are a pair of graphs showing CD4+ and CD8+ T cell subsets in apheresis samples acquired from MM patients (dots with slashes represent non-responders and white dots represent responders).

FIG. 31 is a graph showing treatment schema.

FIGs. 32A, 32B, and 32C are a set of graphs showing clinical outcomes. FIG. 32A is a Swimmer's plot showing best response and progression-free survival (PFS) for each subject. Arrow indicates ongoing response. FIG. 32B is a pair of PET/CT scan images for subject 03 showing resolution of extramedullary disease and malignant pleural effusion post-treatment. FIG. 32C is a Kaplan-Meier plot showing overall survival for Cohort 1. MR=minimal response; MRD=minimal residual disease; PR=partial response; PD=progressive disease; sCR=stringent complete response; SD=stable disease.

FIGs. 33A, 33B, and 33C are a set of graphs showing CART-BCMA expansion and persistence. FIG. 33A is a set of graphs depicting CART-BCMA cell levels over time in peripheral blood for each subject, as measured by flow cytometry (%CAR+ within CD3+ T cells, ▲, left axis) and quantitative PCR for CAR sequence (■, right axis). See FIG. 38 for representative flow cytometry plots. FIG. 33B is a graph showing that peak CART-BCMA levels by qPCR correlate with response: median 102507 vs. 4187 copies/µg DNA for ≥PR vs. <PR, respectively (p=0.016, Mann-Whitney). FIG. 33C is a graph showing that AUC-28 (area under the curve for CART-BCMA levels by qPCR during first 28 days after infusion) correlates with response: median 885181 vs. 26183 (copies)x(days)/µg DNA for ≥PR vs. <PR, respectively (p=0.016, Mann-Whitney).

FIG. 34 is a set of graphs showing soluble BCMA (sBCMA), BAFF, APRIL levels and B cell frequency after CART-BCMA infusions. Peripheral blood serum levels of sBCMA, BAFF, and APRIL (ng/ml, left axis) were measured by ELISA pre- and post-CART-BCMA infusions for each subject as indicated above. Subjects with deepest clinical responses (01 (sCR), 03 (VGPR), 15 (VGPR)) had greatest declines in sBCMA and reciprocal increases in BAFF and APRIL. Peripheral blood B cell frequency (%CD19+ of CD45+CD14- gate, right axis) was assessed by flow cytometry at indicated time points.

FIG. 35 is a set of histograms showing BCMA expression by flow cytometry on gated MM cells in marrow aspirates for each subject, before and after CART-BCMA infusions. Hatched histograms show BCMA; filled histograms show FMO (fluorescence minus one) control. Post-infusion time point is Day 28, unless specified. Percentage of cells expressing BCMA as well as mean BCMA fluorescence intensity (MFI) for each subject are listed in Table 37. Note decreased BCMA expression for subject 03 at relapse (D164). See FIG. 42 for representative gating.

FIGs. 36A, 36B, 36C, and 36D are a set of graphs showing predictors of in vivo CART-BCMA expansion. The ratio of CD4+ to CD8+ T cells (CD4/CD8 ratio) within the apheresis product immediately after collection (FIG. 36A) and within the seed culture at start of manufacturing (i.e. following elutriation step to reduce monocyte contamination) (FIG. 36B) was determined by flow cytometry. In vitro fold expansion (FIG. 36C) was calculated from total cell counts at start and end of

manufacturing. The proportion of CD8+ T cells within the apheresis product with a CD45RO-CD27+ phenotype was assessed by flow cytometry (FIG. 36D). The CD4/CD8 ratio and frequency of CD45RO-CD27+CD8+ T cells pre-manufacturing, and degree of in vitro expansion were associated with peak in vivo CART-BCMA expansion post-infusion (Spearman correlation r and p-value shown).

FIG. 37 is a CONSORT diagram showing subject enrollment.

FIG. 38 is a set of graphs showing representative gating and staining for CART-BCMA cells. Staining is shown for peripheral blood from subject 01, day +7 after first CART-BCMA infusion. Cells are gated by forward and side scatter, then singlets, then CD45+CD14- leukocytes, then T cells (CD3+CD19-). CART-BCMA+ cells were identified using biotinylated recombinant human BCMA-Fc and streptavidin-PE. Negative control was an FMO (fluorescence minus one) tube (lacking biotinylated BCMA-Fc) with streptavidin-PE. The % of CD3+ T cells expressing CART-BCMA was calculated by subtracting CAR+ cells in FMO tube from CAR+ cells in tube with biotinylated BCMA-FC (i.e. in this example 34.7 – 0.9 = 33.8). Activation status of CART-BCMA+ cells was identified by staining for HLA-DR (bottom right panel). The % of CAR+ cells that were activated at each time point was calculated by dividing %HLA-DR+ by (%HLA-DR+ plus %HLA-DR-) (i.e. in this example 32.9/(32.9 + 1.5) = 95.6%).

FIG. 39 is a set of graphs showing absolute number of CART-BCMA+ T cells for each subject. Absolute # of CD3+CAR+ cells per µl of blood was estimated from the absolute lymphocyte count (ALC, reported from the clinical complete blood count (CBC) differential) and the CART-BCMA flow cytometry results (FIG. 38), using the following formula: (ALC) (%CD45+CD14-)(%CD3+CD19-)(%CAR+)/10000. For example, for subject 01 at day+7, ALC was 0.08 x 10^3 cells/µl. Estimated absolute # of circulating CAR+ T cells at this time point is (0.08)(48.3)(72.1)(33.8)/10000 = 0.019 x 10^3 cells/µl.

FIG. 40 is a set of graphs showing serum cytokine changes after CART-BCMA treatment. Levels of 30 peripheral blood cytokines were assessed at multiple time points by Luminex assay. Changes in selected cytokines over first 28 days are depicted. Subjects with deepest responses (01, 03, 15) had greatest fold-increase in cytokines, typically at or just before peak CART-BCMA expansion.

FIGs. 41A and 41B are a pair of graphs showing baseline soluble BCMA (sBCMA) levels, peak expansion, and response. Peripheral blood serum levels of sBCMA were measured by ELISA pre-treatment. FIG. 41A is a graph showing that baseline sBCMA levels did not correlate significantly with peak expansion of CART-BCMA by qPCR (Spearman correlation r=0.43, p=0.25). FIG. 41B is a graph showing that baseline levels of sBCMA were not significantly associated with response (p=0.56, Mann-Whitney test).

FIG. 42 is a set of graphs showing representative gating for myeloma cells and BCMA staining. Bone marrow aspirate cells were gated by forward and side scatter, then by singlets, then on CD3-

CD14- cells. Myeloma cells were identified by gating first on $CD38^{hi}$ cells, then by gating on clonal plasma cells using CD19, CD56, and kappa/lambda staining. In this example, myeloma cells are CD19-CD56+kappa+. The % BCMA + was determined using an FMO tube lacking anti-BCMA antibody.

FIGs. 43A and 43B are a pair of graphs showing baseline BCMA expression on MM cells, peak expansion, and response. BCMA mean fluorescence intensity (MFI) on myeloma cells pre-treatment did not correlate with peak CART-BCMA expansion by qPCR (Spearman correlation r=0.45, p=0.27) (FIG. 43A), nor was it significantly associated with response (p=0.25, Mann-Whitney test) (FIG. 43B). One subject (07) did not have a pre-treatment sample available.

FIGs. 44A and 44B are a set of graphs showing BCMA expression on B cell malignancy cell lines. FIG. 44A is a set of histograms showing the surface expression of BCMA on each cell line. Hatched histograms indicate staining with PE-labeled anti-BCMA antibody and filled histograms show the respective isotype control staining. In FIG. 44B, expression was quantified and the antibody binding capacity (ABC) plotted for each cell line tested.

FIG. 45A is a graph showing % CD27+CD45RO-CD8+ cells in the post-induction cohort and the relapsed/refractory cohort. FIG. 45B is a graph showing CD4/CD8 ratio in the post-induction cohort and the relapsed/refractory cohort. FIG. 45C is a graph showing in vitro population doublings by Day 9 in the post-induction cohort and the relapsed/refractory cohort.

FIG. 46 is a graph showing treatment schema. BM asp/Bx = bone marrow aspirate and biopsy; Cytoxan = cyclophosphamide; D = day; Lenti = lentivirus; Wk = week.

FIGs. 47A-47C are a panel of swimmer's plots showing best response and progression-free survival (PFS) for each subject in Cohort 1 (1-5 x 10^8 CART-BCMA cells alone) (FIG. 47A), Cohort 2 (Cyclophosphamide (Cy) + 1-5 x 10^7 CART-BCMA cells) (FIG. 47B), and Cohort 3 (Cy + 1-5 x 10^8 CART-BCMA cells) (FIG. 47C). Arrow indicates ongoing response. FIG. 47D is a graph showing overall survival (OS) based on cohort, Kaplan-Meier plot. MR=minimal response; MRD=minimal residual disease; PR=partial response; PD=progressive disease; sCR=stringent complete response; SD=stable disease.

FIGs. 48A-48D are graphs showing CART-BCMA expansion and persistence. FIGs. 48A-48C are graphs showing CART-BCMA cell levels over time in peripheral blood for each cohort, as measured by quantitative PCR for CAR sequence. FIG. 48D is a graph showing peak CART-BCMA levels by qPCR for each subject (except subj. 34, for whom peak data not available). Median peak CART-BCMA levels (grey bars) were not significantly different between cohorts (Mann-Whitney).

FIGs. 49A-49I are graphs showing serum cytokines associated with CRS severity and neurotoxicity. Serum cytokine concentrations in pg/ml through day 28 were measured by Luminex assay. FIGs. 49A-49E: The median peak fold increase over baseline for each cytokine was compared between subjects with no cytokine release syndrome (CRS), grade 1 CRS, or grade 2 CRS not receiving

tocilizumab (CRS gr 0-2) and those with grade 3-4 CRS or grade 2 CRS receiving tocilizumab (CRS Gr 3-4 or Gr 2 + toci). The cytokines most significantly associated with CRS severity were IL-6 (FIG. 49A), IFN-γ (FIG. 49B), IL-2Rα (FIG. 49C), MIP-1α (FIG. 49D), and IL-15 (FIG. 49E). FIGs. 49F-49I: Median peak fold increase over baseline for each cytokine was compared between subjects with no neurotoxicity (No Ntx) and those with any grade of neurotoxicity (Any Ntx). The cytokines most significantly associated with neurotoxicity were IL-6 (FIG. 49F), IFN-γ (FIG. 49G), IL-1RA (FIG. 49H), and MIP-1α (FIG. 49I). Stars depict subjects with grade 3-4 neurotoxicity. Exact p-value by Mann-Whitney test is shown. Horizontal lines depict medians. IFN-γ = interferon gamma; IL-1RA = interleukin 1 receptor antagonist; IL-2Rα = interleukin 2 receptor alpha; IL-6 = interleukin 6; IL-15 = interleukin 15. MIP-1α = macrophage inflammatory protein 1 alpha.

FIGs. 50A-50D are graphs showing soluble BCMA (sBCMA), BAFF, and APRIL concentration, and BCMA expression on MM cells pre- and post-CART-BCMA infusions. FIG. 50A: Baseline peripheral blood serum concentration of sBCMA and APRIL for subjects (sub) were significantly increased and decreased, respectively, compared to a panel of healthy donors (HD, n=6) ($p=0.017$, and <0.001, respectively, Mann-Whitney). Baseline BAFF concentrations were not significantly different. Median concentrations are depicted. FIG. 50B: Serial sBCMA concentrations decline after CART-BCMA infusions more significantly in hematologic responders (PR/VGPR/CR/sCR) than non-responders (MR/SD/PD). Mean concentration (ng/ml) + SEM are depicted. *$p<0.05$ by unpaired t-test. FIG. 50C: Representative examples of BCMA expression on MM cells by flow cytometry. See FIG. 42 for gating strategy. FMO=fluorescence minus one. FIG. 50D: BCMA mean fluorescence intensity (MFI) on MM cells over time in 18 subjects with evaluable serial bone marrow aspirates. Median MFI was significantly different between pre-treatment (pre-tx) and day 28 (D28) for responders (4000 vs. 944, $p=0.02$, paired t-test) but not for non-responders (2704 vs. 2140, $p=0.19$). Median MFI was not significantly different between pre-tx and day 90 (D90) for responders (4000 vs.2022, $p=0.26$). *Subj. 15 had no detectable MM cells at D28. #Subj. 03 had no detectable MM cells at D45 (D28 not done) and too few MM cells to characterize at D90. D164 marrow is depicted at D90 time-point.

FIGs. 51A-51I are graphs showing predictors of *in vivo* CART-BCMA expansion and response. Peak blood CART-BCMA expansion, as measured by qPCR (FIG. 51A), as well as total CART-BCMA expansion over first 28 days (calculated as area under the curve (AUC)) (FIG. 51B), were both associated with clinical response. Greater peak CART-BCMA expansion (FIG. 51C) and response (FIG. 51D) were also associated with more severe CRS, defined as grade 3/4 or grade 2 requiring tocilizumab. A higher ratio of CD4+ to CD8+ T cells (CD4/CD8 ratio) within the leukopheresis product, as determined by flow cytometry, also correlated with both peak expansion (FIG. 51E) and response (FIG. 51F), while i*n vitro* proliferation, measured as fold increase of seeded cells during

manufacturing, correlated only with peak expansion (FIG. 51G), but not response (p=0.54, Mann-Whitney test, data not shown). FIGs. 51H-I: A higher proportion of CD8+ T cells within the leukopheresis product with a CD45RO-CD27+ phenotype was significantly associated with peak CART-BCMA expansion (FIG. 51H), and to a lesser degree, response (FIG. 51I). For FIGs. 51A, 51B, 51C, 51F, and 51I, analysis was by Mann-Whitney test; lines represent median values. For FIG. 51D, analysis was by Fisher's exact test. For FIGs. 51E, 51G, and 51H, analysis was by Spearman correlation.

FIG. 52 is a CONSORT diagram showing subject enrollment. ALC = absolute lymphocyte count.

FIGs. 53A-53D are graphs showing additional clinical outcomes for treated subjects. FIG. 53A: Duration of response (DOR) for all subjects with partial response (PR) or better. FIG. 53B: Overall survival (OS) for all subjects. FIG. 53C: Progression-free survival (PFS) by cohort. FIG. 53D: PFS for all subjects. Curves derived by Kaplan-Meier method.

FIGs. 54A-54C are graphs showing expansion of CART-BCMA cells for Cohort 1 (FIG. 54A), Cohort 2 (FIG. 54B) or Cohort 3 (FIG. 54C). The frequency of CAR+ T cells within all peripheral blood CD3+ T cells, as measured by flow cytometry, is depicted for each subject.

FIG. 55 is a panel of graphs showing serum cytokine changes after CART-BCMA treatment. Concentrations (pg/ml) of peripheral blood cytokines were assessed at multiple time-points by Luminex assay. The peak fold increase over baseline for the most frequently elevated cytokines over first 28 days post-infusion are shown, based on cohort.

FIGs. 56A-56L are graphs showing that peak CART-BCMA expansion is not associated with baseline clinical characteristics, baseline BCMA expression or sBCMA concentration. Peak CART-BCMA level (copies/µg genomic DNA) by qPCR was not significantly associated with age at enrollment (above or below median) (FIG. 56A); years from diagnosis (above or below median) (FIG. 56B); presence of del17p by FISH or TP53 mutation by sequencing (FIG. 56C); number (#) of therapeutic lines (above or below median) (FIG. 56D); being penta-refractory to 2 proteasome inhibitors (PIs), 2 immunomodulatory drugs (IMiDs) and daratumumab (dara) (FIG. 56E); receiving therapy just prior to leukapheresis that contained an IMiD (FIG. 56F), a PI (FIG. 56G), dara (FIG. 56H), or cyclophosphamide (Cytoxan) (FIG. 56I); percentage of pre-treatment bone marrow plasma cells (%BM PC) (FIG. 56J); baseline BCMA mean fluorescence intensity (MFI) on BM PC (FIG. 56K); or baseline serum soluble BCMA (sBCMA) concentration (FIG. 56L). For FIGs. 56A-56I, analysis by Mann-Whitney test; line represents median value. For FIGs. 56J-56L, analysis by Spearman correlation.

FIGs. 57A-57L are graphs showing that response is not associated with baseline clinical characteristics, baseline BCMA expression or sBCMA concentration. Clinical response (≥ partial response (PR)) was not significantly associated with age at enrollment (FIG. 57A); years from diagnosis

(FIG. 57B); presence of del17p by FISH or TP53 mutation by sequencing (FIG. 57C); number (#) of therapeutic lines (FIG. 57D); being penta-refractory to 2 proteasome inhibitors (PIs), 2 immunomodulatory drugs (IMiDs) and daratumumab (dara) (FIG. 57E); receiving a regimen just prior to leukapheresis that contained an IMiD, a PI, dara, or cyclophosphamide (Cytoxan) (FIGs. 57F-57I); percentage of pre-treatment bone marrow plasma cells (%BM PC) (FIG. 57J); baseline BCMA mean fluorescence intensity (MFI) on BM PC (FIG. 57K); or baseline serum soluble BCMA (sBCMA) concentration (FIG. 57L). For FIGs. 57C, 57E-57I, analysis by Fisher Exact test. For FIGs. 57A, 57B, 57D, 57J-57L, analysis by Mann-Whitney test; line represents median value.

DESCRIPTION

Definitions

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains.

As used herein, the term "BCMA" refers to B-cell maturation antigen. BCMA (also known as TNFRSF17, BCM or CD269) is a member of the tumor necrosis receptor (TNFR) family and is predominantly expressed on terminally differentiated B cells, e.g., memory B cells, and plasma cells. Its ligand is called B-cell activator of the TNF family (BAFF) and a proliferation inducing ligand (APRIL). BCMA is involved in mediating the survival of plasma cells for mataining long-term humoral immunity. The gene for BCMA is encoded on chromosome 16 producing a primary mRNA transcript of 994 nucleotides in length (NCBI accession NM_001192.2) that encodes a protein of 184 amino acids (NP_001183.2). A second antisense transcript derived from the BCMA locus has been described, which may play a role in regulating BCMA expression. (Laabi Y. et al., Nucleic Acids Res., 1994, 22:1147-1154). Additional transcript variants have been described with unknown significance (Smirnova AS et al. Mol Immunol., 2008, 45(4):1179-1183. A second isoform, also known as TV4, has been identified (Uniprot identifier Q02223-2). As used herein, "BCMA" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type BCMA.

As used herein, the term "CD19" refers to the Cluster of Differentiation 19 protein, which is an antigenic determinant detectable on leukemia precursor cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequence of human CD19 can be found as UniProt/Swiss-Prot Accession No. P15391 and the nucleotide sequence encoding of the human CD19 can be found at Accession No. NM_001178098. As used herein, "CD19" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD19. CD19 is expressed on

most B lineage cancers, including, e.g., acute lymphoblastic leukemia, chronic lymphocyte leukemia and non-Hodgkin lymphoma. Other cells with express CD19 are provided below in the definition of "disease associated with expression of CD19." It is also an early marker of B cell progenitors. See, e.g., Nicholson et al. Mol. Immun. 34 (16-17): 1157-1165 (1997). In one aspect the antigen-binding portion of the CART recognizes and binds an antigen within the extracellular domain of the CD19 protein. In one aspect, the CD19 protein is expressed on a cancer cell.

The term "a" and "an" refers to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

The term "about" when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20% or in some instances ±10%, or in some instances ±5%, or in some instances ±1%, or in some instances ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

The term "Chimeric Antigen Receptor" or alternatively a "CAR" refers to a recombinant polypeptide construct comprising at least an extracellular antigen binding domain, a transmembrane domain and a cytoplasmic signaling domain (also referred to herein as "an intracellular signaling domain") comprising a functional signaling domain derived from a stimulatory molecule as defined below. In some embodiments, the domains in the CAR polypeptide construct are in the same polypeptide chain, e.g., comprise a chimeric fusion protein. In some embodiments, the domains in the CAR polypeptide construct are not contiguous with each other, e.g., are in different polypeptide chains, e.g., as provided in an RCAR as described herein.

In one aspect, the stimulatory molecule of the CAR is the zeta chain associated with the T cell receptor complex. In one aspect, the cytoplasmic signaling domain comprises a primary signaling domain (e.g., a primary signaling domain of CD3-zeta). In one aspect, the cytoplasmic signaling domain further comprises one or more functional signaling domains derived from at least one costimulatory molecule as defined below. In one aspect, the costimulatory molecule is chosen from 4 1BB (i.e., CD137), CD27, ICOS, and/or CD28. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a co-stimulatory molecule and a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an

intracellular signaling domain comprising two functional signaling domains derived from one or more co-stimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an intracellular signaling domain comprising at least two functional signaling domains derived from one or more co-stimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In one aspect the CAR comprises an optional leader sequence at the amino-terminus (N-ter) of the CAR fusion protein. In one aspect, the CAR further comprises a leader sequence at the N-terminus of the extracellular antigen recognition domain, wherein the leader sequence is optionally cleaved from the antigen recognition domain (e.g., an scFv) during cellular processing and localization of the CAR to the cellular membrane.

A CAR that comprises an antigen binding domain (e.g., an scFv, a single domain antibody, or TCR (e.g., a TCR alpha binding domain or TCR beta binding domain)) that targets a specific tumor marker X, wherein X can be a tumor marker as described herein, is also referred to as XCAR. For example, a CAR that comprises an antigen binding domain that targets BCMA is referred to as BCMACAR. The CAR can be expressed in any cell, e.g., an immune effector cell as described herein (e.g., a T cell or an NK cell).

The term "signaling domain" refers to the functional portion of a protein which acts by transmitting information within the cell to regulate cellular activity via defined signaling pathways by generating second messengers or functioning as effectors by responding to such messengers.

The term "antibody," as used herein, refers to a protein, or polypeptide sequence derived from an immunoglobulin molecule, which specifically binds with an antigen. Antibodies can be polyclonal or monoclonal, multiple or single chain, or intact immunoglobulins, and may be derived from natural sources or from recombinant sources. Antibodies can be tetramers of immunoglobulin molecules.

The term "antibody fragment" refers to at least one portion of an intact antibody, or recombinant variants thereof, and refers to the antigen binding domain, e.g., an antigenic determining variable region of an intact antibody, that is sufficient to confer recognition and specific binding of the antibody fragment to a target, such as an antigen. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')2, and Fv fragments, scFv antibody fragments, linear antibodies, single domain antibodies such as sdAb (either VL or VH), camelid VHH domains, and multi-specific molecules formed from antibody fragments such as a bivalent fragment comprising two or more, e.g., two, Fab fragments linked by a disulfide brudge at the hinge region, or two or more, e.g., two isolated CDR or other epitope binding fragments of an antibody linked. An antibody fragment can also be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies,

triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, Nature Biotechnology 23:1126-1136, 2005). Antibody fragments can also be grafted into scaffolds based on polypeptides such as a fibronectin type III (Fn3) (see U.S. Patent No.: 6,703,199, which describes fibronectin polypeptide minibodies).

The term "scFv" refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked via a short flexible polypeptide linker, and capable of being expressed as a single chain polypeptide, and wherein the scFv retains the specificity of the intact antibody from which it is derived. Unless specified, as used herein an scFv may have the VL and VH variable regions in either order, e.g., with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

The terms "complementarity determining region" or "CDR," as used herein, refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. For example, in general, there are three CDRs in each heavy chain variable region (e.g., HCDR1, HCDR2, and HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, and LCDR3). The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of well-known schemes, including those described by Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani et al., (1997) JMB 273,927-948 ("Chothia" numbering scheme), or a combination thereof. Under the Kabat numbering scheme, in some embodiments, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3). Under the Chothia numbering scheme, in some embodiments, the CDR amino acids in the VH are numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3). In a combined Kabat and Chothia numbering scheme, in some embodiments, the CDRs correspond to the amino acid residues that are part of a Kabat CDR, a Chothia CDR, or both. For instance, in some embodiments, the CDRs correspond to amino acid residues 26-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3) in a VH, e.g., a mammalian VH, e.g., a human VH; and amino acid residues 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3) in a VL, e.g., a mammalian VL, e.g., a human VL.

The portion of the CAR composition of the invention comprising an antibody or antibody fragment thereof may exist in a variety of forms, for example, where the antigen binding domain is

expressed as part of a polypeptide chain including, for example, a single domain antibody fragment (sdAb), a single chain antibody (scFv), or e.g., a humanized antibody (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In one aspect, the antigen binding domain of a CAR composition of the invention comprises an antibody fragment. In a further aspect, the CAR comprises an antibody fragment that comprises an scFv.

As used herein, the term “binding domain” or "antibody molecule" (also referred to herein as “anti-target (e.g., BCMA) binding domain”) refers to a protein, e.g., an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term “binding domain” or “antibody molecule” encompasses antibodies and antibody fragments. In an embodiment, an antibody molecule is a multispecific antibody molecule, e.g., it comprises a plurality of immunoglobulin variable domain sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. The term “antibody heavy chain,” refers to the larger of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations, and which normally determines the class to which the antibody belongs.

The term “antibody light chain,” refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa (κ) and lambda (λ) light chains refer to the two major antibody light chain isotypes.

The term “recombinant antibody” refers to an antibody which is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage or yeast expression system. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using recombinant DNA or amino acid sequence technology which is available and well known in the art.

The term "antigen" or "Ag" refers to a molecule that provokes an immune response. This immune response may involve either antibody production, or the activation of specific immunologically-competent cells, or both. The skilled artisan will understand that any macromolecule, including virtually all proteins or peptides, can serve as an antigen. Furthermore, antigens can be derived from recombinant or genomic DNA. A skilled artisan will understand that any DNA, which comprises a nucleotide sequences or a partial nucleotide sequence encoding a protein that elicits an immune response therefore encodes an "antigen" as that term is used herein. Furthermore, one skilled in the art will understand that an antigen need not be encoded solely by a full length nucleotide sequence of a gene. It is readily apparent that the present invention includes, but is not limited to, the use of partial nucleotide sequences of more than one gene and that these nucleotide sequences are arranged in various combinations to encode polypeptides that elicit the desired immune response. Moreover, a skilled artisan will understand that an antigen need not be encoded by a "gene" at all. It is readily apparent that an antigen can be generated synthesized or can be derived from a biological sample, or might be macromolecule besides a polypeptide. Such a biological sample can include, but is not limited to a tissue sample, a tumor sample, a cell or a fluid with other biological components.

The term "anti-tumor effect" refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a decrease in tumor volume, a decrease in the number of tumor cells, a decrease in the number of metastases, an increase in life expectancy, decrease in tumor cell proliferation, decrease in tumor cell survival, or amelioration of various physiological symptoms associated with the cancerous condition. An "anti-tumor effect" can also be manifested by the ability of the peptides, polynucleotides, cells and antibodies of the invention in prevention of the occurrence of tumor in the first place.

The term "anti-cancer effect" refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a decrease in tumor volume, a decrease in the number of cancer cells, a decrease in the number of metastases, an increase in life expectancy, decrease in cancer cell proliferation, decrease in cancer cell survival, or amelioration of various physiological symptoms associated with the cancerous condition. An "anti-cancer effect" can also be manifested by the ability of the peptides, polynucleotides, cells and antibodies in prevention of the occurrence of cancer in the first place. The term "anti-tumor effect" refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a decrease in tumor volume, a decrease in the number of tumor cells, a decrease in tumor cell proliferation, or a decrease in tumor cell survival. The term "autologous" refers to any material derived from the same individual to whom it is later to be re-introduced into the individual.

The term "allogeneic" refers to any material derived from a different animal of the same species as the individual to whom the material is introduced. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. In some aspects, allogeneic material from individuals of the same species may be sufficiently unlike genetically to interact antigenically.

The term "xenogeneic" refers to a graft derived from an animal of a different species.

The term "apheresis" as used herein refers to the art-recognized extracorporeal process by which the blood of a donor or patient is removed from the donor or patient and passed through an apparatus that separates out selected particular constituent(s) and returns the remainder to the circulation of the donor or patient, e.g., by retransfusion. Thus, in the context of "an apheresis sample" refers to a sample obtained using apheresis.

The term "combination" refers to either a fixed combination in one dosage unit form, or a combined administration where a compound of the present invention and a combination partner (e.g. another drug as explained below, also referred to as "therapeutic agent" or "co-agent") may be administered independently at the same time or separately within time intervals, especially where these time intervals allow that the combination partners show a cooperative, e.g. synergistic effect. The single components may be packaged in a kit or separately. One or both of the components (e.g., powders or liquids) may be reconstituted or diluted to a desired dose prior to administration. The terms "co-administration" or "combined administration" or the like as utilized herein are meant to encompass administration of the selected combination partner to a single subject in need thereof (e.g. a patient), and are intended to include treatment regimens in which the agents are not necessarily administered by the same route of administration or at the same time. The term "pharmaceutical combination" as used herein means a product that results from the mixing or combining of more than one active ingredient and includes both fixed and non-fixed combinations of the active ingredients. The term "fixed combination" means that the active ingredients, e.g. a compound of the present invention and a combination partner, are both administered to a patient simultaneously in the form of a single entity or dosage. The term "non-fixed combination" means that the active ingredients, e.g. a compound of the present invention and a combination partner, are both administered to a patient as separate entities either simultaneously, concurrently or sequentially with no specific time limits, wherein such administration provides therapeutically effective levels of the two compounds in the body of the patient. The latter also applies to cocktail therapy, e.g. the administration of three or more active ingredients.

The term "cancer" refers to a disease characterized by the rapid and uncontrolled growth of aberrant cells. Cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body. Examples of various cancers are described herein and include but are not limited to,

breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer and the like. Preferred cancers treated by the methods described herein include multiple myeloma, Hodgkin's lymphoma or non-Hodgkin's lymphoma.

The terms "tumor" and "cancer" are used interchangeably herein, e.g., both terms encompass solid and liquid, e.g., diffuse or circulating, tumors. As used herein, the term "cancer" or "tumor" includes premalignant, as well as malignant cancers and tumors.

"Derived from" as that term is used herein, indicates a relationship between a first and a second molecule. It generally refers to structural similarity between the first molecule and a second molecule and does not connotate or include a process or source limitation on a first molecule that is derived from a second molecule. For example, in the case of an intracellular signaling domain that is derived from a CD3zeta molecule, the intracellular signaling domain retains sufficient CD3zeta structure such that is has the required function, namely, the ability to generate a signal under the appropriate conditions. It does not connotate or include a limitation to a particular process of producing the intracellular signaling domain, e.g., it does not mean that, to provide the intracellular signaling domain, one must start with a CD3zeta sequence and delete unwanted sequence, or impose mutations, to arrive at the intracellular signaling domain.

The phrase "disease associated with expression of BCMA" includes, but is not limited to, a disease associated with a cell which expresses BCMA (e.g., wild-type or mutant BCMA) or condition associated with a cell which expresses BCMA (e.g., wild-type or mutant BCMA) including, e.g., proliferative diseases such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia; or a noncancer related indication associated with a cell which expresses BCMA (e.g., wild-type or mutant BCMA). For the avoidance of doubt, a disease associated with expression of BCMA may include a condition associated with a cell which does not presently express BCMA, e.g., because BCMA expression has been downregulated, e.g., due to treatment with a molecule targeting BCMA, e.g., a BCMA inhibitor described herein, but which at one time expressed BCMA. In one aspect, a cancer associated with expression of BCMA (e.g., wild-type or mutant BCMA) is a hematological cancer. In one aspect, the hematological cancer is a leukemia or a lymphoma. In one aspect, a cancer associated with expression of BCMA (e.g., wild-type or mutant BCMA) is a malignancy of differentiated plasma B cells. In one aspect, a cancer associated with expression of BCMA(e.g., wild-type or mutant BCMA) includes cancers and malignancies including, but not limited to, e.g., one or more acute leukemias including but not limited to, e.g., B-cell acute Lymphoid Leukemia ("BALL"), T-cell acute Lymphoid Leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, e.g., chronic myelogenous

leukemia (CML), Chronic Lymphoid Leukemia (CLL). Additional cancers or hematologic conditions associated with expression of BMCA (e.g., wild-type or mutant BCMA) comprise, but are not limited to, e.g., B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like. In some embodiments, the cancer is multiple myeloma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, or glioblastoma. In embodiments, a disease associated with expression of BCMA includes a plasma cell proliferative disorder, e.g., asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammapathy of undetermined significance (MGUS), Waldenstrom's macroglobulinemia, plasmacytomas (e.g., plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, and POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome). Further diseases associated with expression of BCMA (e.g., wild-type or mutant BCMA) expression include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of BCMA (e.g., wild-type or mutant BCMA), e.g., a cancer described herein, e.g., a prostate cancer (e.g., castrate-resistant or therapy-resistant prostate cancer, or metastatic prostate cancer), pancreatic cancer, or lung cancer.

Non-cancer related conditions that are associated with BCMA (e.g., wild-type or mutant BCMA) include viral infections; e.g., HIV, fungal infections, e.g., C. neoformans; autoimmune disease; e.g. rheumatoid arthritis, system lupus erythematosus (SLE or lupus), pemphigus vulgaris, and Sjogren's syndrome; inflammatory bowel disease, ulcerative colitis; transplant-related allospecific immunity disorders related to mucosal immunity; and unwanted immune responses towards biologics (e.g., Factor VIII) where humoral immunity is important. In embodiments, a non-cancer related indication associated with expression of BCMA includes but is not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation. In some embodiments, the tumor antigen-expressing cell expresses, or at any time expressed, mRNA encoding the tumor antigen. In an embodiment, the tumor antigen -expressing cell produces the tumor antigen protein (e.g., wild-type or mutant), and the tumor antigen protein may be present at normal levels or reduced levels. In an embodiment, the tumor antigen -expressing cell produced detectable levels of a tumor antigen protein at one point, and subsequently produced substantially no detectable tumor antigen protein.

The term "conservative sequence modifications" refers to amino acid modifications that do not significantly affect or alter the binding characteristics of the antibody or antibody fragment containing the amino acid sequence. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into an antibody or antibody fragment of the invention by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis. Conservative substitutions are ones in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, one or more amino acid residues within a CAR of the invention can be replaced with other amino acid residues from the same side chain family and the altered CAR can be tested using the functional assays described herein.

The term "stimulation," refers to a primary response induced by binding of a stimulatory molecule (e.g., a TCR/CD3 complex) with its cognate ligand thereby mediating a signal transduction event, such as, but not limited to, signal transduction via the TCR/CD3 complex. Stimulation can mediate altered expression of certain molecules, such as downregulation of TGF-β, and/or reorganization of cytoskeletal structures, and the like.

The term "stimulatory molecule," refers to a molecule expressed by a T cell that provides the primary cytoplasmic signaling sequence(s) that regulate primary activation of the TCR complex in a stimulatory way for at least some aspect of the T cell signaling pathway. In some embodiments, the ITAM-containing domain within the CAR recapitulates the signaling of the primary TCR independently of endogenous TCR complexes. In one aspect, the primary signal is initiated by, for instance, binding of a TCR/CD3 complex with an MHC molecule loaded with peptide, and which leads to mediation of a T cell response, including, but not limited to, proliferation, activation, differentiation, and the like. A primary cytoplasmic signaling sequence (also referred to as a "primary signaling domain") that acts in a stimulatory manner may contain a signaling motif which is known as immunoreceptor tyrosine-based activation motif or ITAM. Examples of an ITAM containing primary cytoplasmic signaling sequence that is of particular use in the invention includes, but is not limited to, those derived from TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta , CD3 epsilon, CD5, CD22, CD79a, CD79b, CD278 (also known as "ICOS") , FcεRI and CD66d, DAP10 and DAP12. In a specific CAR of the invention, the intracellular signaling domain in any one or more CARS of the invention comprises an intracellular

signaling sequence, e.g., a primary signaling sequence of CD3-zeta. The term "antigen presenting cell" or "APC" refers to an immune system cell such as an accessory cell (e.g., a B-cell, a dendritic cell, and the like) that displays a foreign antigen complexed with major histocompatibility complexes (MHC's) on its surface. T-cells may recognize these complexes using their T-cell receptors (TCRs). APCs process antigens and present them to T-cells.

An "intracellular signaling domain," as the term is used herein, refers to an intracellular portion of a molecule. In embodiments, the intracellular signal domain transduces the effector function signal and directs the cell to perform a specialized function. While the entire intracellular signaling domain can be employed, in many cases it is not necessary to use the entire chain. To the extent that a truncated portion of the intracellular signaling domain is used, such truncated portion may be used in place of the intact chain as long as it transduces the effector function signal. The term intracellular signaling domain is thus meant to include any truncated portion of the intracellular signaling domain sufficient to transduce the effector function signal.

The intracellular signaling domain generates a signal that promotes an immune effector function of the CAR containing cell, e.g., a CART cell. Examples of immune effector function, e.g., in a CART cell, include cytolytic activity and helper activity, including the secretion of cytokines.

In an embodiment, the intracellular signaling domain can comprise a primary intracellular signaling domain. Exemplary primary intracellular signaling domains include those derived from the molecules responsible for primary stimulation, or antigen dependent simulation. In an embodiment, the intracellular signaling domain can comprise a costimulatory intracellular domain. Exemplary costimulatory intracellular signaling domains include those derived from molecules responsible for costimulatory signals, or antigen independent stimulation. For example, in the case of a CART, a primary intracellular signaling domain can comprise a cytoplasmic sequence of a T cell receptor, and a costimulatory intracellular signaling domain can comprise cytoplasmic sequence from co-receptor or costimulatory molecule.

A primary intracellular signaling domain can comprise a signaling motif which is known as an immunoreceptor tyrosine-based activation motif or ITAM. Examples of ITAM containing primary cytoplasmic signaling sequences include, but are not limited to, those derived from CD3 zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3 epsilon, CD5, CD22, CD79a, CD79b, CD278 (also known as "ICOS"), FcεRI, CD66d, DAP10 and DAP12.

The term "zeta" or alternatively "zeta chain", "CD3-zeta" or "TCR-zeta" refers to CD247. Swiss-Prot accession number P20963 provides exemplary human CD3 zeta amino acid sequences. A "zeta stimulatory domain" or alternatively a "CD3-zeta stimulatory domain" or a "TCR-zeta stimulatory

domain" refers to a stimulatory domain of CD3-zeta or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions). In one embodiment, the cytoplasmic domain of zeta comprises residues 52 through 164 of GenBank Acc. No. BAG36664.1 or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions). In one embodiment, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is the sequence provided as SEQ ID NO: 1027 or 1030 or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions).

The term "costimulatory molecule" refers to the cognate binding partner on a T cell that specifically binds with a costimulatory ligand, thereby mediating a costimulatory response by the T cell, such as, but not limited to, proliferation. Costimulatory molecules are cell surface molecules other than antigen receptors or their ligands that are required for an efficient immune response. Costimulatory molecules include, but are not limited to an MHC class I molecule, TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), activating NK cell receptors, BTLA, Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

A costimulatory intracellular signaling domain refers to the intracellular portion of a costimulatory molecule.

The intracellular signaling domain can comprise the entire intracellular portion, or the entire native intracellular signaling domain, of the molecule from which it is derived, or a functional fragment thereof.

The term "4-1BB" refers to CD137 or Tumor necrosis factor receptor superfamily member 9. Swiss-Prot accession number P20963 provides exemplary human 4-1BB amino acid sequences. A "4-1BB costimulatory domain" refers to a costimulatory domain of 4-1BB, or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions). In one

embodiment, the "4-1BB costimulatory domain" is the sequence provided as SEQ ID NO: 1022 or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions).

"Immune effector cell," as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloic-derived phagocytes.

"Immune effector function or immune effector response," as that term is used herein, refers to function or response, e.g., of an immune effector cell, that enhances or promotes an immune attack of a target cell. E.g., an immune effector function or response refers a property of a T or NK cell that promotes killing or the inhibition of growth or proliferation, of a target cell. In the case of a T cell, primary stimulation and co-stimulation are examples of immune effector function or response.

The term "effector function" refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

The term "encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (e.g., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene, cDNA, or RNA, encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. The phrase nucleotide sequence that encodes a protein or a RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

The term "effective amount" or "therapeutically effective amount" are used interchangeably herein, and refer to an amount of a compound, formulation, material, or composition, as described herein effective to achieve a particular biological result.

The term "endogenous" refers to any material from or produced inside an organism, cell, tissue or system.

The term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

The term "expression" refers to the transcription and/or translation of a particular nucleotide sequence driven by a promoter.

The term "transfer vector" refers to a composition of matter which comprises an isolated nucleic acid and which can be used to deliver the isolated nucleic acid to the interior of a cell. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, polynucleotides associated with ionic or amphiphilic compounds, plasmids, and viruses. Thus, the term "transfer vector" includes an autonomously replicating plasmid or a virus. The term should also be construed to further include non-plasmid and non-viral compounds which facilitate transfer of nucleic acid into cells, such as, for example, a polylysine compound, liposome, and the like. Examples of viral transfer vectors include, but are not limited to, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, lentiviral vectors, and the like.

The term "expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, including cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

The term "lentivirus" refers to a genus of the Retroviridae family. Lentiviruses are unique among the retroviruses in being able to infect non-dividing cells; they can deliver a significant amount of genetic information into the DNA of the host cell, so they are one of the most efficient methods of a gene delivery vector. HIV, SIV, and FIV are all examples of lentiviruses.

The term "lentiviral vector" refers to a vector derived from at least a portion of a lentivirus genome, including especially a self-inactivating lentiviral vector as provided in Milone et al., Mol. Ther. 17(8): 1453–1464 (2009). Other examples of lentivirus vectors that may be used in the clinic, include but are not limited to, e.g., the LENTIVECTOR® gene delivery technology from Oxford BioMedica, the LENTIMAX™ vector system from Lentigen and the like. Nonclinical types of lentiviral vectors are also available and would be known to one skilled in the art.

The term "homologous" or "identity" refers to the subunit sequence identity between two polymeric molecules, e.g., between two nucleic acid molecules, such as, two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a subunit position in both of the two

molecules is occupied by the same monomeric subunit; e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous or identical at that position. The homology between two sequences is a direct function of the number of matching or homologous positions; e.g., if half (e.g., five positions in a polymer ten subunits in length) of the positions in two sequences are homologous, the two sequences are 50% homologous; if 90% of the positions (e.g., 9 of 10), are matched or homologous, the two sequences are 90% homologous.

"Humanized" forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. For the most part, humanized antibodies and antibody fragments thereof are human immunoglobulins (recipient antibody or antibody fragment) in which residues from a complementary-determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity, and capacity. In some instances, Fv framework region (FR) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, a humanized antibody/antibody fragment can comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. These modifications can further refine and optimize antibody or antibody fragment performance. In general, the humanized antibody or antibody fragment thereof will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or a significant portion of the FR regions are those of a human immunoglobulin sequence. The humanized antibody or antibody fragment can also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see Jones et al., Nature, 321: 522-525, 1986; Reichmann et al., Nature, 332: 323-329, 1988; Presta, Curr. Op. Struct. Biol., 2: 593-596, 1992.

"Fully human" refers to an immunoglobulin, such as an antibody or antibody fragment, where the whole molecule is of human origin or consists of an amino acid sequence identical to a human form of the antibody or immunoglobulin.

The term "isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

In the context of the present invention, the following abbreviations for the commonly occurring nucleic acid bases are used. "A" refers to adenosine, "C" refers to cytosine, "G" refers to guanosine, "T" refers to thymidine, and "U" refers to uridine.

The term "operably linked" or "transcriptional control" refers to functional linkage between a regulatory sequence and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences can be contiguous with each other and, e.g., where necessary to join two protein coding regions, are in the same reading frame.

The term "parenteral" administration of an immunogenic composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, intratumoral, or infusion techniques.

The term "nucleic acid" or "polynucleotide" refers to deoxyribonucleic acids (DNA) or ribonucleic acids (RNA) and polymers thereof in either single- or double-stranded form. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions, e.g., conservative substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions, e.g., conservative substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19:5081 (1991); Ohtsuka et al., J. Biol. Chem. 260:2605-2608 (1985); and Rossolini et al., Mol. Cell. Probes 8:91-98 (1994)).

The terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments,

substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

The term "promoter" refers to a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a polynucleotide sequence.

The term "promoter/regulatory sequence" refers to a nucleic acid sequence which is required for expression of a gene product operably linked to the promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue specific manner.

The term "constitutive" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell under most or all physiological conditions of the cell.

The term "inducible" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell substantially only when an inducer which corresponds to the promoter is present in the cell.

The term "tissue-specific" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide encodes or specified by a gene, causes the gene product to be produced in a cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

The terms "cancer associated antigen" or "tumor antigen" interchangeably refers to a molecule (typically a protein, carbohydrate or lipid) that is expressed on the surface of a cancer cell, either entirely or as a fragment (e.g., MHC/peptide), and which is useful for the preferential targeting of a pharmacological agent to the cancer cell. In some embodiments, a tumor antigen is a marker expressed by both normal cells and cancer cells, e.g., a lineage marker, e.g., CD19 on B cells. In some embodiments, a tumor antigen is a cell surface molecule that is overexpressed in a cancer cell in comparison to a normal cell, for instance, 1-fold over expression, 2-fold overexpression, 3-fold overexpression or more in comparison to a normal cell. In some embodiments, a tumor antigen is a cell surface molecule that is inappropriately synthesized in the cancer cell, for instance, a molecule that contains deletions, additions or mutations in comparison to the molecule expressed on a normal cell. In some embodiments, a tumor antigen will be expressed exclusively on the cell surface of a cancer cell,

entirely or as a fragment (e.g., MHC/peptide), and not synthesized or expressed on the surface of a normal cell. In some embodiments, the CARs of the present invention includes CARs comprising an antigen binding domain (e.g., antibody or antibody fragment) that binds to a MHC presented peptide. Normally, peptides derived from endogenous proteins fill the pockets of Major histocompatibility complex (MHC) class I molecules, and are recognized by T cell receptors (TCRs) on CD8 + T lymphocytes. The MHC class I complexes are constitutively expressed by all nucleated cells. In cancer, virus-specific and/or tumor-specific peptide/MHC complexes represent a unique class of cell surface targets for immunotherapy. TCR-like antibodies targeting peptides derived from viral or tumor antigens in the context of human leukocyte antigen (HLA)-A1 or HLA-A2 have been described (see, e.g., Sastry et al., J Virol. 2011 85(5):1935-1942; Sergeeva et al., Blood, 2011 117(16):4262-4272; Verma et al., J Immunol 2010 184(4):2156-2165; Willemsen et al., Gene Ther 2001 8(21) :1601-1608 ; Dao et al., Sci Transl Med 2013 5(176) :176ra33 ; Tassev et al., Cancer Gene Ther 2012 19(2):84-100). For example, TCR-like antibody can be identified from screening a library, such as a human scFv phage displayed library.

The term "tumor-supporting antigen" or "cancer-supporting antigen" interchangeably refer to a molecule (typically a protein, carbohydrate or lipid) that is expressed on the surface of a cell that is, itself, not cancerous, but supports the cancer cells, e.g., by promoting their growth or survival e.g., resistance to immune cells. Exemplary cells of this type include stromal cells and myeloid-derived suppressor cells (MDSCs). The tumor-supporting antigen itself need not play a role in supporting the tumor cells so long as the antigen is present on a cell that supports cancer cells.

The term "flexible polypeptide linker" or "linker" as used in the context of an scFv refers to a peptide linker that consists of amino acids such as glycine and/or serine residues used alone or in combination, to link variable heavy and variable light chain regions together. In one embodiment, the flexible polypeptide linker is a Gly/Ser linker and comprises the amino acid sequence (Gly-Gly-Gly-Ser)n (SEQ ID NO: 1038), where n is a positive integer equal to or greater than 1. For example, n=1, n=2, n=3. n=4, n=5 and n=6, n=7, n=8, n=9 and n=10 In one embodiment, the flexible polypeptide linkers include, but are not limited to, (Gly4 Ser)4 (SEQ ID NO: 1039) or (Gly4 Ser)3 (SEQ ID NO: 1040). In another embodiment, the linkers include multiple repeats of (Gly2Ser), (GlySer) or (Gly3Ser) (SEQ ID NO: 1041). Also included within the scope of the invention are linkers described in WO2012/138475, incorporated herein by reference.

As used herein, a 5' cap (also termed an RNA cap, an RNA 7-methylguanosine cap or an RNA m7G cap) is a modified guanine nucleotide that has been added to the "front" or 5' end of a eukaryotic messenger RNA shortly after the start of transcription. The 5' cap consists of a terminal group which is linked to the first transcribed nucleotide. Its presence is critical for recognition by the ribosome and

protection from RNases. Cap addition is coupled to transcription, and occurs co-transcriptionally, such that each influences the other. Shortly after the start of transcription, the 5' end of the mRNA being synthesized is bound by a cap-synthesizing complex associated with RNA polymerase. This enzymatic complex catalyzes the chemical reactions that are required for mRNA capping. Synthesis proceeds as a multi-step biochemical reaction. The capping moiety can be modified to modulate functionality of mRNA such as its stability or efficiency of translation.

As used herein, "in vitro transcribed RNA" refers to RNA, preferably mRNA, that has been synthesized in vitro. Generally, the in vitro transcribed RNA is generated from an in vitro transcription vector. The in vitro transcription vector comprises a template that is used to generate the in vitro transcribed RNA.

As used herein, a "poly(A)" is a series of adenosines attached by polyadenylation to the mRNA. In the preferred embodiment of a construct for transient expression, the polyA is between 50 and 5000 (SEQ ID NO: 1043), preferably greater than 64, more preferably greater than 100, most preferably greater than 300 or 400 (SEQ ID NO: 2024). poly(A) sequences can be modified chemically or enzymatically to modulate mRNA functionality such as localization, stability or efficiency of translation.

As used herein, "polyadenylation" refers to the covalent linkage of a polyadenylyl moiety, or its modified variant, to a messenger RNA molecule. In eukaryotic organisms, most messenger RNA (mRNA) molecules are polyadenylated at the 3' end. The 3' poly(A) tail is a long sequence of adenine nucleotides (often several hundred) added to the pre-mRNA through the action of an enzyme, polyadenylate polymerase. In higher eukaryotes, the poly(A) tail is added onto transcripts that contain a specific sequence, the polyadenylation signal. The poly(A) tail and the protein bound to it aid in protecting mRNA from degradation by exonucleases. Polyadenylation is also important for transcription termination, export of the mRNA from the nucleus, and translation. Polyadenylation occurs in the nucleus immediately after transcription of DNA into RNA, but additionally can also occur later in the cytoplasm. After transcription has been terminated, the mRNA chain is cleaved through the action of an endonuclease complex associated with RNA polymerase. The cleavage site is usually characterized by the presence of the base sequence AAUAAA near the cleavage site. After the mRNA has been cleaved, adenosine residues are added to the free 3' end at the cleavage site.

As used herein, "transient" refers to expression of a non-integrated transgene for a period of hours, days or weeks, wherein the period of time of expression is less than the period of time for expression of the gene if integrated into the genome or contained within a stable plasmid replicon in the host cell.

As used herein, the terms “treat”, “treatment” and “treating” refer to the reduction or amelioration of the progression, severity and/or duration of a proliferative disorder, or the amelioration of one or more symptoms (preferably, one or more discernible symptoms) of a proliferative disorder resulting from the administration of one or more therapies (e.g., one or more therapeutic agents such as a CAR of the invention). In specific embodiments, the terms “treat”, “treatment” and “treating” refer to the amelioration of at least one measurable physical parameter of a proliferative disorder, such as growth of a tumor, not necessarily discernible by the patient. In other embodiments the terms “treat”, “treatment” and “treating” -refer to the inhibition of the progression of a proliferative disorder, either physically by, e.g., stabilization of a discernible symptom, physiologically by, e.g., stabilization of a physical parameter, or both. In other embodiments the terms “treat”, “treatment” and “treating” refer to the reduction or stabilization of tumor size or cancerous cell count.

The term “signal transduction pathway” refers to the biochemical relationship between a variety of signal transduction molecules that play a role in the transmission of a signal from one portion of a cell to another portion of a cell. The phrase “cell surface receptor” includes molecules and complexes of molecules capable of receiving a signal and transmitting signal across the membrane of a cell.

The term “subject” is intended to include living organisms in which an immune response can be elicited (e.g., mammals, human).

The term, a “substantially purified” cell refers to a cell that is essentially free of other cell types. A substantially purified cell also refers to a cell which has been separated from other cell types with which it is normally associated in its naturally occurring state. In some instances, a population of substantially purified cells refers to a homogenous population of cells. In other instances, this term refers simply to cell that have been separated from the cells with which they are naturally associated in their natural state. In some aspects, the cells are cultured in vitro. In other aspects, the cells are not cultured in vitro.

The term “therapeutic” as used herein means a treatment. A therapeutic effect is obtained by reduction, suppression, remission, or eradication of a disease state.

The term “prophylaxis” as used herein means the prevention of or protective treatment for a disease or disease state.

In the context of the present invention, "tumor antigen" or "hyperproliferative disorder antigen" or "antigen associated with a hyperproliferative disorder" refers to antigens that are common to specific hyperproliferative disorders. In certain aspects, the hyperproliferative disorder antigens of the present invention are derived from, cancers including but not limited to primary or metastatic melanoma, thymoma, lymphoma, sarcoma, lung cancer, liver cancer, non-Hodgkin lymphoma, Hodgkin lymphoma,

leukemias, uterine cancer, cervical cancer, bladder cancer, kidney cancer and adenocarcinomas such as breast cancer, prostate cancer (e.g., castrate-resistant or therapy-resistant prostate cancer, or metastatic prostate cancer), ovarian cancer, pancreatic cancer, and the like, or a plasma cell proliferative disorder, e.g., asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammapathy of undetermined significance (MGUS), Waldenstrom's macroglobulinemia, plasmacytomas (e.g., plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, and POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome).

The term "transfected" or "transformed" or "transduced" refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A "transfected" or "transformed" or "transduced" cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

The term "specifically binds," refers to an antibody, or a ligand, which recognizes and binds with a cognate binding partner (e.g., a stimulatory and/or costimulatory molecule present on a T cell) protein present in a sample, but which antibody or ligand does not substantially recognize or bind other molecules in the sample.

"Regulatable chimeric antigen receptor (RCAR)," as used herein, refers to a set of polypeptides, typically two in the simplest embodiments, which when in an immune effector cell, provides the cell with specificity for a target cell, typically a cancer cell, and with intracellular signal generation. In some embodiments, an RCAR comprises at least an extracellular antigen binding domain, a transmembrane domain and a cytoplasmic signaling domain (also referred to herein as "an intracellular signaling domain") comprising a functional signaling domain derived from a stimulatory molecule and/or costimulatory molecule as defined herein in the context of a CAR molecule. In some embodiments, the set of polypeptides in the RCAR are not contiguous with each other, e.g., are in different polypeptide chains. In some embodiments, the RCAR includes a dimerization switch that, upon the presence of a dimerization molecule, can couple the polypeptides to one another, e.g., can couple an antigen binding domain to an intracellular signaling domain. In some embodiments, the RCAR is expressed in a cell (e.g., an immune effector cell) as described herein, e.g., an RCAR-expressing cell (also referred to herein as "RCARX cell"). In an embodiment the RCARX cell is a T cell, and is referred to as a RCART cell. In an embodiment the RCARX cell is an NK cell, and is referred to as a RCARN cell. The RCAR can provide the RCAR-expressing cell with specificity for a target cell, typically a cancer cell, and with regulatable intracellular signal generation or proliferation, which can optimize an immune effector property of the RCAR-expressing cell. In embodiments, an RCAR cell relies at least in part, on

an antigen binding domain to provide specificity to a target cell that comprises the antigen bound by the antigen binding domain.

"Membrane anchor" or "membrane tethering domain", as that term is used herein, refers to a polypeptide or moiety, e.g., a myristoyl group, sufficient to anchor an extracellular or intracellular domain to the plasma membrane.

"Switch domain," as that term is used herein, e.g., when referring to an RCAR, refers to an entity, typically a polypeptide-based entity, that, in the presence of a dimerization molecule, associates with another switch domain. The association results in a functional coupling of a first entity linked to, e.g., fused to, a first switch domain, and a second entity linked to, e.g., fused to, a second switch domain. A first and second switch domain are collectively referred to as a dimerization switch. In embodiments, the first and second switch domains are the same as one another, e.g., they are polypeptides having the same primary amino acid sequence, and are referred to collectively as a homodimerization switch. In embodiments, the first and second switch domains are different from one another, e.g., they are polypeptides having different primary amino acid sequences, and are referred to collectively as a heterodimerization switch. In embodiments, the switch is intracellular. In embodiments, the switch is extracellular. In embodiments, the switch domain is a polypeptide-based entity, e.g., FKBP or FRB-based, and the dimerization molecule is small molecule, e.g., a rapalogue. In embodiments, the switch domain is a polypeptide-based entity, e.g., an scFv that binds a myc peptide, and the dimerization molecule is a polypeptide, a fragment thereof, or a multimer of a polypeptide, e.g., a myc ligand or multimers of a myc ligand that bind to one or more myc scFvs. In embodiments, the switch domain is a polypeptide-based entity, e.g., myc receptor, and the dimerization molecule is an antibody or fragments thereof, e.g., myc antibody.

"Dimerization molecule," as that term is used herein, e.g., when referring to an RCAR, refers to a molecule that promotes the association of a first switch domain with a second switch domain. In embodiments, the dimerization molecule does not naturally occur in the subject, or does not occur in concentrations that would result in significant dimerization. In embodiments, the dimerization molecule is a small molecule, e.g., rapamycin or a rapalogue, e.g, RAD001.

The term "bioequivalent" refers to an amount of an agent other than the reference compound (e.g., RAD001), required to produce an effect equivalent to the effect produced by the reference dose or reference amount of the reference compound (e.g., RAD001). In an embodiment the effect is the level of mTOR inhibition, e.g., as measured by P70 S6 kinase inhibition, e.g., as evaluated in an in vivo or in vitro assay, e.g., as measured by an assay described herein, e.g., the Boulay assay, or measurement of phosphorylated S6 levels by western blot. In an embodiment, the effect is alteration of the ratio of PD-1

positive/PD-1 negative T cells, as measured by cell sorting. In an embodiment a bioequivalent amount or dose of an mTOR inhibitor is the amount or dose that achieves the same level of P70 S6 kinase inhibition as does the reference dose or reference amount of a reference compound. In an embodiment, a bioequivalent amount or dose of an mTOR inhibitor is the amount or dose that achieves the same level of alteration in the ratio of PD-1 positive/PD-1 negative T cells as does the reference dose or reference amount of a reference compound.

The term "low, immune enhancing, dose" when used in conjuction with an mTOR inhibitor, e.g., an allosteric mTOR inhibitor, e.g., RAD001 or rapamycin, or a catalytic mTOR inhibitor, refers to a dose of mTOR inhibitor that partially, but not fully, inhibits mTOR activity, e.g., as measured by the inhibition of P70 S6 kinase activity. Methods for evaluating mTOR activity, e.g., by inhibition of P70 S6 kinase, are discussed herein. The dose is insufficient to result in complete immune suppression but is sufficient to enhance the immune response. In an embodiment, the low, immune enhancing, dose of mTOR inhibitor results in a decrease in the number of PD-1 positive immune effector cells, e.g., T cells or NK cells, and/or an increase in the number of PD-1 negative immune effector cells, e.g., T cells or NK cells, or an increase in the ratio of PD-1 negative immune effector cells (e.g., T cells or NK cells) /PD-1 positive immune effector cells (e.g., T cells or NK cells).

In an embodiment, the low, immune enhancing, dose of mTOR inhibitor results in an increase in the number of naive T cells. In an embodiment, the low, immune enhancing, dose of mTOR inhibitor results in one or more of the following:

an increase in the expression of one or more of the following markers: CD62Lhigh, CD127high, CD27+, and BCL2, e.g., on memory T cells, e.g., memory T cell precursors;

a decrease in the expression of KLRG1, e.g., on memory T cells, e.g., memory T cell precursors; and

an increase in the number of memory T cell precursors, e.g., cells with any one or combination of the following characteristics: increased CD62Lhigh, increased CD127high, increased CD27+, decreased KLRG1, and increased BCL2;

wherein any of the changes described above occurs, e.g., at least transiently, e.g., as compared to a non-treated subject.

"Refractory" as used herein refers to a disease, e.g., cancer, that does not respond to a treatment. In embodiments, a refractory cancer can be resistant to a treatment before or at the beginning of the treatment. In other embodiments, the refractory cancer can become resistant during a treatment. A refractory cancer is also called a resistant cancer.

"Relapsed" or a "relapse" as used herein refers to the reappearance of a disease (e.g., cancer) or the signs and symptoms of a disease such as cancer after a period of improvement or responsiveness, e.g., after prior treatment of a therapy, e.g., cancer therapy. For example, the period of responsiveness may involve the level of cancer cells falling below a certain threshold, e.g., below 20%, 15%, 10%, 5%, 4%, 3%, 2%, or 1%. The reappearance may involve the level of cancer cells rising above a certain threshold, e.g., above 20%, 15%, 10%, 5%, 4%, 3%, 2%, or 1%.

In one aspect, a "responder" of a therapy can be a subject having complete response, very good partial response, or partial response after receiving the therapy. In one aspect, a "non-responder" of a therapy can be a subject having minor response, stable disease, or progressive disease after receiving the therapy. In some embodiments, the subject has multiple myeloma and the response of the subject to a multiple myeloma therapy is determined based on IMWG 2016 criteria, e.g., as disclosed in Kumar, et al., Lancet Oncol. 17, e328-346 (2016), hereby incorporated herein by reference in its entirety, e.g., as described in Table 7.

Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. As another example, a range such as 95-99% identity, includes something with 95%, 96%, 97%, 98% or 99% identity, and includes subranges such as 96-99%, 96-98%, 96-97%, 97-99%, 97-98% and 98-99% identity. This applies regardless of the breadth of the range.

A "gene editing system" as the term is used herein, refers to a system, e.g., one or more molecules, that direct and effect an alteration, e.g., a deletion, of one or more nucleic acids at or near a site of genomic DNA targeted by said system. Gene editing systems are known in the art, and are described more fully below.

Definitions of specific functional groups and chemical terms are described in more detail below. The chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, *Handbook of Chemistry and Physics*, 75th Ed., inside cover, and specific functional groups are generally defined as described therein. Additionally, general principles of organic chemistry, as well as specific functional moieties and reactivity, are described in Thomas Sorrell, *Organic Chemistry*,

University Science Books, Sausalito, 1999; Smith and March, *March's Advanced Organic Chemistry*, 5th Edition, John Wiley & Sons, Inc., New York, 2001; Larock, *Comprehensive Organic Transformations*, VCH Publishers, Inc., New York, 1989; and Carruthers, *Some Modern Methods of Organic Synthesis*, 3rd Edition, Cambridge University Press, Cambridge, 1987.

The term "alkyl," as used herein, refers to a monovalent saturated, straight- or branched-chain hydrocarbon such as a straight or branched group of 1-12, 1-10, or 1-6 carbon atoms, referred to herein as C_1-C_{12} alkyl, C_1-C_{10} alkyl, and C_1-C_6 alkyl, respectively. Examples of alkyl groups include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, sec-pentyl, iso-pentyl, tert-butyl, n-pentyl, neopentyl, n-hexyl, sec-hexyl, and the like.

The terms "alkenyl" and "alkynyl" as used herein refer to unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but that contain at least one double or triple bond, respectively. Exemplary alkenyl groups include, but are not limited to, $-CH=CH_2$ and $-CH_2CH=CH_2$.

The term "aryl" as used herein refers to a monocyclic, bicyclic or polycyclic hydrocarbon ring system, wherein at least one ring is aromatic. Representative aryl groups include fully aromatic ring systems, such as phenyl (e.g., (C_6) aryl), naphthyl (e.g., (C_{10}) aryl), and anthracenyl (e.g., (C_{14}) aryl), and ring systems where an aromatic carbon ring is fused to one or more non-aromatic carbon rings, such as indanyl, phthalimidyl, naphthimidyl, or tetrahydronaphthyl, and the like.

The term "carbocyclyl" as used herein refers to monocyclic, or fused, spiro-fused, and/or bridged bicyclic or polycyclic hydrocarbon ring system containing 3-18 carbon atoms, wherein each ring is either completely saturated or contains one or more units of unsaturation, but where no ring is aromatic. Representative carbocyclyl groups include cycloalkyl groups (*e.g.*, cyclopentyl, cyclobutyl, cyclopentyl, cyclohexyl and the like), and cycloalkenyl groups (*e.g.*, cyclopentenyl, cyclohexenyl, cyclopentadienyl, and the like).

The term "carbonyl" as used herein refers to –C=O.

The term "cyano" as used herein refers to –CN.

The terms "halo" or "halogen" as used herein refer to fluorine (fluoro, –F), chlorine (chloro, –Cl), bromine (bromo, –Br), or iodine (iodo, –I).

The term "heteroalkyl" as used herein refers to a monovalent saturated straight or branched alkyl chain wherein at least one carbon atom in the chain is replaced with a heteroatom, such as O, S, or N, provided that upon substitution, the chain comprises at least one carbon atom. In some embodiments, a heteroalkyl group may comprise, e.g., 1-12, 1-10, or 1-6 carbon atoms, referred to herein as C_1-C_{12} heteroalkyl, C_1-C_{10} heteroalkyl, and C_1-C_6 heteroalkyl. In certain instances, a heteroalkyl group comprises 1, 2, 3, or 4 independently selected heteroatoms in place of 1, 2, 3, or 4

individual carbon atoms in the alkyl chain. Representative heteroalkyl groups include –$CH_2NHC(O)CH_3$, -$CH_2CH_2OCH_3$, -$CH_2CH_2NHCH_3$, -$CH_2CH_2N(CH_3)CH_3$, and the like.

The term "heteroaryl" as used herein refers to a monocyclic, bicyclic or polycyclic ring system wherein at least one ring is both aromatic and comprises a heteroatom; and wherein no other rings are heterocyclyl (as defined below). Representative heteroaryl groups include ring systems where (i) each ring comprises a heteroatom and is aromatic, *e.g.*, imidazolyl, oxazolyl, thiazolyl, triazolyl, pyrrolyl, furanyl, thiophenyl pyrazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolizinyl, purinyl, naphthyridinyl, and pteridinyl; (ii) each ring is aromatic or carbocyclyl, at least one aromatic ring comprises a heteroatom and at least one other ring is a hydrocarbon ring or *e.g.*, indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, pyrido[2,3-*b*]-1,4-oxazin-3(4H)-one, thiazolo-[4,5-*c*]-pyridinyl, 4,5,6,7-tetrahydrothieno[2,3-*c*]pyridinyl, 5,6-dihydro-4H-thieno[2,3-*c*]pyrrolyl, 4,5,6,7,8-tetrahydroquinolinyl and 5,6,7,8-tetrahydroisoquinolinyl; and (iii) each ring is aromatic or carbocyclyl, and at least one aromatic ring shares a bridgehead heteroatom with another aromatic ring, *e.g.*, 4H-quinolizinyl. In certain embodiments, the heteroaryl is a monocyclic or bicyclic ring, wherein each of said rings contains 5 or 6 ring atoms where 1, 2, 3, or 4 of said ring atoms are a heteroatom independently selected from N, O, and S.

The term "heterocyclyl" as used herein refers to a monocyclic, or fused, spiro-fused, and/or bridged bicyclic and polycyclic ring systems where at least one ring is saturated or partially unsaturated (but not aromatic) and comprises a heteroatom. A heterocyclyl can be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure and any of the ring atoms can be optionally substituted. Representative heterocyclyls include ring systems in which (i) every ring is non-aromatic and at least one ring comprises a heteroatom, *e.g.*, tetrahydrofuranyl, tetrahydrothienyl, pyrrolidinyl, pyrrolidonyl, piperidinyl, pyrrolinyl, decahydroquinolinyl, oxazolidinyl, piperazinyl, dioxanyl, dioxolanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, and quinuclidinyl; (ii) at least one ring is non-aromatic and comprises a heteroatom and at least one other ring is an aromatic carbon ring, *e.g.*, 1,2,3,4-tetrahydroquinolinyl; and (iii) at least one ring is non-aromatic and comprises a heteroatom and at least one other ring is aromatic and comprises a heteroatom, *e.g.*, 3,4-dihydro-1H-pyrano[4,3-c]pyridinyl, and 1,2,3,4-tetrahydro-2,6-naphthyridinyl. In certain embodiments, the heterocyclyl is a monocyclic or bicyclic ring, wherein each of said rings contains 3-7 ring atoms where 1, 2, 3, or 4 of said ring atoms are a heteroatom independently selected from N, O, and S.

As described herein, compounds of the invention may contain "optionally substituted" moieties. In general, the term "substituted", whether preceded by the term "optionally" or not, means that one or

more hydrogens of the designated moiety are replaced with a suitable substituent. Unless otherwise indicated, an "optionally substituted" group may have a suitable substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at each position. Combinations of substituents envisioned under this invention are preferably those that result in the formation of stable or chemically feasible compounds. The term "stable", as used herein, refers to compounds that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein.

The term "oxo" as used herein refers to =O.

The term "thiocarbonyl" as used herein refers to C=S.

As used herein, the term "pharmaceutically acceptable salt" refers to those salts which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, Berge et al., describe pharmaceutically acceptable salts in detail in *J. Pharmaceutical Sciences*, 1977, 66, 1–19, incorporated herein by reference. Pharmaceutically acceptable salts of the compounds of this invention include those derived from suitable inorganic and organic acids and bases. Examples of pharmaceutically acceptable, nontoxic acid addition salts are salts of an amino group formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid, and perchloric acid or with organic acids such as acetic acid, oxalic acid, maleic acid, tartaric acid, citric acid, succinic acid, or malonic acid or by using other methods known in the art such as ion exchange. Other pharmaceutically acceptable salts include adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, hemisulfate, heptanoate, hexanoate, hydroiodide, 2–hydroxy–ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2–naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3–phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p-toluenesulfonate, undecanoate, valerate salts, and the like. Salts derived from appropriate bases include alkali metal, alkaline earth metal, ammonium and $N^+(C_{1-4}$ alkyl$)_4^-$ salts. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like. Further pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, lower alkyl sulfonate, and aryl sulfonate.

The term "solvate" refers to forms of the compound that are associated with a solvent, usually by a solvolysis reaction. This physical association may include hydrogen bonding. Conventional solvents include water, methanol, ethanol, acetic acid, DMSO, THF, diethyl ether, and the like. The compounds of Formula (I), Formula (I-a), and/or Formula (II) may be prepared, *e.g.*, in crystalline form, and may be solvated. Suitable solvates include pharmaceutically acceptable solvates and further include both stoichiometric solvates and non-stoichiometric solvates. In certain instances, the solvate will be capable of isolation, for example, when one or more solvent molecules are incorporated in the crystal lattice of a crystalline solid. "Solvate" encompasses both solution-phase and isolable solvates. Representative solvates include hydrates, ethanolates, and methanolates.

The term "hydrate" refers to a compound which is associated with water. Typically, the number of the water molecules contained in a hydrate of a compound is in a definite ratio to the number of the compound molecules in the hydrate. Therefore, a hydrate of a compound may be represented, for example, by the general formula R·x H_2O, wherein R is the compound and wherein x is a number greater than 0. A given compound may form more than one type of hydrates, including, *e.g.*, monohydrates (x is 1), lower hydrates (x is a number greater than 0 and smaller than 1, *e.g.*, hemihydrates (R·0.5 H_2O)), and polyhydrates (x is a number greater than 1, *e.g.*, dihydrates (R·2 H_2O) and hexahydrates (R·6 H_2O)).

It is to be understood that compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or the arrangement of their atoms in space are termed "isomers". Isomers that differ in the arrangement of their atoms in space are termed "stereoisomers".

Stereoisomers that are not mirror images of one another are termed "diastereomers" and those that are non-superimposable mirror images of each other are termed "enantiomers". When a compound has an asymmetric center, for example, it is bonded to four different groups and a pair of enantiomers is possible. An enantiomer can be characterized by the absolute configuration of its asymmetric center and is described by the R- and S-sequencing rules of Cahn and Prelog, or by the manner in which the molecule rotates the plane of polarized light and designated as dextrorotatory or levorotatory (*i.e.*, as (+) or (-)-isomers respectively). A chiral compound can exist as either individual enantiomer or as a mixture thereof. A mixture containing equal proportions of the enantiomers is called a "racemic mixture".

The term "tautomers" refer to compounds that are interchangeable forms of a particular compound structure, and that vary in the displacement of hydrogen atoms and electrons. Thus, two structures may be in equilibrium through the movement of π electrons and an atom (usually H). For example, enols and ketones are tautomers because they are rapidly interconverted by treatment with either acid or base. Another example of tautomerism is the aci- and nitro- forms of phenylnitromethane that are likewise formed by treatment with acid or base.

Tautomeric forms may be relevant to the attainment of the optimal chemical reactivity and biological activity of a compound of interest.

Unless otherwise stated, structures depicted herein are also meant to include all isomeric (*e.g.*, enantiomeric, diastereomeric, and geometric (or conformational)) forms of the structure; for example, the R and S configurations for each asymmetric center, Z and E double bond isomers, and Z and E conformational isomers. Therefore, single stereochemical isomers as well as enantiomeric, diastereomeric, and geometric (or conformational) mixtures of the present compounds are within the scope of the invention. Unless otherwise stated, all tautomeric forms of the compounds of the invention are within the scope of the invention. Additionally, unless otherwise stated, structures depicted herein are also meant to include compounds that differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures including the replacement of hydrogen by deuterium or tritium, or the replacement of a carbon by a ^{13}C- or ^{14}C-enriched carbon are within the scope of this invention. Such compounds are useful, for example, as analytical tools, as probes in biological assays, or as therapeutic agents in accordance with the present invention.

Where a particular enantiomer is preferred, it may, in some embodiments be provided substantially free of the corresponding enantiomer, and may also be referred to as "optically enriched." "Optically-enriched," as used herein, means that the compound is made up of a significantly greater proportion of one enantiomer. In certain embodiments the compound is made up of at least about 90% by weight of a preferred enantiomer. In other embodiments the compound is made up of at least about 95%, 98%, or 99% by weight of a preferred enantiomer. Preferred enantiomers may be isolated from racemic mixtures by any method known to those skilled in the art, including chiral high pressure liquid chromatography (HPLC) and the formation and crystallization of chiral salts or prepared by asymmetric syntheses. See, for example, Jacques et al., *Enantiomers, Racemates and Resolutions* (Wiley Interscience, New York, 1981); Wilen, et al., *Tetrahedron* 33:2725 (1977); Eliel, E.L. *Stereochemistry of Carbon Compounds* (McGraw-Hill, NY, 1962); Wilen, S.H. *Tables of Resolving Agents and Optical Resolutions* p. 268 (E.L. Eliel, Ed., Univ. of Notre Dame Press, Notre Dame, IN 1972).

Various aspects of the compositions and methods herein are described in further detail below. Additional definitions are set out throughout the specification.

Detailed Description

The present invention provides, at least in part, a method of treating a subject having a disease associated with BCMA expression, comprising administering to the subject an effective amount of a cell (e.g., a population of cells) that expresses a CAR molecule that binds BCMA (a "BCMA CAR-expressing cell"). In some embodiments, the disease associated with expression of BCMA is a

hematologic cancer, e.g., ALL, CLL, DLBCL, or multiple myeloma. In some embodiments, the BCMA CAR-expressing cell therapy is administered based on the acquisition of a level of a biomarker from a patient sample. In some embodiments, the BCMA CAR-expressing cell therapy is administered to the subject in combination with a second therapy. In some embodiments, the BCMA CAR-expressing cell therapy and the second therapy are administered simultaneously or sequentially.

Chimeric antigen receptor (CAR)

In one aspect, disclosed herein are methods using a cell (e.g., a population of cells) that expresses a CAR molecule. In one aspect, an exemplary CAR construct comprises an optional leader sequence (e.g., a leader sequence described herein), an antigen binding domain (e.g., an antigen binding domain described herein), a hinge (e.g., a hinge region described herein), a transmembrane domain (e.g., a transmembrane domain described herein), and an intracellular stimulatory domain (e.g., an intracellular stimulatory domain described herein). In one aspect, an exemplary CAR construct comprises an optional leader sequence (e.g., a leader sequence described herein), an extracellular antigen binding domain (e.g., an antigen binding domain described herein), a hinge (e.g., a hinge region described herein), a transmembrane domain (e.g., a transmembrane domain described herein), an intracellular costimulatory signaling domain (e.g., a costimulatory signaling domain described herein) and/or an intracellular primary signaling domain (e.g., a primary signaling domain described herein).

Sequences of non-limiting examples of various components that can be part of a CAR molecule described herein, are listed in **Table 1**, where "aa" stands for amino acids, and "na" stands for nucleic acids that encode the corresponding peptide.

Table 1. Sequences of various components of CAR (aa – amino acid sequence, na – nucleic acid sequence).

SEQ ID NO:	description	Sequence
1007	EF-1 promoter	CGTGAGGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATCGC CCACAGTCCCCGAGAAGTTGGGGGGAGGGGTCGGCAATTGAA CCGGTGCCTAGAGAAGGTGGCGCGGGGTAAACTGGGAAAGT GATGTCGTGTACTGGCTCCGCCTTTTTCCCGAGGGTGGGGGAG AACCGTATATAAGTGCAGTAGTCGCCGTGAACGTTCTTTTTCG CAACGGGTTTGCCGCCAGAACACAGGTAAGTGCCGTGTGTGG TTCCCGCGGGCCTGGCCTCTTTACGGGTTATGGCCCTTGCGTG CCTTGAATTACTTCCACCTGGCTGCAGTACGTGATTCTTGATC CCGAGCTTCGGGTTGGAAGTGGGTGGGAGAGTTCGAGGCCTT GCGCTTAAGGAGCCCCTTCGCCTCGTGCTTGAGTTGAGGCCTG GCCTGGGCGCTGGGGCCGCCGCGTGCGAATCTGGTGGCACCT TCGCGCCTGTCTCGCTGCTTTCGATAAGTCTCTAGCCATTTAA AATTTTTGATGACCTGCTGCGACGCTTTTTTTCTGGCAAGATA GTCTTGTAAATGCGGGCCAAGATCTGCACACTGGTATTTCGGT

		TTTTGGGGCCGCGGGCGGCGACGGGGCCCGTGCGTCCCAGCG CACATGTTCGGCGAGGCGGGGCCTGCGAGCGCGGCCACCGAG AATCGGACGGGGGTAGTCTCAAGCTGGCCGGCCTGCTCTGGT GCCTGGCCTCGCGCCGCCGTGTATCGCCCCGCCCTGGGCGGC AAGGCTGGCCCGGTCGGCACCAGTTGCGTGAGCGGAAAGATG GCCGCTTCCCGGCCCTGCTGCAGGGAGCTCAAAATGGAGGAC GCGGCGCTCGGGAGAGCGGGCGGGTGAGTCACCCACACAAA GGAAAAGGGCCTTTCCGTCCTCAGCCGTCGCTTCATGTGACTC CACGGAGTACCGGGCGCCGTCCAGGCACCTCGATTAGTTCTC GAGCTTTTGGAGTACGTCGTCTTTAGGTTGGGGGGAGGGGTTT TATGCGATGGAGTTTCCCCACACTGAGTGGGTGGAGACTGAA GTTAGGCCAGCTTGGCACTTGATGTAATTCTCCTTGGAATTTG CCCTTTTTGAGTTTGGATCTTGGTTCATTCTCAAGCCTCAGAC AGTGGTTCAAAGTTTTTTTCTTCCATTTCAGGTGTCGTGA
1008	Leader (aa)	MALPVTALLLPLALLLHAARP
1009	Leader (na)	ATGGCCCTGCCTGTGACAGCCCTGCTGCTGCCTCTGGCTCTGC TGCTGCATGCCGCTAGACCC
1010	Leader (na)	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTC TGCTCCACGCCGCTCGGCCC
1011	CD8 hinge (aa)	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD
1012	CD8 hinge (na)	ACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCCCACC ATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTGCCGG CCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTT CGCCTGTGAT
1013	Ig4 hinge (aa)	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLGKM
1014	Ig4 hinge (na)	GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGCCCCCG AGTTCCTGGGCGGACCCAGCGTGTTCCTGTTCCCCCCCAAGCC CAAGGACACCCTGATGATCAGCCGGACCCCCGAGGTGACCTG TGTGGTGGTGGACGTGTCCCAGGAGGACCCCGAGGTCCAGTT CAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGAC CAAGCCCCGGGAGGAGCAGTTCAATAGCACCTACCGGGTGGT GTCCGTGCTGACCGTGCTGCACCAGGACTGGCTGAACGGCAA GGAATACAAGTGTAAGGTGTCCAACAAGGGCCTGCCCAGCAG CATCGAGAAAACCATCAGCAAGGCCAAGGGCCAGCCTCGGG AGCCCCAGGTGTACACCCTGCCCCCTAGCCAAGAGGAGATGA CCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCT ACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAG CCCGAGAACAACTACAAGACCACCCCCCCTGTGCTGGACAGC GACGGCAGCTTCTTCCTGTACAGCCGGCTGACCGTGGACAAG AGCCGGTGGCAGGAGGGCAACGTCTTTAGCTGCTCCGTGATG CACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGC CTGTCCCTGGGCAAGATG
1015	IgD hinge (aa)	RWPESPKAQASSVPTAQPQAEGSLAKATTAPATTRNTGRGGEEK KKEKEKEEQEERETKTPECPSHTQPLGVYLLTPAVQDLWLRDKA TFTCFVVGSDLKDAHLTWEVAGKVPTGGVEEGLLERHSNGSQS

		QHSRLTLPRSLWNAGTSVTCTLNHPSLPPQRLMALREPAAQAPV KLSLNLLASSDPPEAASWLLCEVSGFSPPNILLMWLEDQREVNTS GFAPARPPPQPGSTTFWAWSVLRVPAPPSPQPATYTCVVSHEDS RTLLNASRSLEVSYVTDH
1016	IgD hinge (na)	AGGTGGCCCGAAAGTCCCAAGGCCCAGGCATCTAGTGTTCCT ACTGCACAGCCCCAGGCAGAAGGCAGCCTAGCCAAAGCTACT ACTGCACCTGCCACTACGCGCAATACTGGCCGTGGCGGGGAG GAGAAGAAAAAGGAGAAAGAGAAAGAAGAACAGGAAGAGA GGGAGACCAAGACCCCTGAATGTCCATCCCATACCCAGCCGC TGGGCGTCTATCTCTTGACTCCCGCAGTACAGGACTTGTGGCT TAGAGATAAGGCCACCTTTACATGTTTCGTCGTGGGCTCTGAC CTGAAGGATGCCCATTTGACTTGGGAGGTTGCCGGAAAGGTA CCCACAGGGGGGGTTGAGGAAGGGTTGCTGGAGCGCCATTCC AATGGCTCTCAGAGCCAGCACTCAAGACTCACCCTTCCGAGA TCCCTGTGGAACGCCGGGACCTCTGTCACATGTACTCTAAATC ATCCTAGCCTGCCCCCACAGCGTCTGATGGCCCTTAGAGAGC CAGCCGCCCAGGCACCAGTTAAGCTTAGCCTGAATCTGCTCG CCAGTAGTGATCCCCCAGAGGCCGCCAGCTGGCTCTTATGCG AAGTGTCCGGCTTTAGCCCGCCCAACATCTTGCTCATGTGGCT GGAGGACCAGCGAGAAGTGAACACCAGCGGCTTCGCTCCAGC CCGGCCCCCACCCCAGCCGGGTTCTACCACATTCTGGGCCTGG AGTGTCTTAAGGGTCCCAGCACCACCTAGCCCCCAGCCAGCC ACATACACCTGTGTTGTGTCCCATGAAGATAGCAGGACCCTG CTAAATGCTTCTAGGAGTCTGGAGGTTTCCTACGTGACTGACC ATT
1017	GS hinge/linker (aa)	GGGGSGGGGS
1018	GS hinge/linker (na)	GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC
1019	CD8 transmembrane (TM) (aa)	IYIWAPLAGTCGVLLLSLVITLYC
1020	CD8 transmembrane (TM) (na)	ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTTC TCCTGTCACTGGTTATCACCCTTTACTGC
1021	CD8 TM (na)	ATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGC TGCTTTCACTCGTGATCACTCTTTACTGT
1022	4-1BB intracellular domain (aa)	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL
1023	4-1BB intracellular domain (na)	AAACGGGGCAGAAAGAAACTCCTGTATATATTCAAACAACCA TTTATGAGACCAGTACAAACTACTCAAGAGGAAGATGGCTGT AGCTGCCGATTTCCAGAAGAAGAAGAAGGAGGATGTGAACT G
1024	4-1BB intracellular domain (na)	AAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGT TCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTG
1025	CD27 (aa)	QRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPAC SP

1026	CD27 (na)	AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAAC ATGACTCCCCGCCGCCCCGGGCCCACCCGCAAGCATTACCAG CCCTATGCCCCACCACGCGACTTCGCAGCCTATCGCTCC
1027	CD3-zeta (aa)	RVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDP EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKG HDGLYQGLSTATKDTYDALHMQALPPR
1028	CD3-zeta (na)	AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACAA GCAGGGCCAGAACCAGCTCTATAACGAGCTCAATCTAGGACG AAGAGAGGAGTACGATGTTTTGGACAAGAGACGTGGCCGGG ACCCTGAGATGGGGGGAAAGCCGAGAAGGAAGAACCCTCAG GAAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGA GGCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGGG GCAAGGGGCACGATGGCCTTTACCAGGGTCTCAGTACAGCCA CCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCCC CTCGC
1029	CD3-zeta (na)	CGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGG AGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGA CCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAG AGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGG CAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCAC CAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCC TCGG
1030	CD3-zeta (aa)	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDP EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKG HDGLYQGLSTATKDTYDALHMQALPPR
1031	CD3-zeta (na)	AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACCAG CAGGGCCAGAACCAGCTCTATAACGAGCTCAATCTAGGACGA AGAGAGGAGTACGATGTTTTGGACAAGAGACGTGGCCGGGA CCCTGAGATGGGGGGAAAGCCGAGAAGGAAGAACCCTCAGG AAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGAG GCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGGGG CAAGGGGCACGATGGCCTTTACCAGGGTCTCAGTACAGCCAC CAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCCCC TCGC
1032	linker	GGGGS
1033	linker	GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC
1034	PD-1 extracellular domain (aa)	Pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdklaafpedrs qpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslraelrvterraevptahp spsprpagqfqtlv
1035	PD-1 extracellular domain (na)	Cccggatggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcactcttggtt gtgactgagggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatcattcgtgctgaact ggtaccgcatgagcccgtcaaaccagaccgacaagctcgccgcgtttccggaagatcggtcgcaac cgggacaggattgtcggttccgcgtgactcaactgccgaatggcagagacttccacatgagcgtggtc cgcgctaggcgaaacgactccgggacctacctgtgcggagccatctcgctggcgcctaaggcccaa atcaaagagagcttgagggccgaactgagagtgaccgagcgcagagctgaggtgccaactgcacat ccatccccatcgcctcggcctgcggggcagtttcagaccctggtc

1036	PD-1 CAR (aa) with signal	Malpvtalllplalllhaarppgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwy rmspsnqtdklaafpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqik eslraelrvterraevptahpspsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaaggav htrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeee eggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqegly nelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr
1037	PD-1 CAR (na)	Atggccctccctgtcactgccctgcttctccccctcgcactcctgctccacgccgctagaccacccgg atggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcactcttggttgtgactg agggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatcattcgtgctgaactggtaccg catgagcccgtcaaaccagaccgacaagctcgccgcgtttccggaagatcggtcgcaaccgggaca ggattgtcggttccgcgtgactcaactgccgaatggcagagacttccacatgagcgtggtccgcgcta ggcgaaacgactccgggacctacctgtgcggagccatctcgctggcgcctaaggcccaaatcaaag agagcttgagggccgaactgagagtgaccgagcgcagagctgaggtgccaactgcacatccatccc catcgcctcggcctgcggggcagtttcagaccctggtcacgaccactccggcgccgcgcccaccga ctccggccccaactatcgcgagccagcccctgtcgctgaggccggaagcatgccgccctgccgccg gaggtgctgtgcatacccggggattggacttcgcatgcgacatctacatttgggctcctctcgccggaa cttgtggcgtgctccttctgtccctggtcatcaccctgtactgcaagcggggtcggaaaaagcttctgta cattttcaagcagcccttcatgaggcccgtgcaaaccacccaggaggaggacggttgctcctgccggt tccccgaagaggaagaaggaggttgcgagctgcgcgtgaagttctcccggagcgccgacgccccc gcctataagcagggccagaaccagctgtacaacgaactgaacctgggacggcgggaagagtacgat gtgctggacaagcggcgcggccgggaccccgaaatgggcgggaagcctagaagaaagaaccctc aggaaggcctgtataacgagctgcagaaggacaagatggccgaggcctactccgaaattgggatga agggagagcggcggaggggaaaggggcacgacggcctgtaccaaggactgtccaccgccaccaa ggacacatacgatgccctgcacatgcaggcccttcccccctcgc
1038	linker	(Gly-Gly-Gly-Ser)n, where n = 1-10
1039	linker	(Gly4 Ser)4
1040	linker	(Gly4 Ser)3
1041	linker	(Gly3Ser)
1042	linker	ASGGGGSGGRASGGGGS
1043	polyA	$[a]_{50\text{-}5000}$
1044	PD1 CAR (aa)	Pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdklaafpedrs qpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslraelrvterraevptahp spsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagt cgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapay kqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigm kgerrrgkghdglyqglstatkdtydalhmqalppr
1045	ICOS intracellular domain (aa)	TKKKYSSSVHDPNGEYMFMRAVNTAKKSRLTDVTL
1046	ICOS intracellular domain (na)	ACAAAAAAGAAGTATTCATCCAGTGTGCACGACCCTAACGGT GAATACATGTTCATGAGAGCAGTGAACACAGCCAAAAAATCC AGACTCACAGATGTGACCCTA
1047	ICOS TM domain (aa)	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD FWLPIGCAAFVVVCILGCILICWL
1048	ICOS TM domain (na)	ACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCCCACC ATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTGCCGG CCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACTT CGCCTGTGATTTCTGGTTACCCATAGGATGTGCAGCCTTTGTT GTAGTCTGCATTTTGGGATGCATACTTATTTGTTGGCTT

1049	CD28 intracellular domain (aa)	RSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS
1050	CD28 intracellular domain (na)	AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAAC ATGACTCCCCGCCGCCCCGGGCCCACCCGCAAGCATTACCAG CCCTATGCCCCACCACGCGACTTCGCAGCCTATCGCTCC

CAR Antigen Binding Domain

In one aspect, the portion of the CAR comprising the antigen binding domain comprises an antigen binding domain that targets a tumor antigen, e.g., a tumor antigen described herein. In some embodiments, the antigen binding domain binds to: CD19; CD123; CD22; CD30; CD171; CS-1; C-type lectin-like molecule-1, CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3; TNF receptor family member; B-cell maturation antigen (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2; Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21; vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3; transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6

complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1, melanoma antigen recognized by T cells 1; Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like, Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); or immunoglobulin lambda-like polypeptide 1 (IGLL1).

The antigen binding domain can be any domain that binds to an antigen, including but not limited to a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, and a functional fragment thereof, including but not limited to a single-domain antibody such as a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) of camelid derived nanobody, and to an alternative scaffold known in the art to function as antigen binding domain, such as a recombinant fibronectin domain, a T cell receptor (TCR), or a fragment there of, e.g., single chain TCR, and the like. In some instances, it is beneficial for the antigen binding domain to be derived from the same species in which the CAR will ultimately be used in. For

example, for use in humans, it may be beneficial for the antigen binding domain of the CAR to comprise human or humanized residues for the antigen binding domain of an antibody or antibody fragment.

CAR Transmembrane domain

With respect to the transmembrane domain, in various embodiments, a CAR can be designed to comprise a transmembrane domain that is attached to the extracellular domain of the CAR. A transmembrane domain can include one or more additional amino acids adjacent to the transmembrane region, e.g., one or more amino acid associated with the extracellular region of the protein from which the transmembrane was derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the extracellular region) and/or one or more additional amino acids associated with the intracellular region of the protein from which the transmembrane protein is derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the intracellular region). In one aspect, the transmembrane domain is one that is associated with one of the other domains of the CAR. In some instances, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins, e.g., to minimize interactions with other members of the receptor complex. In one aspect, the transmembrane domain is capable of homodimerization with another CAR on the cell surface of a CAR-expressing cell. In a different aspect, the amino acid sequence of the transmembrane domain may be modified or substituted so as to minimize interactions with the binding domains of the native binding partner present in the same CART.

The transmembrane domain may be derived either from a natural or from a recombinant source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. In one aspect the transmembrane domain is capable of signaling to the intracellular domain(s) whenever the CAR has bound to a target. A transmembrane domain of particular use in this invention may include at least the transmembrane region(s) of e.g., the alpha, beta or zeta chain of the T-cell receptor, CD28, CD27, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154. In some embodiments, a transmembrane domain may include at least the transmembrane region(s) of, e.g., KIR2DS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, IL2R beta, IL2R gamma, IL7R α, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKG2D, NKG2C.

In some instances, the transmembrane domain can be attached to the extracellular region of the CAR, e.g., the antigen binding domain of the CAR, via a hinge, e.g., a hinge from a human protein. For example, in one embodiment, the hinge can be a human Ig (immunoglobulin) hinge, e.g., an IgG4 hinge, or a CD8a hinge. In one embodiment, the hinge or spacer comprises (e.g., consists of) the amino acid sequence of SEQ ID NO: 1011. In one aspect, the transmembrane domain comprises (e.g., consists of) a transmembrane domain of SEQ ID NO: 1019.

In one aspect, the hinge or spacer comprises an IgG4 hinge. For example, in one embodiment, the hinge or spacer comprises a hinge of the amino acid sequence of SEQ ID NO: 1013. In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of SEQ ID NO: 1014.

In one aspect, the hinge or spacer comprises an IgD hinge. For example, in one embodiment, the hinge or spacer comprises a hinge of the amino acid sequence of SEQ ID NO: 1015. In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of SEQ ID NO: 1016.

In one aspect, the transmembrane domain may be recombinant, in which case it will comprise predominantly hydrophobic residues such as leucine and valine. In one aspect a triplet of phenylalanine, tryptophan and valine can be found at each end of a recombinant transmembrane domain.

Optionally, a short oligo- or polypeptide linker, between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the cytoplasmic region of the CAR. A glycine-serine doublet provides a particularly suitable linker. For example, in one aspect, the linker comprises the amino acid sequence of SEQ ID NO: 1017. In some embodiments, the linker is encoded by a nucleotide sequence of SEQ ID NO: 1018.

In one aspect, the hinge or spacer comprises a KIR2DS2 hinge.

Cytoplasmic domain

The cytoplasmic domain or region of the CAR includes an intracellular signaling domain. An intracellular signaling domain is generally responsible for activation of at least one of the normal effector functions of the immune cell in which the CAR has been introduced.

Examples of intracellular signaling domains for use in a CAR described herein include the cytoplasmic sequences of the T cell receptor (TCR) and co-receptors that act in concert to initiate signal transduction following antigen receptor engagement, as well as any derivative or variant of these sequences and any recombinant sequence that has the same functional capability.

It is known that signals generated through the TCR alone are insufficient for full activation of the T cell and that a secondary and/or costimulatory signal is also required. Thus, T cell activation can

be said to be mediated by two distinct classes of cytoplasmic signaling sequences: those that initiate antigen-dependent primary activation through the TCR (primary intracellular signaling domains) and those that act in an antigen-independent manner to provide a secondary or costimulatory signal (secondary cytoplasmic domain, e.g., a costimulatory domain).

A primary signaling domain regulates primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary intracellular signaling domains that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs.

Examples of ITAM containing primary intracellular signaling domains that are of particular use in the invention include those of TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta , CD3 epsilon, CD5, CD22, CD79a, CD79b, CD278 (also known as "ICOS"), FcεRI, DAP10, DAP12, and CD66d. In one embodiment, a CAR of the invention comprises an intracellular signaling domain, e.g., a primary signaling domain of CD3-zeta, e.g., a CD3-zeta sequence described herein.

In one embodiment, a primary signaling domain comprises a modified ITAM domain, e.g., a mutated ITAM domain which has altered (e.g., increased or decreased) activity as compared to the native ITAM domain. In one embodiment, a primary signaling domain comprises a modified ITAM-containing primary intracellular signaling domain, e.g., an optimized and/or truncated ITAM-containing primary intracellular signaling domain. In an embodiment, a primary signaling domain comprises one, two, three, four or more ITAM motifs.

Costimulatory Signaling Domain

The intracellular signalling domain of the CAR can comprise the CD3-zeta signaling domain by itself or it can be combined with any other desired intracellular signaling domain(s) useful in the context of a CAR of the invention. For example, the intracellular signaling domain of the CAR can comprise a CD3 zeta chain portion and a costimulatory signaling domain. The costimulatory signaling domain refers to a portion of the CAR comprising the intracellular domain of a costimulatory molecule. In one embodiment, the intracellular domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD28. In one aspect, the intracellular domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of ICOS.

A costimulatory molecule can be a cell surface molecule other than an antigen receptor or its ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that specifically binds with CD83, and the like. For example, CD27 costimulation has been demonstrated to enhance expansion, effector function, and survival of human CART cells in vitro and augments human

T cell persistence and antitumor activity in vivo (Song et al. Blood. 2012; 119(3):696-706). Further examples of such costimulatory molecules include CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp30, NKp44, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, NKG2D, NKG2C and PAG/Cbp.

The intracellular signaling sequences within the cytoplasmic portion of the CAR may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example, between 2 and 10 amino acids (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids) in length may form the linkage between intracellular signaling sequence. In one embodiment, a glycine-serine doublet can be used as a suitable linker. In one embodiment, a single amino acid, e.g., an alanine, a glycine, can be used as a suitable linker.

In one aspect, the intracellular signaling domain is designed to comprise two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains. In an embodiment, the two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains, are separated by a linker molecule, e.g., a linker molecule described herein. In one embodiment, the intracellular signaling domain comprises two costimulatory signaling domains. In some embodiments, the linker molecule is a glycine residue. In some embodiments, the linker is an alanine residue.

In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD28. In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of 4-1BB. In one aspect, the signaling domain of 4-1BB is a signaling domain of SEQ ID NO: 1022. In one aspect, the signaling domain of CD3-zeta is a signaling domain of SEQ ID NO: 1027.

In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD27. In one aspect, the signaling domain of CD27 comprises an amino acid sequence of SEQ ID NO: 1025. In one aspect, the signalling domain of CD27 is encoded by a nucleic acid sequence of SEQ ID NO: 1026.

In one aspect, the CAR-expressing cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target or a different target (e.g., a target other than a cancer associated antigen described herein or a different cancer associated antigen described herein, *e.g.*, CD19, CD33, CLL-1, CD34, FLT3, or folate receptor beta). In one embodiment, the second CAR includes an antigen binding domain to a target expressed

the same cancer cell type as the cancer associated antigen. In one embodiment, the CAR-expressing cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. While not wishing to be bound by theory, placement of a costimulatory signaling domain, *e.g.*, 4-1BB, CD28, ICOS, CD27 or OX-40, onto the first CAR, and the primary signaling domain, *e.g.*, CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In one embodiment, the CAR expressing cell comprises a first cancer associated antigen CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a costimulatory domain and a second CAR that targets a different target antigen (e.g., an antigen expressed on that same cancer cell type as the first target antigen) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing cell comprises a first CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a primary signaling domain and a second CAR that targets an antigen other than the first target antigen (e.g., an antigen expressed on the same cancer cell type as the first target antigen) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In another aspect, the disclosure features a population of CAR-expressing cells, e.g., CART cells. In some embodiments, the population of CAR-expressing cells comprises a mixture of cells expressing different CARs. For example, in one embodiment, the population of CART cells can include a first cell expressing a CAR having an antigen binding domain to a cancer associated antigen described herein, and a second cell expressing a CAR having a different antigen binding domain, e.g., an antigen binding domain to a different a cancer associated antigen described herein, e.g., an antigen binding domain to a cancer associated antigen described herein that differs from the cancer associate antigen bound by the antigen binding domain of the CAR expressed by the first cell. As another example, the population of CAR-expressing cells can include a first cell expressing a CAR that includes an antigen binding domain to a cancer associated antigen described herein, and a second cell expressing a CAR that includes an antigen binding domain to a target other than a cancer associate antigen as described herein. In one embodiment, the population of CAR-expressing cells includes, e.g., a first cell expressing a CAR that includes a primary intracellular signaling domain, and a second cell expressing a CAR that includes a secondary signaling domain.

In another aspect, the disclosure features a population of cells wherein at least one cell in the population expresses a CAR having an antigen binding domain to a cancer associated antigen described herein, and a second cell expressing another agent, e.g., an agent which enhances the activity of a CAR-expressing cell. For example, in one embodiment, the agent can be an agent which inhibits an inhibitory

molecule. Inhibitory molecules, e.g., PD-1, can, in some embodiments, decrease the ability of a CAR-expressing cell to mount an immune effector response. Examples of inhibitory molecules include PD-1, PD-L1, CTLA4, TIM3, CEACAM (CEACAM-1, CEACAM-3, and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF (e.g., TGFbeta). In one embodiment, the agent which inhibits an inhibitory molecule comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD-1, PD-L1, CTLA4, TIM3, CEACAM (CEACAM-1, CEACAM-3, and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta, or a fragment of any of these, and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27, OX40 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD-1 or a fragment thereof, and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28 signaling domain described herein and/or a CD3 zeta signaling domain described herein).

BCMA CAR

In one aspect, the CAR disclosed herein binds to BCMA. Exemplary BCMA CARs can include sequences disclosed in Table 1 or 16 of WO2016/014565, incorporated herein by reference. The BCMA CAR construct can include an optional leader sequence; an optional hinge domain, e.g., a CD8 hinge domain; a transmembrane domain, e.g., a CD8 transmembrane domain; an intracellular domain, e.g., a 4-1BB intracellular domain; and a functional signaling domain, e.g., a CD3 zeta domain. In certain embodiments, the domains are contiguous and in the same reading frame to form a single fusion protein. In other embodiments, the domain are in separate polypeptides, e.g., as in an RCAR molecule as described herein.

The sequences of exemplary BCMA CAR molecules or fragments thereof are disclosed in Tables 2-5. In certain embodiments, the full length BCMA CAR molecule includes one or more CDRs, VH, VL, scFv, or full-length sequences of, BCMA-1, BCMA-2, BCMA-3, BCMA-4, BCMA-5, BCMA-6, BCMA-7, BCMA-8, BCMA-9, BCMA-10, BCMA-11, BCMA-12, BCMA-13, BCMA-14, BCMA-15, 149362, 149363, 149364, 149365, 149366, 149367, 149368, 149369, BCMA_EBB-C1978-A4, BCMA_EBB-C1978-G1, BCMA_EBB-C1979-C1, BCMA_EBB-C1978-C7, BCMA_EBB-C1978-D10, BCMA_EBB-C1979-C12, BCMA_EBB-C1980-G4, BCMA_EBB-C1980-D2, BCMA_EBB-C1978-A10, BCMA_EBB-C1978-D4, BCMA_EBB-C1980-A2, BCMA_EBB-C1981-C3,

BCMA_EBB-C1978-G4, A7D12.2, C11D5.3, C12A3.2, or C13F12.1, as disclosed in Tables 2-5, or a sequence substantially (e.g., 95-99%) identical thereto.

Additional exemplary BCMA-targeting sequences that can be used in the anti-BCMA CAR constructs are disclosed in WO 2017/021450, WO 2017/011804, WO 2017/025038, WO 2016/090327, WO 2016/130598, WO 2016/210293, WO 2016/090320, WO 2016/014789, WO 2016/094304, WO 2016/154055, WO 2015/166073, WO 2015/188119, WO 2015/158671, US 9,243,058, US 8,920,776, US 9,273,141, US 7,083,785, US 9,034,324, US 2007/0049735, US 2015/0284467, US 2015/0051266, US 2015/0344844, US 2016/0131655, US 2016/0297884, US 2016/0297885, US 2017/0051308, US 2017/0051252, US 2017/0051252, WO 2016/020332, WO 2016/087531, WO 2016/079177, WO 2015/172800, WO 2017/008169, US 9,340,621, US 2013/0273055, US 2016/0176973, US 2015/0368351, US 2017/0051068, US 2016/0368988, and US 2015/0232557, herein incorporated by reference in their entirety. In some embodiments, additional exemplary BCMA CAR constructs are generated using the VH and VL sequences from PCT Publication WO2012/0163805 (the contents of which are hereby incorporated by reference in its entirety).

Table 2. Amino Acid and Nucleic Acid Sequences of exemplary anti-BCMA scFv domains and BCMA CAR molecules. The amino acid sequences variable heavy chain and variable light chain sequences for each scFv is also provided.

Name/ Description	SEQ ID NO:	Sequence
139109		
139109- aa ScFv domain	49	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIQLTQSPSSLSASV GDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYSTPYTFGQGTKVEIK
139109- nt ScFv domain	64	GAAGTGCAATTGGTGGAATCAGGGGGAGGACTTGTGCAGCCTGGAGGAT CGCTGAGACTGTCATGTGCCGTGTCCGGCTTTGCCCTGTCCAACCACGG GATGTCCTGGGTCCGCCGCGCGCCTGGAAAGGGCCTCGAATGGGTGTCG GGTATTGTGTACAGCGGTAGCACCTACTATGCCGCATCCGTGAAGGGGA GATTCACCATCAGCCGGGACAACTCCAGGAACACTCTGTACCTCCAAAT GAATTCGCTGAGGCCAGAGGACACTGCCATCTACTACTGCTCCGCGCAT GGCGGAGAGTCCGACGTCTGGGGACAGGGGACCACCGTGACCGTGTCTA GCGCGTCCGGCGGAGGCGGCAGCGGGGGTCGGGCATCAGGGGGCGGCGG ATCGGACATCCAGCTCACCCAGTCCCCGAGCTCGCTGTCCGCCTCCGTG GGAGATCGGGTCACCATCACGTGCCGCGCCAGCCAGTCGATTTCCTCCT ACCTGAACTGGTACCAACAGAAGCCCGGAAAAGCCCCGAAGCTTCTCAT CTACGCCGCCTCGAGCCTGCAGTCAGGAGTGCCCTCACGGTTCTCCGGC TCCGGTTCCGGTACTGATTTCACCCTGACCATTTCCTCCCTGCAACCGG AGGACTTCGCTACTTACTACTGCCAGCAGTCGTACTCCACCCCCTACAC TTTCGGACAAGGCACCAAGGTCGAAATCAAG

139109- aa VH	79	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139109- aa VL	94	DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPYTF GQGTKVEIK
139109- aa Full CAR	109	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSDIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSY STPYTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLY NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139109- nt Full CAR	124	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGGTGGAATCAGGGGGAGGACTTGT GCAGCCTGGAGGATCGCTGAGACTGTCATGTGCCGTGTCCGGCTTTGCC CTGTCCAACCACGGGATGTCCTGGGTCCGCCGCGCGCCTGGAAAGGGCC TCGAATGGGTGTCGGGTATTGTGTACAGCGGTAGCACCTACTATGCCGC ATCCGTGAAGGGGAGATTCACCATCAGCCGGGACAACTCCAGGAACACT CTGTACCTCCAAATGAATTCGCTGAGGCCAGAGGACACTGCCATCTACT ACTGCTCCGCGCATGGCGGAGAGTCCGACGTCTGGGGACAGGGGACCAC CGTGACCGTGTCTAGCGCGTCCGGCGGAGGCGGCAGCGGGGGTCGGGCA TCAGGGGGCGGCGGATCGGACATCCAGCTCACCCAGTCCCCGAGCTCGC TGTCCGCCTCCGTGGGAGATCGGGTCACCATCACGTGCCGCGCCAGCCA GTCGATTTCCTCCTACCTGAACTGGTACCAACAGAAGCCCGGAAAAGCC CCGAAGCTTCTCATCTACGCCGCCTCGAGCCTGCAGTCAGGAGTGCCCT CACGGTTCTCCGGCTCCGGTTCCGGTACTGATTTCACCCTGACCATTTC CTCCCTGCAACCGGAGGACTTCGCTACTTACTACTGCCAGCAGTCGTAC TCCACCCCCTACACTTTCGGACAAGGCACCAAGGTCGAAATCAAGACCA CTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCA GCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCC GTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCC CTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCT TTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCC GGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAG CCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTAC AACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGC GGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCC CCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACG ACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGC TCTTCACATGCAGGCCCTGCCGCCTCGG
Full CAR without leader sequence	392	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIQLTQSPSSLSASV GDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYSTPYTFGQGTKVEIKTTTPAP RPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGT

		CGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE EEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRD PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQ GLSTATKDTYDALHMQALPPR
Full CAR without linker, without leader sequence	393	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSDIQLTQSPSSLSASVGDRVTITCRASQSISSY LNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQSYSTPYTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRG RKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLY NELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
139103		
139103- aa ScFv domain	39	QVQLVESGGGLVQPGRSLRLSCAASGFTFSNYAMSWVRQAPGKGLGWVS GISRSGENTYYADSVKGRFTISRDNSKNTLYLQMNSLRDEDTAVYYCAR SPAHYYGGMDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIVLTQSPGT LSLSPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLIYGASRRATGI PDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSWTFGQGTKLEI K
139103- nt ScFv domain	54	CAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGCAACCCGGAAGAT CGCTTAGACTGTCGTGTGCCGCCAGCGGGTTCACTTTCTCGAACTACGC GATGTCCTGGGTCCGCCAGGCACCCGGAAAGGGACTCGGTTGGGTGTCC GGCATTTCCCGGTCCGGCGAAAATACCTACTACGCCGACTCCGTGAAGG GCCGCTTCACCATCTCAAGGGACAACAGCAAAAACACCCTGTACTTGCA AATGAACTCCCTGCGGGATGAAGATACAGCCGTGTACTATTGCGCCCGG TCGCCTGCCCATTACTACGGCGGAATGGACGTCTGGGGACAGGGAACCA CTGTGACTGTCAGCAGCGCGTCGGGTGGCGGCGGCTCAGGGGGTCGGGC CTCCGGGGGGGGAGGGTCCGACATCGTGCTGACCCAGTCCCCGGGAACC CTGAGCCTGAGCCCGGGAGAGCGCGCGACCCTGTCATGCCGGGCATCCC AGAGCATTAGCTCCTCCTTTCTCGCCTGGTATCAGCAGAAGCCCGGACA GGCCCCGAGGCTGCTGATCTACGGCGCTAGCAGAAGGGCTACCGGAATC CCAGACCGGTTCTCCGGCTCCGGTTCCGGGACCGATTTCACCCTTACTA TCTCGCGCCTGGAACCTGAGGACTCCGCCGTCTACTACTGCCAGCAGTA CCACTCATCCCCGTCGTGGACGTTCGGACAGGGCACCAAGCTGGAGATT AAG
139103- aa VH	69	QVQLVESGGGLVQPGRSLRLSCAASGFTFSNYAMSWVRQAPGKGLGWVS GISRSGENTYYADSVKGRFTISRDNSKNTLYLQMNSLRDEDTAVYYCAR SPAHYYGGMDVWGQGTTVTVSS
139103- aa VL	84	DIVLTQSPGTLSLSPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLI YGASRRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSW TFGQGTKLEIK
139103- aa Full CAR	99	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGRSLRLSCAASGFT FSNYAMSWVRQAPGKGLGWVSGISRSGENTYYADSVKGRFTISRDNSKN TLYLQMNSLRDEDTAVYYCARSPAHYYGGMDVWGQGTTVTVSSASGGGG SGGRASGGGGSDIVLTQSPGTLSLSPGERATLSCRASQSISSSFLAWYQ QKPGQAPRLLIYGASRRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVY YCQQYHSSPSWTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK

		QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139103- nt Full CAR	114	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGT GCAACCCGGAAGATCGCTTAGACTGTCGTGTGCCGCCAGCGGGTTCACT TTCTCGAACTACGCGATGTCCTGGGTCCGCCAGGCACCCGGAAAGGGAC TCGGTTGGGTGTCCGGCATTTCCCGGTCCGGCGAAAATACCTACTACGC CGACTCCGTGAAGGGCCGCTTCACCATCTCAAGGGACAACAGCAAAAAC ACCCTGTACTTGCAAATGAACTCCCTGCGGGATGAAGATACAGCCGTGT ACTATTGCGCCCGGTCGCCTGCCCATTACTACGGCGGAATGGACGTCTG GGGACAGGGAACCACTGTGACTGTCAGCAGCGCGTCGGGTGGCGGCGGC TCAGGGGGTCGGGCCTCCGGGGGGGGAGGGTCCGACATCGTGCTGACCC AGTCCCCGGGAACCCTGAGCCTGAGCCCGGGAGAGCGCGCGACCCTGTC ATGCCGGGCATCCCAGAGCATTAGCTCCTCCTTTCTCGCCTGGTATCAG CAGAAGCCCGGACAGGCCCCGAGGCTGCTGATCTACGGCGCTAGCAGAA GGGCTACCGGAATCCCAGACCGGTTCTCCGGCTCCGGTTCCGGGACCGA TTTCACCCTTACTATCTCGCGCCTGGAACCTGAGGACTCCGCCGTCTAC TACTGCCAGCAGTACCACTCATCCCCGTCGTGGACGTTCGGACAGGGCA CCAAGCTGGAGATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139105		
139105- aa ScFv domain	40	QVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVS GISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCSV HSFLAYWGQGTLVTVSSASGGGGSGGRASGGGGSDIVMTQTPLSLPVTP GEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPYTFGQGTKVEIK
139105- nt ScFv domain	55	CAAGTGCAACTCGTCGAATCCGGTGGAGGTCTGGTCCAACCTGGTAGAA GCCTGAGACTGTCGTGTGCGGCCAGCGGATTCACCTTTGATGACTATGC TATGCACTGGGTGCGGCAGGCCCCAGGAAAGGGCCTGGAATGGGTGTCG GGAATTAGCTGGAACTCCGGGTCCATTGGCTACGCCGACTCCGTGAAGG GCCGCTTCACCATCTCCCGCGACAACGCAAAGAACTCCCTGTACTTGCA AATGAACTCGCTCAGGGCTGAGGATACCGCGCTGTACTACTGCTCCGTG CATTCCTTCCTGGCCTACTGGGGACAGGGAACTCTGGTCACCGTGTCGA GCGCCTCCGGCGGCGGGGGCTCGGGTGGACGGGCCTCGGGCGGAGGGGG GTCCGACATCGTGATGACCCAGACCCCGCTGAGCTTGCCCGTGACTCCC GGAGAGCCTGCATCCATCTCCTGCCGGTCATCCCAGTCCCTTCTCCACT CCAACGGATACAACTACCTCGACTGGTACCTCCAGAAGCCGGGACAGAG CCCTCAGCTTCTGATCTACCTGGGGTCAAATAGAGCCTCAGGAGTGCCG GATCGGTTCAGCGGATCTGGTTCGGGAACTGATTTCACTCTGAAGATTT

		CCCGCGTGGAAGCCGAGGACGTGGGCGTCTACTACTGTATGCAGGCGCT GCAGACCCCCTATACCTTCGGCCAAGGGACGAAAGTGGAGATCAAG
139105- aa VH	70	QVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVS GISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCSV HSFLAYWGQGTLVTVSS
139105- aa VL	85	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSP QLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQ TPYTFGQGTKVEIK
139105- aa Full CAR	100	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGRSLRLSCAASGFT FDDYAMHWVRQAPGKGLEWVSGISWNSGSIGYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTALYYCSVHSFLAYWGQGTLVTVSSASGGGGSGGRA SGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQ KPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYY CMQALQTPYTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRP AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLY IFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQG QNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKD KMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139105- nt Full CAR	115	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAACTCGTCGAATCCGGTGGAGGTCTGGT CCAACCTGGTAGAAGCCTGAGACTGTCGTGTGCGGCCAGCGGATTCACC TTTGATGACTATGCTATGCACTGGGTGCGGCAGGCCCCAGGAAAGGGCC TGGAATGGGTGTCGGGAATTAGCTGGAACTCCGGGTCCATTGGCTACGC CGACTCCGTGAAGGGCCGCTTCACCATCTCCCGCGACAACGCAAAGAAC TCCCTGTACTTGCAAATGAACTCGCTCAGGGCTGAGGATACCGCGCTGT ACTACTGCTCCGTGCATTCCTTCCTGGCCTACTGGGGACAGGGAACTCT GGTCACCGTGTCGAGCGCCTCCGGCGGCGGGGGCTCGGGTGGACGGGCC TCGGGCGGAGGGGGGTCCGACATCGTGATGACCCAGACCCCGCTGAGCT TGCCCGTGACTCCCGGAGAGCCTGCATCCATCTCCTGCCGGTCATCCCA GTCCCTTCTCCACTCCAACGGATACAACTACCTCGACTGGTACCTCCAG AAGCCGGGACAGAGCCCTCAGCTTCTGATCTACCTGGGGTCAAATAGAG CCTCAGGAGTGCCGGATCGGTTCAGCGGATCTGGTTCGGGAACTGATTT CACTCTGAAGATTTCCCGCGTGGAAGCCGAGGACGTGGGCGTCTACTAC TGTATGCAGGCGCTGCAGACCCCCTATACCTTCGGCCAAGGGACGAAAG TGGAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCC TACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATA TCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTC ACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGG ACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACT GCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGG CAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCC GCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGAT AAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAA GAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAA GGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139111		
139111- aa ScFv domain	41	EVQLLESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIVMTQTPLSLSVTP

		GQPASISCKSSQSLLRNDGKTPLYWYLQKAGQPPQLLIYEVSNRFSGVP DRFSGSGSGTDFTLKISRVEAEDVGAYYCMQNIQFPSFGGGTKLEIK
139111- nt ScFv domain	56	GAAGTGCAATTGTTGGAATCTGGAGGAGGACTTGTGCAGCCTGGAGGAT CACTGAGACTTTCGTGTGCGGTGTCAGGCTTCGCCCTGAGCAACCACGG CATGAGCTGGGTGCGGAGAGCCCCGGGGAAGGGTCTGGAATGGGTGTCC GGGATCGTCTACTCCGGTTCAACTTACTACGCCGCAAGCGTGAAGGGTC GCTTCACCATTTCCCGCGATAACTCCCGGAACACCCTGTACCTCCAAAT GAACTCCCTGCGGCCCGAGGACACCGCCATCTACTACTGTTCCGCGCAT GGAGGAGAGTCCGATGTCTGGGGACAGGGCACTACCGTGACCGTGTCGA GCGCCTCGGGGGGGAGGAGGCTCCGGCGGTCGCGCCTCCGGGGGGGGTGG CAGCGACATTGTGATGACGCAGACTCCACTCTCGCTGTCCGTGACCCCG GGACAGCCCGCGTCCATCTCGTGCAAGAGCTCCCAGAGCCTGCTGAGGA ACGACGGAAAGACTCCTCTGTATTGGTACCTCCAGAAGGCTGGACAGCC CCCGCAACTGCTCATCTACGAAGTGTCAAATCGCTTCTCCGGGGTGCCG GATCGGTTTTCCGGCTCGGGATCGGGCACCGACTTCACCCTGAAAATCT CCAGGGTCGAGGCCGAGGACGTGGGAGCCTACTACTGCATGCAAAACAT CCAGTTCCCTTCCTTCGGCGGCGGCACAAAGCTGGAGATTAAG
139111- aa VH	71	EVQLLESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139111- aa VL	86	DIVMTQTPLSLSVTPGQPASISCKSSQSLLRNDGKTPLYWYLQKAGQPP QLLIYEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGAYYCMQNIQ FPSFGGGTKLEIK
139111- aa Full CAR	101	MALPVTALLLPLALLLHAARPEVQLLESGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSDIVMTQTPLSLSVTPGQPASISCKSSQSLLRNDGKTPLYWYLQ KAGQPPQLLIYEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGAYY CMQNIQFPSFGGGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPA AGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYI FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQ NQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139111- nt Full CAR	116	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGTTGGAATCTGGAGGAGGACTTGT GCAGCCTGGAGGATCACTGAGACTTTCGTGTGCGGTGTCAGGCTTCGCC CTGAGCAACCACGGCATGAGCTGGGTGCGGAGAGCCCCGGGGAAGGGTC TGGAATGGGTGTCCGGGATCGTCTACTCCGGTTCAACTTACTACGCCGC AAGCGTGAAGGGTCGCTTCACCATTTCCCGCGATAACTCCCGGAACACC CTGTACCTCCAAATGAACTCCCTGCGGCCCGAGGACACCGCCATCTACT ACTGTTCCGCGCATGGAGGAGAGTCCGATGTCTGGGGACAGGGCACTAC CGTGACCGTGTCGAGCGCCTCGGGGGGGAGGAGGCTCCGGCGGTCGCGCC TCCGGGGGGGGTGGCAGCGACATTGTGATGACGCAGACTCCACTCTCGC TGTCCGTGACCCCGGGACAGCCCGCGTCCATCTCGTGCAAGAGCTCCCA GAGCCTGCTGAGGAACGACGGAAAGACTCCTCTGTATTGGTACCTCCAG AAGGCTGGACAGCCCCCGCAACTGCTCATCTACGAAGTGTCAAATCGCT TCTCCGGGGTGCCGGATCGGTTTTCCGGCTCGGGATCGGGCACCGACTT CACCCTGAAAATCTCCAGGGTCGAGGCCGAGGACGTGGGAGCCTACTAC TGCATGCAAAACATCCAGTTCCCTTCCTTCGGCGGCGGCACAAAGCTGG AGATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTAC CATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCA GCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCT

		ACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACT CGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATC TTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACG GCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCG CGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAG AACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACG TGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCG CAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAG ATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAG GCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGA CACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139100		
139100- aa ScFv domain	42	QVQLVQSGAEVRKTGASVKVSCKASGYIFDNFGINWVRQAPGQGLEWMG WINPKNNNTNYAQKFQGRVTITADESTNTAYMEVSSLRSEDTAVYYCAR GPYYYQSYMDVWGQGTMVTVSSASGGGGSGGRASGGGGSDIVMTQTPLS LPVTPGEPASISCRSSQSLLHSNGYNYLNWYLQKPGQSPQLLIYLGSKR ASGVPDRFSGSGSGTDFTLHITRVGAEDVGVYYCMQALQTPYTFGQGTK LEIK
139100- nt ScFv domain	57	CAAGTCCAACTCGTCCAGTCCGGCGCAGAAGTCAGAAAAACCGGTGCTA GCGTGAAAGTGTCCTGCAAGGCCTCCGGCTACATTTTCGATAACTTCGG AATCAACTGGGTCAGACAGGCCCCGGGCCAGGGGCTGGAATGGATGGGA TGGATCAACCCCAAGAACAACAACACCAACTACGCACAGAAGTTCCAGG GCCGCGTGACTATCACCGCCGATGAATCGACCAATACCGCCTACATGGA GGTGTCCTCCCTGCGGTCGGAGGACACTGCCGTGTATTACTGCGCGAGG GGCCCATACTACTACCAAAGCTACATGGACGTCTGGGGACAGGGAACCA TGGTGACCGTGTCATCCGCCTCCGGTGGTGGAGGCTCCGGGGGGCGGGC TTCAGGAGGCGGAGGAAGCGATATTGTGATGACCCAGACTCCGCTTAGC CTGCCCGTGACTCCTGGAGAACCGGCCTCCATTTCCTGCCGGTCCTCGC AATCACTCCTGCATTCCAACGGTTACAACTACCTGAATTGGTACCTCCA GAAGCCTGGCCAGTCGCCCCAGTTGCTGATCTATCTGGGCTCGAAGCGC GCCTCCGGGGTGCCTGACCGGTTTAGCGGATCTGGGAGCGGCACGGACT TCACTCTCCACATCACCCGCGTGGGAGCGGAGGACGTGGGAGTGTACTA CTGTATGCAGGCGCTGCAGACTCCGTACACATTCGGACAGGGCACCAAG CTGGAGATCAAG
139100- aa VH	72	QVQLVQSGAEVRKTGASVKVSCKASGYIFDNFGINWVRQAPGQGLEWMG WINPKNNNTNYAQKFQGRVTITADESTNTAYMEVSSLRSEDTAVYYCAR GPYYYQSYMDVWGQGTMVTVSS
139100- aa VL	87	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLNWYLQKPGQSP QLLIYLGSKRASGVPDRFSGSGSGTDFTLHITRVGAEDVGVYYCMQALQ TPYTFGQGTKLEIK
139100- aa Full CAR	102	MALPVTALLLPLALLLHAARPQVQLVQSGAEVRKTGASVKVSCKASGYI FDNFGINWVRQAPGQGLEWMGWINPKNNNTNYAQKFQGRVTITADESTN TAYMEVSSLRSEDTAVYYCARGPYYYQSYMDVWGQGTMVTVSSASGGGG SGGRASGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYL NWYLQKPGQSPQLLIYLGSKRASGVPDRFSGSGSGTDFTLHITRVGAED VGVYYCMQALQTPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRP EACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAP AYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN ELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR

139100- nt Full CAR	117	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTCCAACTCGTCCAGTCCGGCGCAGAAGTCAG AAAAACCGGTGCTAGCGTGAAAGTGTCCTGCAAGGCCTCCGGCTACATT TTCGATAACTTCGGAATCAACTGGGTCAGACAGGCCCCGGGCCAGGGGC TGGAATGGATGGGATGGATCAACCCCAAGAACAACAACACCAACTACGC ACAGAAGTTCCAGGGCCGCGTGACTATCACCGCCGATGAATCGACCAAT ACCGCCTACATGGAGGTGTCCTCCCTGCGGTCGGAGGACACTGCCGTGT ATTACTGCGCGAGGGGCCCATACTACTACCAAAGCTACATGGACGTCTG GGGACAGGGAACCATGGTGACCGTGTCATCCGCCTCCGGTGGTGGAGGC TCCGGGGGGCGGGCTTCAGGAGGCGGAGGAAGCGATATTGTGATGACCC AGACTCCGCTTAGCCTGCCCGTGACTCCTGGAGAACCGGCCTCCATTTC CTGCCGGTCCTCGCAATCACTCCTGCATTCCAACGGTTACAACTACCTG AATTGGTACCTCCAGAAGCCTGGCCAGTCGCCCCAGTTGCTGATCTATC TGGGCTCGAAGCGCGCCTCCGGGGTGCCTGACCGGTTTAGCGGATCTGG GAGCGGCACGGACTTCACTCTCCACATCACCCGCGTGGGAGCGGAGGAC GTGGGAGTGTACTACTGTATGCAGGCGCTGCAGACTCCGTACACATTCG GACAGGGCACCAAGCTGGAGATCAAGACCACTACCCCAGCACCGAGGCC ACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCG GAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTG ACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGG GGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGG AAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGA CTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGA AGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCA GCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTC GGAGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGA AATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAAC GAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGA AAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACT CAGCACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTG CCGCCTCGG
139101		
139101- aa ScFv domain	43	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSDAMTWVRQAPGKGLEWVS VISGSGGTTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK LDSSGYYYARGPRYWGQGTLVTVSSASGGGGSGGRASGGGGSDIQLTQS PSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYGASTLAS GVPARFSGSGSGTHFTLTINSLQSEDSATYYCQQSYKRASFGQGTKVEI K
139101- nt ScFv domain	58	CAAGTGCAACTTCAAGAATCAGGCGGAGGACTCGTGCAGCCCGGAGGAT CATTGCGGCTCTCGTGCGCCGCCTCGGGCTTCACCTTCTCGAGCGACGC CATGACCTGGGTCCGCCAGGCCCCGGGGAAGGGGCTGGAATGGGTGTCT GTGATTTCCGGCTCCGGGGGAACTACGTACTACGCCGATTCCGTGAAAG GTCGCTTCACTATCTCCCGGGACAACAGCAAGAACACCCTTTATCTGCA AATGAATTCCCTCCGCGCCGAGGACACCGCCGTGTACTACTGCGCCAAG CTGGACTCCTCGGGCTACTACTATGCCCGGGGTCCGAGATACTGGGGAC AGGGAACCCTCGTGACCGTGTCCTCCGCGTCCGGCGGAGGAGGGTCGGG AGGGCGGGCCTCCGGCGGCGGCGGTTCGGACATCCAGCTGACCCAGTCC CCATCCTCACTGAGCGCAAGCGTGGGCGACAGAGTCACCATTACATGCA GGGCGTCCCAGAGCATCAGCTCCTACCTGAACTGGTACCAACAGAAGCC TGGAAAGGCTCCTAAGCTGTTGATCTACGGGGCTTCGACCCTGGCATCC GGGGTGCCCGCGAGGTTTAGCGGAAGCGGTAGCGGCACTCACTTCACTC TGACCATTAACAGCCTCCAGTCCGAGGATTCAGCCACTTACTACTGTCA

		GCAGTCCTACAAGCGGGCCAGCTTCGGACAGGGCACTAAGGTCGAGATC AAG
139101- aa VH	73	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSDAMTWVRQAPGKGLEWVS VISGSGGTTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK LDSSGYYYARGPRYWGQGTLVTVSS
139101- aa VL	88	DIQLTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY GASTLASGVPARFSGSGSGTHFTLTINSLQSEDSATYYCQQSYKRASFG QGTKVEIK
139101- aa Full CAR	103	MALPVTALLLPLALLLHAARPQVQLQESGGGLVQPGGSLRLSCAASGFT FSSDAMTWVRQAPGKGLEWVSVISGSGGTTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCAKLDSSGYYYARGPRYWGQGTLVTVSSASG GGGSGGRASGGGGSDIQLTQSPSSLSASVGDRVTITCRASQSISSYLNW YQQKPGKAPKLLIYGASTLASGVPARFSGSGSGTHFTLTINSLQSEDSA TYYCQQSYKRASFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139101- nt Full CAR	118	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAACTTCAAGAATCAGGCGGAGGACTCGT GCAGCCCGGAGGATCATTGCGGCTCTCGTGCGCCGCCTCGGGCTTCACC TTCTCGAGCGACGCCATGACCTGGGTCCGCCAGGCCCCGGGGAAGGGGC TGGAATGGGTGTCTGTGATTTCCGGCTCCGGGGGAACTACGTACTACGC CGATTCCGTGAAAGGTCGCTTCACTATCTCCCGGGACAACAGCAAGAAC ACCCTTTATCTGCAAATGAATTCCCTCCGCGCCGAGGACACCGCCGTGT ACTACTGCGCCAAGCTGGACTCCTCGGGCTACTACTATGCCCGGGGTCC GAGATACTGGGGACAGGGAACCCTCGTGACCGTGTCCTCCGCGTCCGGC GGAGGAGGGTCGGGAGGGCGGGCCTCCGGCGGCGGCGGTTCGGACATCC AGCTGACCCAGTCCCCATCCTCACTGAGCGCAAGCGTGGGCGACAGAGT CACCATTACATGCAGGGCGTCCCAGAGCATCAGCTCCTACCTGAACTGG TACCAACAGAAGCCTGGAAAGGCTCCTAAGCTGTTGATCTACGGGGCTT CGACCCTGGCATCCGGGGTGCCCGCGAGGTTTAGCGGAAGCGGTAGCGG CACTCACTTCACTCTGACCATTAACAGCCTCCAGTCCGAGGATTCAGCC ACTTACTACTGTCAGCAGTCCTACAAGCGGGCCAGCTTCGGACAGGGCA CTAAGGTCGAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139102		
139102- aa ScFv domain	44	QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYGITWVRQAPGQGLEWMG WISAYNGNTNYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR GPYYYYMDVWGKGTMVTVSSASGGGGSGGRASGGGGSEIVMTQSPLSLP

		VTPGEPASISCRSSQSLLYSNGYNYVDWYLQKPGQSPQLLIYLGSNRAS GVPDRFSGSGSGTDFKLQISRVEAEDVGIYYCMQGRQFPYSFGQGTKVE IK
139102- nt ScFv domain	59	CAAGTCCAACTGGTCCAGAGCGGTGCAGAAGTGAAGAAGCCCGGAGCGA GCGTGAAAGTGTCCTGCAAGGCTTCCGGGTACACCTTCTCCAACTACGG CATCACTTGGGTGCGCCAGGCCCCGGGACAGGGCCTGGAATGGATGGGG TGGATTTCCGCGTACAACGGCAATACGAACTACGCTCAGAAGTTCCAGG GTAGAGTGACCATGACTAGGAACACCTCCATTTCCACCGCCTACATGGA ACTGTCCTCCCTGCGGAGCGAGGACACCGCCGTGTACTATTGCGCCCGG GGACCATACTACTACTACATGGATGTCTGGGGGAAGGGGACTATGGTCA CCGTGTCATCCGCCTCGGGAGGCGGCGGATCAGGAGGACGCGCCTCTGG TGGTGGAGGATCGGAGATCGTGATGACCCAGAGCCCTCTCTCCTTGCCC GTGACTCCTGGGGAGCCCGCATCCATTTCATGCCGGAGCTCCCAGTCAC TTCTCTACTCCAACGGCTATAACTACGTGGATTGGTACCTCCAAAAGCC GGGCCAGAGCCCGCAGCTGCTGATCTACCTGGGCTCGAACAGGGCCAGC GGAGTGCCTGACCGGTTCTCCGGGTCGGGAAGCGGGACCGACTTCAAGC TGCAAATCTCGAGAGTGGAGGCCGAGGACGTGGGAATCTACTACTGTAT GCAGGGCCGCCAGTTTCCGTACTCGTTCGGACAGGGCACCAAAGTGGAA ATCAAG
139102- aa VH	74	QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYGITWVRQAPGQGLEWMG WISAYNGNTNYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR GPYYYYMDVWGKGTMVTVSS
139102- aa VL	89	EIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYVDWYLQKPGQSP QLLIYLGSNRASGVPDRFSGSGSGTDFKLQISRVEAEDVGIYYCMQGRQ FPYSFGQGTKVEIK
139102- aa Full CAR	104	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVSCKASGYT FSNYGITWVRQAPGQGLEWMGWISAYNGNTNYAQKFQGRVTMTRNTSIS TAYMELSSLRSEDTAVYYCARGPYYYYMDVWGKGTMVTVSSASGGGGSG GRASGGGGSEIVMTQSPLSLPVTPGEPASISCRSSQSLLYSNGYNYVDW YLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFKLQISRVEAEDVG IYYCMQGRQFPYSFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEA CRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKK LLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNEL QKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPP R
139102- nt Full CAR	119	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTCCAACTGGTCCAGAGCGGTGCAGAAGTGAA GAAGCCCGGAGCGAGCGTGAAAGTGTCCTGCAAGGCTTCCGGGTACACC TTCTCCAACTACGGCATCACTTGGGTGCGCCAGGCCCCGGGACAGGGCC TGGAATGGATGGGGTGGATTTCCGCGTACAACGGCAATACGAACTACGC TCAGAAGTTCCAGGGTAGAGTGACCATGACTAGGAACACCTCCATTTCC ACCGCCTACATGGAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGTGT ACTATTGCGCCCGGGGACCATACTACTACTACATGGATGTCTGGGGGAA GGGGACTATGGTCACCGTGTCATCCGCCTCGGGAGGCGGCGGATCAGGA GGACGCGCCTCTGGTGGTGGAGGATCGGAGATCGTGATGACCCAGAGCC CTCTCTCCTTGCCCGTGACTCCTGGGGAGCCCGCATCCATTTCATGCCG GAGCTCCCAGTCACTTCTCTACTCCAACGGCTATAACTACGTGGATTGG TACCTCCAAAAGCCGGGCCAGAGCCCGCAGCTGCTGATCTACCTGGGCT CGAACAGGGCCAGCGGAGTGCCTGACCGGTTCTCCGGGTCGGGAAGCGG GACCGACTTCAAGCTGCAAATCTCGAGAGTGGAGGCCGAGGACGTGGGA ATCTACTACTGTATGCAGGGCCGCCAGTTTCCGTACTCGTTCGGACAGG

		GCACCAAAGTGGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCAC CCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCA TGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCG CCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCT GCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAG CTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTC AAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGG CTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTAC AAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAG AGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGG CGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTC CAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGG AACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCAC CGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCT CGG
139104		
139104- aa ScFv domain	45	EVQLLETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVLTQSPATLSVSP GESATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRASGIPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQQYGSSLTFGGGTKVEIK
139104- nt ScFv domain	60	GAAGTGCAATTGCTCGAAACTGGAGGAGGTCTGGTGCAACCTGGAGGAT CACTTCGCCTGTCCTGCGCCGTGTCGGGCTTTGCCCTGTCCAACCATGG AATGAGCTGGGTCCGCCGCGCGCCGGGGAAGGGCCTCGAATGGGTGTCC GGCATCGTCTACTCCGGCTCCACCTACTACGCCGCGTCCGTGAAGGGCC GGTTCACGATTTCACGGGACAACTCGCGGAACACCCTGTACCTCCAAAT GAATTCCCTTCGGCCGGAGGATACTGCCATCTACTACTGCTCCGCCCAC GGTGGCGAATCCGACGTCTGGGGCCAGGGAACCACCGTGACCGTGTCCA GCGCGTCCGGGGGAGGAGGAAGCGGGGGTAGAGCATCGGGTGGAGGCGG ATCAGAGATCGTGCTGACCCAGTCCCCCGCCACCTTGAGCGTGTCACCA GGAGAGTCCGCCACCCTGTCATGCCGCGCCAGCCAGTCCGTGTCCTCCA ACCTGGCTTGGTACCAGCAGAAGCCGGGGCAGGCCCCTAGACTCCTGAT CTATGGGGCGTCGACCCGGGCATCTGGAATTCCCGATAGGTTCAGCGGA TCGGGCTCGGGCACTGACTTCACTCTGACCATCTCCTCGCTGCAAGCCG AGGACGTGGCTGTGTACTACTGTCAGCAGTACGGAAGCTCCCTGACTTT CGGTGGCGGGACCAAAGTCGAGATTAAG
139104- aa VH	75	EVQLLETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139104- aa VL	90	EIVLTQSPATLSVSPGESATLSCRASQSVSSNLAWYQQKPGQAPRLLIY GASTRASGIPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYGSSLTFG GGTKVEIK
139104- aa Full CAR	105	MALPVTALLLPLALLLHAARPEVQLLETGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSEIVLTQSPATLSVSPGESATLSCRASQSVSSNLAWYQQKPGQA PRLLIYGASTRASGIPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYG SSLTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAV HTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPF MRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYN ELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAY SEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

139104- nt Full CAR	120	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGCTCGAAACTGGAGGAGGTCTGGT GCAACCTGGAGGATCACTTCGCCTGTCCTGCGCCGTGTCGGGCTTTGCC CTGTCCAACCATGGAATGAGCTGGGTCCGCCGCGCGCCGGGGAAGGGCC TCGAATGGGTGTCCGGCATCGTCTACTCCGGCTCCACCTACTACGCCGC GTCCGTGAAGGGCCGGTTCACGATTTCACGGGACAACTCGCGGAACACC CTGTACCTCCAAATGAATTCCCTTCGGCCGGAGGATACTGCCATCTACT ACTGCTCCGCCCACGGTGGCGAATCCGACGTCTGGGGCCAGGGAACCAC CGTGACCGTGTCCAGCGCGTCCGGGGGAGGAGGAAGCGGGGGTAGAGCA TCGGGTGGAGGCGGATCAGAGATCGTGCTGACCCAGTCCCCCGCCACCT TGAGCGTGTCACCAGGAGAGTCCGCCACCCTGTCATGCCGCGCCAGCCA GTCCGTGTCCTCCAACCTGGCTTGGTACCAGCAGAAGCCGGGGCAGGCC CCTAGACTCCTGATCTATGGGGCGTCGACCCGGGCATCTGGAATTCCCG ATAGGTTCAGCGGATCGGGCTCGGGCACTGACTTCACTCTGACCATCTC CTCGCTGCAAGCCGAGGACGTGGCTGTGTACTACTGTCAGCAGTACGGA AGCTCCCTGACTTTCGGTGGCGGGACCAAAGTCGAGATTAAGACCACTA CCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCC TCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTG CATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTC TGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTA CTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTC ATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGT TCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCG CAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTACAAC GAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGGA GAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCA AGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTAT AGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACG GACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCT TCACATGCAGGCCCTGCCGCCTCGG
139106		
139106- aa ScFv domain	46	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVMTQSPATLSVSP GERATLSCRASQSVSSKLAWYQQKPGQAPRLLMYGASIRATGIPDRFSG SGSGTEFTLTISSLEPEDFAVYYCQQYGSSSWTFGQGTKVEIK
139106- nt ScFv domain	61	GAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGTGCAACCTGGAGGAT CATTGAGACTGAGCTGCGCAGTGTCGGGATTCGCCCTGAGCAACCATGG AATGTCCTGGGTCAGAAGGGCCCCTGGAAAAGGCCTCGAATGGGTGTCA GGGATCGTGTACTCCGGTTCCACTTACTACGCCGCCTCCGTGAAGGGGC GCTTCACTATCTCACGGGATAACTCCCGCAATACCCTGTACCTCCAAAT GAACAGCCTGCGGCCGGAGGATACCGCCATCTACTACTGTTCCGCCCAC GGTGGAGAGTCTGACGTCTGGGGCCAGGGAACTACCGTGACCGTGTCCT CCGCGTCCGGCGGTGGAGGGAGCGGCGGCCGCGCCAGCGGCGGCGGAGG CTCCGAGATCGTGATGACCCAGAGCCCCGCTACTCTGTCGGTGTCGCCC GGAGAAAGGGCGACCCTGTCCTGCCGGGCGTCGCAGTCCGTGAGCAGCA AGCTGGCTTGGTACCAGCAGAAGCCGGGCCAGGCACCACGCCTGCTTAT GTACGGTGCCTCCATTCGGGCCACCGGAATCCCGGACCGGTTCTCGGGG TCGGGGTCCGGTACCGAGTTCACACTGACCATTTCCTCGCTCGAGCCCG AGGACTTTGCCGTCTATTACTGCCAGCAGTACGGCTCCTCCTCATGGAC GTTCGGCCAGGGGACCAAGGTCGAAATCAAG

139106- aa VH	76	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139106- aa VL	91	EIVMTQSPATLSVSPGERATLSCRASQSVSSKLAWYQQKPGQAPRLLMY GASIRATGIPDRFSGSGSGTEFTLTISSLEPEDFAVYYCQQYGSSSWTF GQGTKVEIK
139106- aa Full CAR	106	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSEIVMTQSPATLSVSPGERATLSCRASQSVSSKLAWYQQKPGQA PRLLMYGASIRATGIPDRFSGSGSGTEFTLTISSLEPEDFAVYYCQQYG SSSWTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLY NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139106- nt Full CAR	121	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGT GCAACCTGGAGGATCATTGAGACTGAGCTGCGCAGTGTCGGGATTCGCC CTGAGCAACCATGGAATGTCCTGGGTCAGAAGGGCCCCTGGAAAAGGCC TCGAATGGGTGTCAGGGATCGTGTACTCCGGTTCCACTTACTACGCCGC CTCCGTGAAGGGGCGCTTCACTATCTCACGGGATAACTCCCGCAATACC CTGTACCTCCAAATGAACAGCCTGCGGCCGGAGGATACCGCCATCTACT ACTGTTCCGCCCACGGTGGAGAGTCTGACGTCTGGGGCCAGGGAACTAC CGTGACCGTGTCCTCCGCGTCCGGCGGTGGAGGGAGCGGCGGCCGCGCC AGCGGCGGCGGAGGCTCCGAGATCGTGATGACCCAGAGCCCCGCTACTC TGTCGGTGTCGCCCGGAGAAAGGGCGACCCTGTCCTGCCGGGCGTCGCA GTCCGTGAGCAGCAAGCTGGCTTGGTACCAGCAGAAGCCGGGCCAGGCA CCACGCCTGCTTATGTACGGTGCCTCCATTCGGGCCACCGGAATCCCGG ACCGGTTCTCGGGGTCGGGGTCCGGTACCGAGTTCACACTGACCATTTC CTCGCTCGAGCCCGAGGACTTTGCCGTCTATTACTGCCAGCAGTACGGC TCCTCCTCATGGACGTTCGGCCAGGGGACCAAGGTCGAAATCAAGACCA CTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCA GCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCC GTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCC CTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCT TTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCC GGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAG CCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTAC AACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGC GGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCC CCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACG ACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGC TCTTCACATGCAGGCCCTGCCGCCTCGG
139107		
139107- aa ScFv domain	47	EVQLVETGGGVVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVLTQSPGTLSLSP GERATLSCRASQSVGSTNLAWYQQKPGQAPRLLIYDASNRATGIPDRFS GGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPPWTFGQGTKVEIK

139107- nt ScFv domain	62	GAAGTGCAATTGGTGGAGACTGGAGGAGGAGTGGTGCAACCTGGAGGAA GCCTGAGACTGTCATGCGCGGTGTCGGGCTTCGCCCTCTCCAACCACGG AATGTCCTGGGTCCGCCGGGCCCCTGGGAAAGGACTTGAATGGGTGTCC GGCATCGTGTACTCGGGTTCCACCTACTACGCGGCCTCAGTGAAGGGCC GGTTTACTATTAGCCGCGACAACTCCAGAAACACACTGTACCTCCAAAT GAACTCGCTGCGGCCGGAAGATACCGCTATCTACTACTGCTCCGCCCAT GGGGGAGAGTCGGACGTCTGGGGACAGGGCACCACTGTCACTGTGTCCA GCGCTTCCGGCGGTGGTGGAAGCGGGGGACGGGCCTCAGGAGGCGGTGG CAGCGAGATTGTGCTGACCCAGTCCCCCGGGACCCTGAGCCTGTCCCCG GGAGAAAGGGCCACCCTCTCCTGTCGGGCATCCCAGTCCGTGGGGTCTA CTAACCTTGCATGGTACCAGCAGAAGCCCGGCCAGGCCCCTCGCCTGCT GATCTACGACGCGTCCAATAGAGCCACCGGCATCCCGGATCGCTTCAGC GGAGGCGGATCGGGCACCGACTTCACCCTCACCATTTCAAGGCTGGAAC CGGAGGACTTCGCCGTGTACTACTGCCAGCAGTATGGTTCGTCCCCACC CTGGACGTTCGGCCAGGGGACTAAGGTCGAGATCAAG
139107- aa VH	77	EVQLVETGGGVVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139107- aa VL	92	EIVLTQSPGTLSLSPGERATLSCRASQSVGSTNLAWYQQKPGQAPRLLI YDASNRATGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPPW TFGQGTKVEIK
139107- aa Full CAR	107	MALPVTALLLPLALLLHAARPEVQLVETGGGVVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVGSTNLAWYQQKPGQ APRLLIYDASNRATGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQQY GSSPPWTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAG GAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQ LYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139107- nt Full CAR	122	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGGTGGAGACTGGAGGAGGAGTGGT GCAACCTGGAGGAAGCCTGAGACTGTCATGCGCGGTGTCGGGCTTCGCC CTCTCCAACCACGGAATGTCCTGGGTCCGCCGGGCCCCTGGGAAAGGAC TTGAATGGGTGTCCGGCATCGTGTACTCGGGTTCCACCTACTACGCGGC CTCAGTGAAGGGCCGGTTTACTATTAGCCGCGACAACTCCAGAAACACA CTGTACCTCCAAATGAACTCGCTGCGGCCGGAAGATACCGCTATCTACT ACTGCTCCGCCCATGGGGGAGAGTCGGACGTCTGGGGACAGGGCACCAC TGTCACTGTGTCCAGCGCTTCCGGCGGTGGTGGAAGCGGGGGACGGGCC TCAGGAGGCGGTGGCAGCGAGATTGTGCTGACCCAGTCCCCCGGGACCC TGAGCCTGTCCCCGGGAGAAAGGGCCACCCTCTCCTGTCGGGCATCCCA GTCCGTGGGGTCTACTAACCTTGCATGGTACCAGCAGAAGCCCGGCCAG GCCCCTCGCCTGCTGATCTACGACGCGTCCAATAGAGCCACCGGCATCC CGGATCGCTTCAGCGGAGGCGGATCGGGCACCGACTTCACCCTCACCAT TTCAAGGCTGGAACCGGAGGACTTCGCCGTGTACTACTGCCAGCAGTAT GGTTCGTCCCCACCCTGGACGTTCGGCCAGGGGACTAAGGTCGAGATCA AGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGC CTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGT GGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTT GGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAG

		CAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTT CATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAA ATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGG ACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAA GAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCA GAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAG GCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTA TGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139108		
139108- aa ScFv domain	48	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVS YISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR ESGDGMDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIQMTQSPSSLSA SVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRF SGSGSGTDFTLTISSLQPEDFATYYCQQSYTLAFGQGTKVDIK
139108- nt ScFv domain	63	CAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGAAACCTGGAGGAT CATTGAGACTGTCATGCGCGGCCTCGGGATTCACGTTCTCCGATTACTA CATGAGCTGGATTCGCCAGGCTCCGGGGAAGGGACTGGAATGGGTGTCC TACATTTCCTCATCCGGCTCCACCATCTACTACGCGGACTCCGTGAAGG GGAGATTCACCATTAGCCGCGATAACGCCAAGAACAGCCTGTACCTTCA GATGAACTCCCTGCGGGCTGAAGATACTGCCGTCTACTACTGCGCAAGG GAGAGCGGAGATGGGATGGACGTCTGGGGACAGGGTACCACTGTGACCG TGTCGTCGGCCTCCGGCGGAGGGGGTTCGGGTGGAAGGGCCAGCGGCGG CGGAGGCAGCGACATCCAGATGACCCAGTCCCCCTCATCGCTGTCCGCC TCCGTGGGCGACCGCGTCACCATCACATGCCGGGCCTCACAGTCGATCT CCTCCTACCTCAATTGGTATCAGCAGAAGCCCGGAAAGGCCCCTAAGCT TCTGATCTACGCAGCGTCCTCCCTGCAATCCGGGGTCCCATCTCGGTTC TCCGGCTCGGGCAGCGGTACCGACTTCACTCTGACCATCTCGAGCCTGC AGCCGGAGGACTTCGCCACTTACTACTGTCAGCAAAGCTACACCCTCGC GTTTGGCCAGGGCACCAAAGTGGACATCAAG
139108- aa VH	78	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVS YISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR ESGDGMDVWGQGTTVTVSS
139108- aa VL	93	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYTLAFGQ GTKVDIK
139108- aa Full CAR	108	MALPVTALLLPLALLLHAARPQVQLVESGGGLVKPGGSLRLSCAASGFT FSDYYMSWIRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAVYYCARESGDGMDVWGQGTTVTVSSASGGGGSGG RASGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPG KAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ SYTLAFGQGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLY NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139108- nt Full CAR	123	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGT GAAACCTGGAGGATCATTGAGACTGTCATGCGCGGCCTCGGGATTCACG TTCTCCGATTACTACATGAGCTGGATTCGCCAGGCTCCGGGGAAGGGAC TGGAATGGGTGTCCTACATTTCCTCATCCGGCTCCACCATCTACTACGC GGACTCCGTGAAGGGGAGATTCACCATTAGCCGCGATAACGCCAAGAAC

		AGCCTGTACCTTCAGATGAACTCCCTGCGGGCTGAAGATACTGCCGTCT ACTACTGCGCAAGGGAGAGCGGAGATGGGATGGACGTCTGGGGACAGGG TACCACTGTGACCGTGTCGTCGGCCTCCGGCGGAGGGGGTTCGGGTGGA AGGGCCAGCGGCGGCGGAGGCAGCGACATCCAGATGACCCAGTCCCCCT CATCGCTGTCCGCCTCCGTGGGCGACCGCGTCACCATCACATGCCGGGC CTCACAGTCGATCTCCTCCTACCTCAATTGGTATCAGCAGAAGCCCGGA AAGGCCCCTAAGCTTCTGATCTACGCAGCGTCCTCCCTGCAATCCGGGG TCCCATCTCGGTTCTCCGGCTCGGGCAGCGGTACCGACTTCACTCTGAC CATCTCGAGCCTGCAGCCGGAGGACTTCGCCACTTACTACTGTCAGCAA AGCTACACCCTCGCGTTTGGCCAGGGCACCAAAGTGGACATCAAGACCA CTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCA GCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCC GTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCC CTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCT TTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCC GGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAG CCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTAC AACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGC GGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCC CCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACG ACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGC TCTTCACATGCAGGCCCTGCCGCCTCGG
139110		
139110- aa ScFv domain	50	QVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVS YISSSGNTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR STMVREDYWGQGTLVTVSSASGGGGSGGRASGGGGSDIVLTQSPLSLPV TLGQPASISCKSSESLVHNSGKTYLNWFHQRPGQSPRRLIYEVSNRDSG VPDRFTGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPGTFGQGTKLEI K
139110- nt ScFv domain	65	CAAGTGCAACTGGTGCAAAGCGGAGGAGGATTGGTCAAACCCGGAGGAA GCCTGAGACTGTCATGCGCGGCCTCTGGATTCACCTTCTCCGATTACTA CATGTCATGGATCAGACAGGCCCCGGGGAAGGGCCTCGAATGGGTGTCC TACATCTCGTCCTCCGGGAACACCATCTACTACGCCGACAGCGTGAAGG GCCGCTTTACCATTTCCCGCGACAACGCAAAGAACTCGCTGTACCTTCA GATGAATTCCCTGCGGGCTGAAGATACCGCGGTGTACTATTGCGCCCGG TCCACTATGGTCCGGGAGGACTACTGGGGACAGGGCACACTCGTGACCG TGTCCAGCGCGAGCGGGGGTGGAGGCAGCGGTGGACGCGCCTCCGGCGG CGGCGGTTCAGACATCGTGCTGACTCAGTCGCCCCTGTCGCTGCCGGTC ACCCTGGGCCAACCGGCCTCAATTAGCTGCAAGTCCTCGGAGAGCCTGG TGCACAACTCAGGAAAGACTTACCTGAACTGGTTCCATCAGCGGCCTGG ACAGTCCCCACGGAGGCTCATCTATGAAGTGTCCAACAGGGATTCGGGG GTGCCCGACCGCTTCACTGGCTCCGGGTCCGGCACCGACTTCACCTTGA AAATCTCCAGAGTGGAAGCCGAGGACGTGGGCGTGTACTACTGTATGCA GGGTACCCACTGGCCTGGAACCTTTGGACAAGGAACTAAGCTCGAGATT AAG
139110- aa VH	80	QVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVS YISSSGNTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR STMVREDYWGQGTLVTVSS

139110- aa VL	95	DIVLTQSPLSLPVTLGQPASISCKSSESLVHNSGKTYLNWFHQRPGQSP RRLIYEVSNRDSGVPDRFTGSGSGTDFTLKISRVEAEDVGVYYCMQGTH WPGTFGQGTKLEIK
139110- aa Full CAR	110	MALPVTALLLPLALLLHAARPQVQLVQSGGGLVKPGGSLRLSCAASGFT FSDYYMSWIRQAPGKGLEWVSYISSSGNTIYYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAVYYCARSTMVREDYWGQGTLVTVSSASGGGGSGG RASGGGGSDIVLTQSPLSLPVTLGQPASISCKSSESLVHNSGKTYLNWF HQRPGQSPRRLIYEVSNRDSGVPDRFTGSGSGTDFTLKISRVEAEDVGV YYCMQGTHWPGTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139110- nt Full CAR	125	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAACTGGTGCAAAGCGGAGGAGGATTGGT CAAACCCGGAGGAAGCCTGAGACTGTCATGCGCGGCCTCTGGATTCACC TTCTCCGATTACTACATGTCATGGATCAGACAGGCCCCGGGGAAGGGCC TCGAATGGGTGTCCTACATCTCGTCCTCCGGGAACACCATCTACTACGC CGACAGCGTGAAGGGCCGCTTTACCATTTCCCGCGACAACGCAAAGAAC TCGCTGTACCTTCAGATGAATTCCCTGCGGGCTGAAGATACCGCGGTGT ACTATTGCGCCCGGTCCACTATGGTCCGGGAGGACTACTGGGGACAGGG CACACTCGTGACCGTGTCCAGCGCGAGCGGGGGTGGAGGCAGCGGTGGA CGCGCCTCCGGCGGCGGCGGTTCAGACATCGTGCTGACTCAGTCGCCCC TGTCGCTGCCGGTCACCCTGGGCCAACCGGCCTCAATTAGCTGCAAGTC CTCGGAGAGCCTGGTGCACAACTCAGGAAAGACTTACCTGAACTGGTTC CATCAGCGGCCTGGACAGTCCCCACGGAGGCTCATCTATGAAGTGTCCA ACAGGGATTCGGGGGTGCCCGACCGCTTCACTGGCTCCGGGTCCGGCAC CGACTTCACCTTGAAAATCTCCAGAGTGGAAGCCGAGGACGTGGGCGTG TACTACTGTATGCAGGGTACCCACTGGCCTGGAACCTTTGGACAAGGAA CTAAGCTCGAGATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139112		
139112- aa ScFv domain	51	QVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSDIRLTQSPSPLSASV GDRVTITCQASEDINKFLNWYHQTPGKAPKLLIYDASTLQTGVPSRFSG SGSGTDFTLTINSLQPEDIGTYYCQQYESLPLTFGGGTKVEIK
139112- nt ScFv domain	66	CAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGTGCAACCCGGTGGAA GCCTTAGGCTGTCGTGCGCCGTCAGCGGGTTTGCTCTGAGCAACCATGG AATGTCCTGGGTCCGCCGGGCACCGGGAAAAGGGCTGGAATGGGTGTCC

		GGCATCGTGTACAGCGGGTCAACCTATTACGCCGCGTCCGTGAAGGGCA GATTCACTATCTCAAGAGACAACAGCCGGAACACCCTGTACTTGCAAAT GAATTCCCTGCGCCCCGAGGACACCGCCATCTACTACTGCTCCGCCCAC GGAGGAGAGTCGGACGTGTGGGGCCAGGGAACGACTGTGACTGTGTCCA GCGCATCAGGAGGGGGTGGTTCGGGCGGCCGGGCCTCGGGGGGAGGAGG TTCCGACATTCGGCTGACCCAGTCCCCGTCCCCACTGTCGGCCTCCGTC GGCGACCGCGTGACCATCACTTGTCAGGCGTCCGAGGACATTAACAAGT TCCTGAACTGGTACCACCAGACCCCTGGAAAGGCCCCCAAGCTGCTGAT CTACGATGCCTCGACCCTTCAAACTGGAGTGCCTAGCCGGTTCTCCGGG TCCGGCTCCGGCACTGATTTCACTCTGACCATCAACTCATTGCAGCCGG AAGATATCGGGACCTACTATTGCCAGCAGTACGAATCCCTCCCGCTCAC ATTCGGCGGGGGAACCAAGGTCGAGATTAAG
139112- aa VH	81	QVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139112- aa VL	96	DIRLTQSPSPLSASVGDRVTITCQASEDINKFLNWYHQTPGKAPKLLIY DASTLQTGVPSRFSGSGSGTDFTLTINSLQPEDIGTYYCQQYESLPLTF GGGTKVEIK
139112- aa Full CAR	111	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSDIRLTQSPSPLSASVGDRVTITCQASEDINKFLNWYHQTPGKA PKLLIYDASTLQTGVPSRFSGSGSGTDFTLTINSLQPEDIGTYYCQQYE SLPLTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLY NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139112- nt Full CAR	126	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAACTCGTGGAATCTGGTGGAGGACTCGT GCAACCCGGTGGAAGCCTTAGGCTGTCGTGCGCCGTCAGCGGGTTTGCT CTGAGCAACCATGGAATGTCCTGGGTCCGCCGGGCACCGGGAAAAGGGC TGGAATGGGTGTCCGGCATCGTGTACAGCGGGTCAACCTATTACGCCGC GTCCGTGAAGGGCAGATTCACTATCTCAAGAGACAACAGCCGGAACACC CTGTACTTGCAAATGAATTCCCTGCGCCCCGAGGACACCGCCATCTACT ACTGCTCCGCCCACGGAGGAGAGTCGGACGTGTGGGGCCAGGGAACGAC TGTGACTGTGTCCAGCGCATCAGGAGGGGGTGGTTCGGGCGGCCGGGCC TCGGGGGGAGGAGGTTCCGACATTCGGCTGACCCAGTCCCCGTCCCCAC TGTCGGCCTCCGTCGGCGACCGCGTGACCATCACTTGTCAGGCGTCCGA GGACATTAACAAGTTCCTGAACTGGTACCACCAGACCCCTGGAAAGGCC CCCAAGCTGCTGATCTACGATGCCTCGACCCTTCAAACTGGAGTGCCTA GCCGGTTCTCCGGGTCCGGCTCCGGCACTGATTTCACTCTGACCATCAA CTCATTGCAGCCGGAAGATATCGGGACCTACTATTGCCAGCAGTACGAA TCCCTCCCGCTCACATTCGGCGGGGGAACCAAGGTCGAGATTAAGACCA CTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCA GCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCC GTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCC CTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCT TTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCC GGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAG CCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTAC

		AACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGC GGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCC CCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACG ACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGC TCTTCACATGCAGGCCCTGCCGCCTCGG
139113		
139113- aa ScFv domain	52	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSETTLTQSPATLSVSP GERATLSCRASQSVGSNLAWYQQKPGQGPRLLIYGASTRATGIPARFSG SGSGTEFTLTISSLQPEDFAVYYCQQYNDWLPVTFGQGTKVEIK
139113- nt ScFv domain	67	GAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGTGCAACCTGGAGGAT CATTGCGGCTCTCATGCGCTGTCTCCGGCTTCGCCCTGTCAAATCACGG GATGTCGTGGGTCAGACGGGCCCCGGGAAAGGGTCTGGAATGGGTGTCG GGGATTGTGTACAGCGGCTCCACCTACTACGCCGCTTCGGTCAAGGGCC GCTTCACTATTTCACGGGACAACAGCCGCAACACCCTCTATCTGCAAAT GAACTCTCTCCGCCCGGAGGATACCGCCATCTACTACTGCTCCGCACAC GGCGGCGAATCCGACGTGTGGGGACAGGGAACCACTGTCACCGTGTCGT CCGCATCCGGTGGCGGAGGATCGGGTGGCCGGGCCTCCGGGGGCGGCGG CAGCGAGACTACCCTGACCCAGTCCCCTGCCACTCTGTCCGTGAGCCCG GGAGAGAGAGCCACCCTTAGCTGCCGGGCCAGCCAGAGCGTGGGCTCCA ACCTGGCCTGGTACCAGCAGAAGCCAGGACAGGGTCCCAGGCTGCTGAT CTACGGAGCCTCCACTCGCGCGACCGGCATCCCCGCGAGGTTCTCCGGG TCGGGTTCCGGGACCGAGTTCACCCTGACCATCTCCTCCCTCCAACCGG AGGACTTCGCGGTGTACTACTGTCAGCAGTACAACGATTGGCTGCCCGT GACATTTGGACAGGGGACGAAGGTGGAAATCAAA
139113- aa VH	82	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139113- aa VL	97	ETTLTQSPATLSVSPGERATLSCRASQSVGSNLAWYQQKPGQGPRLLIY GASTRATGIPARFSGSGSGTEFTLTISSLQPEDFAVYYCQQYNDWLPVT FGQGTKVEIK
139113- aa Full CAR	112	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSETTLTQSPATLSVSPGERATLSCRASQSVGSNLAWYQQKPGQG PRLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQPEDFAVYYCQQYN DWLPVTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG AVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQ PFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139113- nt Full CAR	127	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGGTGGAAACTGGAGGAGGACTTGT GCAACCTGGAGGATCATTGCGGCTCTCATGCGCTGTCTCCGGCTTCGCC CTGTCAAATCACGGGATGTCGTGGGTCAGACGGGCCCCGGGAAAGGGTC TGGAATGGGTGTCGGGGATTGTGTACAGCGGCTCCACCTACTACGCCGC TTCGGTCAAGGGCCGCTTCACTATTTCACGGGACAACAGCCGCAACACC CTCTATCTGCAAATGAACTCTCTCCGCCCGGAGGATACCGCCATCTACT ACTGCTCCGCACACGGCGGCGAATCCGACGTGTGGGGACAGGGAACCAC TGTCACCGTGTCGTCCGCATCCGGTGGCGGAGGATCGGGTGGCCGGGCC

		TCCGGGGGCGGCGGCAGCGAGACTACCCTGACCCAGTCCCCTGCCACTC TGTCCGTGAGCCCGGGAGAGAGAGCCACCCTTAGCTGCCGGGCCAGCCA GAGCGTGGGCTCCAACCTGGCCTGGTACCAGCAGAAGCCAGGACAGGGT CCCAGGCTGCTGATCTACGGAGCCTCCACTCGCGCGACCGGCATCCCCG CGAGGTTCTCCGGGTCGGGTTCCGGGACCGAGTTCACCCTGACCATCTC CTCCCTCCAACCGGAGGACTTCGCGGTGTACTACTGTCAGCAGTACAAC GATTGGCTGCCCGTGACATTTGGACAGGGGACGAAGGTGGAAATCAAAA CCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTC CCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGG GCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGG CCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCAC TCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAA CCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCAT GCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATT CAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACA AGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAA TCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCC ACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGA CGCTCTTCACATGCAGGCCCTGCCGCCTCGG
139114		
139114- aa ScFv domain	53	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSSASGGGGSGGRASGGGGSEIVLTQSPGTLSLSP GERATLSCRASQSIGSSSLAWYQQKPGQAPRLLMYGASSRASGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYAGSPPFTFGQGTKVEIK
139114- nt ScFv domain	68	GAAGTGCAATTGGTGGAATCTGGTGGAGGACTTGTGCAACCTGGAGGAT CACTGAGACTGTCATGCGCGGTGTCCGGTTTTGCCCTGAGCAATCATGG GATGTCGTGGGTCCGGCGCGCCCCCGGAAAGGGTCTGGAATGGGTGTCG GGTATCGTCTACTCCGGGAGCACTTACTACGCCGCGAGCGTGAAGGGCC GCTTCACCATTTCCCGCGATAACTCCCGCAACACCCTGTACTTGCAAAT GAACTCGCTCCGGCCTGAGGACACTGCCATCTACTACTGCTCCGCACAC GGAGGAGAATCCGACGTGTGGGGCCAGGGAACTACCGTGACCGTCAGCA GCGCCTCCGGCGGCGGGGGCTCAGGCGGACGGGCTAGCGGCGGCGGTGG CTCCGAGATCGTGCTGACCCAGTCGCCTGGCACTCTCTCGCTGAGCCCC GGGGAAAGGGCAACCCTGTCCTGTCGGGCCAGCCAGTCCATTGGATCAT CCTCCCTCGCCTGGTATCAGCAGAAACCGGGACAGGCTCCGCGGCTGCT TATGTATGGGGCCAGCTCAAGAGCCTCCGGCATTCCCGACCGGTTCTCC GGGTCCGGTTCCGGCACCGATTTCACCCTGACTATCTCGAGGCTGGAGC CAGAGGACTTCGCCGTGTACTACTGCCAGCAGTACGCGGGGTCCCCGCC GTTCACGTTCGGACAGGGAACCAAGGTCGAGATCAAG
139114- aa VH	83	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGKGLEWVS GIVYSGSTYYAASVKGRFTISRDNSRNTLYLQMNSLRPEDTAIYYCSAH GGESDVWGQGTTVTVSS
139114- aa VL	98	EIVLTQSPGTLSLSPGERATLSCRASQSIGSSSLAWYQQKPGQAPRLLM YGASSRASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYAGSPPF TFGQGTKVEIK
139114- aa Full CAR	113	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAVSGFA LSNHGMSWVRRAPGKGLEWVSGIVYSGSTYYAASVKGRFTISRDNSRNT LYLQMNSLRPEDTAIYYCSAHGGESDVWGQGTTVTVSSASGGGGSGGRA SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSIGSSSLAWYQQKPGQ

		APRLLMYGASSRASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQY AGSPPFTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAG GAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQ LYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
139114- nt Full CAR	128	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAATTGGTGGAATCTGGTGGAGGACTTGT GCAACCTGGAGGATCACTGAGACTGTCATGCGCGGTGTCCGGTTTTGCC CTGAGCAATCATGGGATGTCGTGGGTCCGGCGCGCCCCCGGAAAGGGTC TGGAATGGGTGTCGGGTATCGTCTACTCCGGGAGCACTTACTACGCCGC GAGCGTGAAGGGCCGCTTCACCATTTCCCGCGATAACTCCCGCAACACC CTGTACTTGCAAATGAACTCGCTCCGGCCTGAGGACACTGCCATCTACT ACTGCTCCGCACACGGAGGAGAATCCGACGTGTGGGGCCAGGGAACTAC CGTGACCGTCAGCAGCGCCTCCGGCGGCGGGGGCTCAGGCGGACGGGCT AGCGGCGGCGGTGGCTCCGAGATCGTGCTGACCCAGTCGCCTGGCACTC TCTCGCTGAGCCCCGGGGAAAGGGCAACCCTGTCCTGTCGGGCCAGCCA GTCCATTGGATCATCCTCCCTCGCCTGGTATCAGCAGAAACCGGGACAG GCTCCGCGGCTGCTTATGTATGGGGCCAGCTCAAGAGCCTCCGGCATTC CCGACCGGTTCTCCGGGTCCGGTTCCGGCACCGATTTCACCCTGACTAT CTCGAGGCTGGAGCCAGAGGACTTCGCCGTGTACTACTGCCAGCAGTAC GCGGGGTCCCCGCCGTTCACGTTCGGACAGGGAACCAAGGTCGAGATCA AGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGC CTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGT GGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTT GGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAG CAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTT CATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAA ATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGG ACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAA GAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCA GAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAG GCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTA TGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149362		
149362-aa ScFv domain	129	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSYYYWGWIRQPPGKGLEW IGSIYYSGSAYYNPSLKSRVTISVDTSKNQFSLRLSSVTAADTAVYYCA RHWQEWPDAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSETTLTQSPAFM SATPGDKVIISCKASQDIDDAMNWYQQKPGEAPLFIIQSATSPVPGIPP RFSGSGFGTDFSLTINNIESEDAAYYFCLQHDNFPLTFGQGTKLEIK
149362-nt ScFv domain	150	CAAGTGCAGCTTCAGGAAAGCGGACCGGGCCTGGTCAAGCCATCCGAAA CTCTCTCCCTGACTTGCACTGTGTCTGGCGGTTCCATCTCATCGTCGTA CTACTACTGGGGCTGGATTAGGCAGCCGCCCGGAAAGGGACTGGAGTGG ATCGGAAGCATCTACTATTCCGGCTCGGCGTACTACAACCCTAGCCTCA AGTCGAGAGTGACCATCTCCGTGGATACCTCCAAGAACCAGTTTTCCCT GCGCCTGAGCTCCGTGACCGCCGCTGACACCGCCGTGTACTACTGTGCT CGGCATTGGCAGGAATGGCCCGATGCCTTCGACATTTGGGGCCAGGGCA CTATGGTCACTGTGTCATCCGGGGGTGGAGGCAGCGGGGGAGGAGGGTC CGGGGGGGGAGGTTCAGAGACAACCTTGACCCAGTCACCCGCATTCATG TCCGCCACTCCGGGAGACAAGGTCATCATCTCGTGCAAAGCGTCCCAGG

		ATATCGACGATGCCATGAATTGGTACCAGCAGAAGCCTGGCGAAGCGCC GCTGTTCATTATCCAATCCGCAACCTCGCCCGTGCCTGGAATCCCACCG CGGTTCAGCGGCAGCGGTTTCGGAACCGACTTTTCCCTGACCATTAACA ACATTGAGTCCGAGGACGCCGCCTACTACTTCTGCCTGCAACACGACAA CTTCCCTCTCACGTTCGGCCAGGGAACCAAGCTGGAAATCAAG
149362-aa VH	171	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSYYYWGWIRQPPGKGLEW IGSIYYSGSAYYNPSLKSRVTISVDTSKNQFSLRLSSVTAADTAVYYCA RHWQEWPDAFDIWGQGTMVTVSS
149362-aa VL	192	ETTLTQSPAFMSATPGDKVIISCKASQDIDDAMNWYQQKPGEAPLFIIQ SATSPVPGIPPRFSGSGFGTDFSLTINNIESEDAAYYFCLQHDNFPLTF GQGTKLEIK
149362-aa Full CAR	213	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGGS ISSSYYYWGWIRQPPGKGLEWIGSIYYSGSAYYNPSLKSRVTISVDTSK NQFSLRLSSVTAADTAVYYCARHWQEWPDAFDIWGQGTMVTVSSGGGGS GGGGSGGGGSETTLTQSPAFMSATPGDKVIISCKASQDIDDAMNWYQQK PGEAPLFIIQSATSPVPGIPPRFSGSGFGTDFSLTINNIESEDAAYYFC LQHDNFPLTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPA AGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYI FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQ NQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149362-nt Full CAR	234	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAGCTTCAGGAAAGCGGACCGGGCCTGGT CAAGCCATCCGAAACTCTCTCCCTGACTTGCACTGTGTCTGGCGGTTCC ATCTCATCGTCGTACTACTACTGGGGCTGGATTAGGCAGCCGCCCGGAA AGGGACTGGAGTGGATCGGAAGCATCTACTATTCCGGCTCGGCGTACTA CAACCCTAGCCTCAAGTCGAGAGTGACCATCTCCGTGGATACCTCCAAG AACCAGTTTTCCCTGCGCCTGAGCTCCGTGACCGCCGCTGACACCGCCG TGTACTACTGTGCTCGGCATTGGCAGGAATGGCCCGATGCCTTCGACAT TTGGGGCCAGGGCACTATGGTCACTGTGTCATCCGGGGGTGGAGGCAGC GGGGGAGGAGGGTCCGGGGGGGGAGGTTCAGAGACAACCTTGACCCAGT CACCCGCATTCATGTCCGCCACTCCGGGAGACAAGGTCATCATCTCGTG CAAAGCGTCCCAGGATATCGACGATGCCATGAATTGGTACCAGCAGAAG CCTGGCGAAGCGCCGCTGTTCATTATCCAATCCGCAACCTCGCCCGTGC CTGGAATCCCACCGCGGTTCAGCGGCAGCGGTTTCGGAACCGACTTTTC CCTGACCATTAACAACATTGAGTCCGAGGACGCCGCCTACTACTTCTGC CTGCAACACGACAACTTCCCTCTCACGTTCGGCCAGGGAACCAAGCTGG AAATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTAC CATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCA GCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCT ACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACT CGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATC TTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACG GCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCG CGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAG AACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACG TGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCG CAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAG ATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAG GCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGA CACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149363		

149363-aa ScFv domain	130	VNLRESGPALVKPTQTLTLTCTFSGFSLRTSGMCVSWIRQPPGKALEWL ARIDWDEDKFYSTSLKTRLTISKDTSDNQVVLRMTNMDPADTATYYCAR SGAGGTSATAFDIWGPGTMVTVSSGGGGSGGGGSGGGGSDIQMTQSPSS LSASVGDRVTITCRASQDIYNNLAWFQLKPGSAPRSLMYAANKSQSGVP SRFSGSASGTDFTLTISSLQPEDFATYYCQHYYRFPYSFGQGTKLEIK
149363-nt ScFv domain	151	CAAGTCAATCTGCGCGAATCCGGCCCCGCCTTGGTCAAGCCTACCCAGA CCCTCACTCTGACCTGTACTTTCTCCGGCTTCTCCCTGCGGACTTCCGG GATGTGCGTGTCCTGGATCAGACAGCCTCCGGGAAAGGCCCTGGAGTGG CTCGCTCGCATTGACTGGGATGAGGACAAGTTCTACTCCACCTCACTCA AGACCAGGCTGACCATCAGCAAAGATACCTCTGACAACCAAGTGGTGCT CCGCATGACCAACATGGACCCAGCCGACACTGCCACTTACTACTGCGCG AGGAGCGGAGCGGGCGGAACCTCCGCCACCGCCTTCGATATTTGGGGCC CGGGTACCATGGTCACCGTGTCAAGCGGAGGAGGGGGTCCGGGGGCGG CGGTTCCGGGGGAGGCGGATCGGACATTCAGATGACTCAGTCACCATCG TCCCTGAGCGCTAGCGTGGGCGACAGAGTGACAATCACTTGCCGGGCAT CCCAGGACATCTATAACAACCTTGCGTGGTTCCAGCTGAAGCCTGGTTC CGCACCGCGGTCACTTATGTACGCCGCCAACAAGAGCCAGTCGGGAGTG CCGTCCCGGTTTTCCGGTTCGGCCTCGGGAACTGACTTCACCCTGACGA TCTCCAGCCTGCAACCCGAGGATTTCGCCACCTACTACTGCCAGCACTA CTACCGCTTTCCCTACTCGTTCGGACAGGGAACCAAGCTGGAAATCAAG
149363-aa VH	172	QVNLRESGPALVKPTQTLTLTCTFSGFSLRTSGMCVSWIRQPPGKALEW LARIDWDEDKFYSTSLKTRLTISKDTSDNQVVLRMTNMDPADTATYYCA RSGAGGTSATAFDIWGPGTMVTVSS
149363-aa VL	193	DIQMTQSPSSLSASVGDRVTITCRASQDIYNNLAWFQLKPGSAPRSLMY AANKSQSGVPSRFSGSASGTDFTLTISSLQPEDFATYYCQHYYRFPYSF GQGTKLEIK
149363-aa Full CAR	214	MALPVTALLLPLALLLHAARPQVNLRESGPALVKPTQTLTLTCTFSGFS LRTSGMCVSWIRQPPGKALEWLARIDWDEDKFYSTSLKTRLTISKDTSD NQVVLRMTNMDPADTATYYCARSGAGGTSATAFDIWGPGTMVTVSSGGG GSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQDIYNNLAWFQ LKPGSAPRSLMYAANKSQSGVPSRFSGSASGTDFTLTISSLQPEDFATY YCQHYYRFPYSFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLL YIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQ GQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149363-nt Full CAR	235	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTCAATCTGCGCGAATCCGGCCCCGCCTTGGT CAAGCCTACCCAGACCCTCACTCTGACCTGTACTTTCTCCGGCTTCTCC CTGCGGACTTCCGGGATGTGCGTGTCCTGGATCAGACAGCCTCCGGGAA AGGCCCTGGAGTGGCTCGCTCGCATTGACTGGGATGAGGACAAGTTCTA CTCCACCTCACTCAAGACCAGGCTGACCATCAGCAAAGATACCTCTGAC AACCAAGTGGTGCTCCGCATGACCAACATGGACCCAGCCGACACTGCCA CTTACTACTGCGCGAGGAGCGGAGCGGGCGGAACCTCCGCCACCGCCTT CGATATTTGGGGCCCGGGTACCATGGTCACCGTGTCAAGCGGAGGAGGG GGGTCCGGGGGCGGCGGTTCCGGGGGAGGCGGATCGGACATTCAGATGA CTCAGTCACCATCGTCCCTGAGCGCTAGCGTGGGCGACAGAGTGACAAT CACTTGCCGGGCATCCCAGGACATCTATAACAACCTTGCGTGGTTCCAG CTGAAGCCTGGTTCCGCACCGCGGTCACTTATGTACGCCGCCAACAAGA GCCAGTCGGGAGTGCCGTCCCGGTTTTCCGGTTCGGCCTCGGGAACTGA CTTCACCCTGACGATCTCCAGCCTGCAACCCGAGGATTTCGCCACCTAC TACTGCCAGCACTACTACCGCTTTCCCTACTCGTTCGGACAGGGAACCA

		AGCTGGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGC TCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGA CCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCG ATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCT TTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTG TACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGG AGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGA ACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAG GGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGT ACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAA GCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCA GAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCAC CAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149364		
149364-aa ScFv domain	131	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVS SISSSSSYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAK TIAAVYAFDIWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPLSLPV TPEEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPYTFGQGTKLEI K
149364-nt ScFv domain	152	GAAGTGCAGCTTGTCGAATCCGGGGGGGGACTGGTCAAGCCGGGCGGAT CACTGAGACTGTCCTGCGCCGCGAGCGGCTTCACGTTCTCCTCCTACTC CATGAACTGGGTCCGCCAAGCCCCCGGGAAGGGACTGGAATGGGTGTCC TCTATCTCCTCGTCGTCGTCCTACATCTACTACGCCGACTCCGTGAAGG GAAGATTCACCATTTCCCGCGACAACGCAAAGAACTCACTGTACTTGCA AATGAACTCACTCCGGGCCGAAGATACTGCTGTGTACTATTGCGCCAAG ACTATTGCCGCCGTCTACGCTTTCGACATCTGGGGCCAGGGAACCACCG TGACTGTGTCGTCCGGTGGTGGTGGCTCGGGCGGAGGAGGAAGCGGCGG CGGGGGGTCCGAGATTGTGCTGACCCAGTCGCCACTGAGCCTCCCTGTG ACCCCCGAGGAACCCGCCAGCATCAGCTGCCGGTCCAGCCAGTCCCTGC TCCACTCCAACGGATACAATTACCTCGATTGGTACCTTCAGAAGCCTGG ACAAAGCCCGCAGCTGCTCATCTACTTGGGATCAAACCGCGCGTCAGGA GTGCCTGACCGGTTCTCCGGCTCGGGCAGCGGTACCGATTTCACCCTGA AAATCTCCAGGGTGGAGGCAGAGGACGTGGGAGTGTATTACTGTATGCA GGCGCTGCAGACTCCGTACACATTTGGGCAGGGCACCAAGCTGGAGATC AAG
149364-aa VH	173	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVS SISSSSSYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAK TIAAVYAFDIWGQGTTVTVSS
149364-aa VL	194	EIVLTQSPLSLPVTPEEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSP QLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQ TPYTFGQGTKLEIK
149364-aa Full CAR	215	MALPVTALLLPLALLLHAARPEVQLVESGGGLVKPGGSLRLSCAASGFT FSSYSMNWVRQAPGKGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAVYYCAKTIAAVYAFDIWGQGTTVTVSSGGGGSGG GGSGGGGSEIVLTQSPLSLPVTPEEPASISCRSSQSLLHSNGYNYLDWY LQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGV YYCMQALQTPYTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK

		QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149364-nt Full CAR	236	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTTGTCGAATCCGGGGGGGGACTGGT CAAGCCGGGCGGATCACTGAGACTGTCCTGCGCCGCGAGCGGCTTCACG TTCTCCTCCTACTCCATGAACTGGGTCCGCCAAGCCCCCGGGAAGGGAC TGGAATGGGTGTCCTCTATCTCCTCGTCGTCGTCCTACATCTACTACGC CGACTCCGTGAAGGGAAGATTCACCATTTCCCGCGACAACGCAAAGAAC TCACTGTACTTGCAAATGAACTCACTCCGGGCCGAAGATACTGCTGTGT ACTATTGCGCCAAGACTATTGCCGCCGTCTACGCTTTCGACATCTGGGG CCAGGGAACCACCGTGACTGTGTCGTCCGGTGGTGGTGGCTCGGGCGGA GGAGGAAGCGGCGGCGGGGGGTCCGAGATTGTGCTGACCCAGTCGCCAC TGAGCCTCCCTGTGACCCCCGAGGAACCCGCCAGCATCAGCTGCCGGTC CAGCCAGTCCCTGCTCCACTCCAACGGATACAATTACCTCGATTGGTAC CTTCAGAAGCCTGGACAAAGCCCGCAGCTGCTCATCTACTTGGGATCAA ACCGCGCGTCAGGAGTGCCTGACCGGTTCTCCGGCTCGGGCAGCGGTAC CGATTTCACCCTGAAAATCTCCAGGGTGGAGGCAGAGGACGTGGGAGTG TATTACTGTATGCAGGCGCTGCAGACTCCGTACACATTTGGGCAGGGCA CCAAGCTGGAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149365		
149365-aa ScFv domain	132	EVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVS YISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR DLRGAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSSYVLTQSPSVSAAPG YTATISCGGNNIGTKSVHWYQQKPGQAPLLVIRDDSVRPSKIPGRFSGS NSGNMATLTISGVQAGDEADFYCQVWDSDSEHVVFGGGTKLTVL
149365-nt ScFv domain	153	GAAGTCCAGCTCGTGGAGTCCGGCGGAGGCCTTGTGAAGCCTGGAGGTT CGCTGAGACTGTCCTGCGCCGCCTCCGGCTTCACCTTCTCCGACTACTA CATGTCCTGGATCAGACAGGCCCCGGGAAAGGGCCTGGAATGGGTGTCC TACATCTCGTCATCGGGCAGCACTATCTACTACGCGGACTCAGTGAAGG GGCGGTTCACCATTTCCCGGGATAACGCGAAGAACTCGCTGTATCTGCA AATGAACTCACTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCCGC GATCTCCGCGGGGCATTTGACATCTGGGGACAGGGAACCATGGTCACAG TGTCCAGCGGAGGGGGAGGATCGGGTGGCGGAGGTTCCGGGGGTGGAGG CTCCTCCTACGTGCTGACTCAGAGCCCAAGCGTCAGCGCTGCGCCCGGT TACACGGCAACCATCTCCTGTGGCGGAAACAACATTGGGACCAAGTCTG TGCACTGGTATCAGCAGAAGCCGGGCCAAGCTCCCCTGTTGGTGATCCG CGATGACTCCGTGCGGCCTAGCAAAATTCCGGGACGGTTCTCCGGCTCC AACAGCGGCAATATGGCCACTCTCACCATCTCGGGAGTGCAGGCCGGAG

		ATGAAGCCGACTTCTACTGCCAAGTCTGGGACTCAGACTCCGAGCATGT GGTGTTCGGGGGCGGAACCAAGCTGACTGTGCTC
149365-aa VH	174	EVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVS YISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR DLRGAFDIWGQGTMVTVSS
149365-aa VL	195	SYVLTQSPSVSAAPGYTATISCGGNNIGTKSVHWYQQKPGQAPLLVIRD DSVRPSKIPGRFSGSNSGNMATLTISGVQAGDEADFYCQVWDSDSEHVV FGGGTKLTVL
149365-aa Full CAR	216	MALPVTALLLPLALLLHAARPEVQLVESGGGLVKPGGSLRLSCAASGFT FSDYYMSWIRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAVYYCARDLRGAFDIWGQGTMVTVSSGGGGSGGGG SGGGGSSYVLTQSPSVSAAPGYTATISCGGNNIGTKSVHWYQQKPGQAP LLVIRDDSVRPSKIPGRFSGSNSGNMATLTISGVQAGDEADFYCQVWDS DSEHVVFGGGTKLTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG AVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQ PFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149365-nt Full CAR	237	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTCCAGCTCGTGGAGTCCGGCGGAGGCCTTGT GAAGCCTGGAGGTTCGCTGAGACTGTCCTGCGCCGCCTCCGGCTTCACC TTCTCCGACTACTACATGTCCTGGATCAGACAGGCCCCGGGAAAGGGCC TGGAATGGGTGTCCTACATCTCGTCATCGGGCAGCACTATCTACTACGC GGACTCAGTGAAGGGGCGGTTCACCATTTCCCGGGATAACGCGAAGAAC TCGCTGTATCTGCAAATGAACTCACTGAGGGCCGAGGACACCGCCGTGT ACTACTGCGCCCGCGATCTCCGCGGGGCATTTGACATCTGGGGACAGGG AACCATGGTCACAGTGTCCAGCGGAGGGGGAGGATCGGGTGGCGGAGGT TCCGGGGGTGGAGGCTCCTCCTACGTGCTGACTCAGAGCCCAAGCGTCA GCGCTGCGCCCGGTTACACGGCAACCATCTCCTGTGGCGGAAACAACAT TGGGACCAAGTCTGTGCACTGGTATCAGCAGAAGCCGGGCCAAGCTCCC CTGTTGGTGATCCGCGATGACTCCGTGCGGCCTAGCAAAATTCCGGGAC GGTTCTCCGGCTCCAACAGCGGCAATATGGCCACTCTCACCATCTCGGG AGTGCAGGCCGGAGATGAAGCCGACTTCTACTGCCAAGTCTGGGACTCA GACTCCGAGCATGTGGTGTTCGGGGGCGGAACCAAGCTGACTGTGCTCA CCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTC CCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGG GCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGG CCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCAC TCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAA CCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCAT GCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATT CAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTC TACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACA AGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAA TCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAA GCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCC ACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGA CGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149366		
149366-aa ScFv domain	133	QVQLVQSGAEVKKPGASVKVSCKPSGYTVTSHYIHWVRRAPGQGLEWMG MINPSGGVTAYSQTLQGRVTMTSDTSSSTVYMELSSLRSEDTAMYYCAR EGSGSGWYFDFWGRGTLVTVSSGGGGSGGGGSGGGGSSYVLTQPPSVSV

		SPGQTASITCSGDGLSKKYVSWYQQKAGQSPVVLISRDKERPSGIPDRF SGSNSADTATLTISGTQAMDEADYYCQAWDDTTVVFGGGTKLTVL
149366-nt ScFv domain	154	CAAGTGCAGCTGGTGCAGAGCGGGGCCGAAGTCAAGAAGCCGGGAGCCT CCGTGAAAGTGTCCTGCAAGCCTTCGGGATACACCGTGACCTCCCACTA CATTCATTGGGTCCGCCGCGCCCCCGGCCAAGGACTCGAGTGGATGGGC ATGATCAACCCTAGCGGCGGAGTGACCGCGTACAGCCAGACGCTGCAGG GACGCGTGACTATGACCTCGGATACCTCCTCCTCCACCGTCTATATGGA ACTGTCCAGCCTGCGGTCCGAGGATACCGCCATGTACTACTGCGCCCGG GAAGGATCAGGCTCCGGGTGGTATTTCGACTTCTGGGGAAGAGGCACCC TCGTGACTGTGTCATCTGGGGGAGGGGGTTCCGGTGGTGGCGGATCGGG AGGAGGCGGTTCATCCTACGTGCTGACCCAGCCACCCTCCGTGTCCGTG AGCCCCGGCCAGACTGCATCGATTACATGTAGCGGCGACGGCCTCTCCA AGAAATACGTGTCGTGGTACCAGCAGAAGGCCGGACAGAGCCCGGTGGT GCTGATCTCAAGAGATAAGGAGCGGCCTAGCGGAATCCCGGACAGGTTC TCGGGTTCCAACTCCGCGGACACTGCTACTCTGACCATCTCGGGGACCC AGGCTATGGACGAAGCCGATTACTACTGCCAAGCCTGGGACGACACTAC TGTCGTGTTTGGAGGGGGCACCAAGTTGACCGTCCTT
149366-aa VH	175	QVQLVQSGAEVKKPGASVKVSCKPSGYTVTSHYIHWVRRAPGQGLEWMG MINPSGGVTAYSQTLQGRVTMTSDTSSSTVYMELSSLRSEDTAMYYCAR EGSGSGWYFDFWGRGTLVTVSS
149366-aa VL	196	SYVLTQPPSVSVSPGQTASITCSGDGLSKKYVSWYQQKAGQSPVVLISR DKERPSGIPDRFSGSNSADTATLTISGTQAMDEADYYCQAWDDTTVVFG GGTKLTVL
149366-aa Full CAR	217	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVSCKPSGYT VTSHYIHWVRRAPGQGLEWMGMINPSGGVTAYSQTLQGRVTMTSDTSSS TVYMELSSLRSEDTAMYYCAREGSGSGWYFDFWGRGTLVTVSSGGGGSG GGGSGGGGSSYVLTQPPSVSVSPGQTASITCSGDGLSKKYVSWYQQKAG QSPVVLISRDKERPSGIPDRFSGSNSADTATLTISGTQAMDEADYYCQA WDDTTVVFGGGTKLTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAG GAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQ LYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149366-nt Full CAR	238	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAGCTGGTGCAGAGCGGGGCCGAAGTCAA GAAGCCGGGAGCCTCCGTGAAAGTGTCCTGCAAGCCTTCGGGATACACC GTGACCTCCCACTACATTCATTGGGTCCGCCGCGCCCCCGGCCAAGGAC TCGAGTGGATGGGCATGATCAACCCTAGCGGCGGAGTGACCGCGTACAG CCAGACGCTGCAGGGACGCGTGACTATGACCTCGGATACCTCCTCCTCC ACCGTCTATATGGAACTGTCCAGCCTGCGGTCCGAGGATACCGCCATGT ACTACTGCGCCCGGGAAGGATCAGGCTCCGGGTGGTATTTCGACTTCTG GGGAAGAGGCACCCTCGTGACTGTGTCATCTGGGGGAGGGGGTTCCGGT GGTGGCGGATCGGGAGGAGGCGGTTCATCCTACGTGCTGACCCAGCCAC CCTCCGTGTCCGTGAGCCCCGGCCAGACTGCATCGATTACATGTAGCGG CGACGGCCTCTCCAAGAAATACGTGTCGTGGTACCAGCAGAAGGCCGGA CAGAGCCCGGTGGTGCTGATCTCAAGAGATAAGGAGCGGCCTAGCGGAA TCCCGGACAGGTTCTCGGGTTCCAACTCCGCGGACACTGCTACTCTGAC CATCTCGGGGACCCAGGCTATGGACGAAGCCGATTACTACTGCCAAGCC TGGGACGACACTACTGTCGTGTTTGGAGGGGGCACCAAGTTGACCGTCC TTACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGC CTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGT GGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTT

		GGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAG CAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTT CATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAA ATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGG ACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAA GAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCA GAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAG GCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTA TGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149367		
149367-aa ScFv domain	134	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEW IGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCA RAGIAARLRGAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSDIVMTQSPS SVSASVGDRVIITCRASQGIRNWLAWYQQKPGKAPNLLIYAASNLQSGV PSRFSGSGSGADFTLTISSLQPEDVATYYCQKYNSAPFTFGPGTKVDIK
149367-nt ScFv domain	155	CAAGTGCAGCTTCAGGAGAGCGGCCCGGGACTCGTGAAGCCGTCCCAGA CCCTGTCCCTGACTTGCACCGTGTCGGGAGGAAGCATCTCGAGCGGAGG CTACTATTGGTCGTGGATTCGGCAGCACCCTGGAAAGGGCCTGGAATGG ATCGGCTACATCTACTACTCCGGCTCGACCTACTACAACCCATCGCTGA AGTCCAGAGTGACAATCTCAGTGGACACGTCCAAGAATCAGTTCAGCCT GAAGCTCTCTTCCGTGACTGCGGCCGACACCGCCGTGTACTACTGCGCA CGCGCTGGAATTGCCGCCCGGCTGAGGGGTGCCTTCGACATTTGGGGAC AGGGCACCATGGTCACCGTGTCCTCCGGCGGCGGAGGTTCCGGGGGTGG AGGCTCAGGAGGAGGGGGGTCCGACATCGTCATGACTCAGTCGCCCTCA AGCGTCAGCGCGTCCGTCGGGGACAGAGTGATCATCACCTGTCGGGCGT CCCAGGGAATTCGCAACTGGCTGGCCTGGTATCAGCAGAAGCCCGGAAA GGCCCCCAACCTGTTGATCTACGCCGCCTCAAACCTCCAATCCGGGGTG CCGAGCCGCTTCAGCGGCTCCGGTTCGGGTGCCGATTTCACTCTGACCA TCTCCTCCCTGCAACCTGAAGATGTGGCTACCTACTACTGCCAAAAGTA CAACTCCGCACCTTTTACTTTCGGACCGGGGACCAAAGTGGACATTAAG
149367-aa VH	176	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEW IGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCA RAGIAARLRGAFDIWGQGTMVTVSS
149367-aa VL	197	DIVMTQSPSSVSASVGDRVIITCRASQGIRNWLAWYQQKPGKAPNLLIY AASNLQSGVPSRFSGSGSGADFTLTISSLQPEDVATYYCQKYNSAPFTF GPGTKVDIK
149367-aa Full CAR	218	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSQTLSLTCTVSGGS ISSGGYYWSWIRQHPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSK NQFSLKLSSVTAADTAVYYCARAGIAARLRGAFDIWGQGTMVTVSSGGG GSGGGGSGGGGSDIVMTQSPSSVSASVGDRVIITCRASQGIRNWLAWYQ QKPGKAPNLLIYAASNLQSGVPSRFSGSGSGADFTLTISSLQPEDVATY YCQKYNSAPFTFGPGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLL YIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQ GQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
149367-nt Full CAR	239	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAGCTTCAGGAGAGCGGCCCGGGACTCGT GAAGCCGTCCCAGACCCTGTCCCTGACTTGCACCGTGTCGGGAGGAAGC ATCTCGAGCGGAGGCTACTATTGGTCGTGGATTCGGCAGCACCCTGGAA

		AGGGCCTGGAATGGATCGGCTACATCTACTACTCCGGCTCGACCTACTA CAACCCATCGCTGAAGTCCAGAGTGACAATCTCAGTGGACACGTCCAAG AATCAGTTCAGCCTGAAGCTCTCTTCCGTGACTGCGGCCGACACCGCCG TGTACTACTGCGCACGCGCTGGAATTGCCGCCCGGCTGAGGGGTGCCTT CGACATTTGGGGACAGGGCACCATGGTCACCGTGTCCTCCGGCGGCGGA GGTTCCGGGGGTGGAGGCTCAGGAGGAGGGGGGTCCGACATCGTCATGA CTCAGTCGCCCTCAAGCGTCAGCGCGTCCGTCGGGGACAGAGTGATCAT CACCTGTCGGGCGTCCCAGGGAATTCGCAACTGGCTGGCCTGGTATCAG CAGAAGCCCGGAAAGGCCCCCAACCTGTTGATCTACGCCGCCTCAAACC TCCAATCCGGGGTGCCGAGCCGCTTCAGCGGCTCCGGTTCGGGTGCCGA TTTCACTCTGACCATCTCCTCCCTGCAACCTGAAGATGTGGCTACCTAC TACTGCCAAAAGTACAACTCCGCACCTTTTACTTTCGGACCGGGGACCA AAGTGGACATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGC TCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGA CCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCG ATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCT TTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTG TACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGG AGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGA ACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAG GGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGT ACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAA GCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCA GAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCAC CAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
149368		
149368-aa ScFv domain	135	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMG GIIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCAR RGGYQLLRWDVGLLRSAFDIWGQGTMVTVSSGGGGSGGGGSGGGGSSYV LTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVLYGKNN RPSGVPDRFSGSRSGTTASLTITGAQAEDEADYYCSSRDSSGDHLRVFG TGTKVTVL
149368-nt ScFv domain	156	CAAGTGCAGCTGGTCCAGTCGGGCGCCGAGGTCAAGAAGCCCGGGAGCT CTGTGAAAGTGTCCTGCAAGGCCTCCGGGGGCACCTTTAGCTCCTACGC CATCTCCTGGGTCCGCCAAGCACCGGGTCAAGGCCTGGAGTGGATGGGG GGAATTATCCCTATCTTCGGCACTGCCAACTACGCCCAGAAGTTCCAGG GACGCGTGACCATTACCGCGGACGAATCCACCTCCACCGCTTATATGGA GCTGTCCAGCTTGCGCTCGGAAGATACCGCCGTGTACTACTGCGCCCGG AGGGGTGGATACCAGCTGCTGAGATGGGACGTGGGCCTCCTGCGGTCGG CGTTCGACATCTGGGGCCAGGGCACTATGGTCACTGTGTCCAGCGGAGG AGGCGGATCGGGAGGCGGCGGATCAGGGGGAGGCGGTTCCAGCTACGTG CTTACTCAACCCCCTTCGGTGTCCGTGGCCCCGGGACAGACCGCCAGAA TCACTTGCGGAGGAAACAACATTGGGTCCAAGAGCGTGCATTGGTACCA GCAGAAGCCAGGACAGGCCCCTGTGCTGGTGCTCTACGGGAAGAACAAT CGGCCCAGCGGAGTGCCGGACAGGTTCTCGGGTTCACGCTCCGGTACAA CCGCTTCACTGACTATCACCGGGGCCCAGGCAGAGGATGAAGCGGACTA CTACTGTTCCTCCCGGGATTCATCCGGCGACCACCTCCGGGTGTTCGGA ACCGGAACGAAGGTCACCGTGCTG
149368-aa VH	177	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMG GIIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCAR RGGYQLLRWDVGLLRSAFDIWGQGTMVTVSS

149368-aa VL	198	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVLYG KNNRPSGVPDRFSGSRSGTTASLTITGAQAEDEADYYCSSRDSSGDHLR VFGTGTKVTVL
149368-aa Full CAR	219	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVSCKASGGT FSSYAISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQGRVTITADESTS TAYMELSSLRSEDTAVYYCARRGGYQLLRWDVGLLRSAFDIWGQGTMVT VSSGGGGSGGGGSGGGGSSYVLTQPPSVSVAPGQTARITCGGNNIGSKS VHWYQQKPGQAPVLVLYGKNNRPSGVPDRFSGSRSGTTASLTITGAQAE DEADYYCSSRDSSGDHLRVFGTGTKVTVLTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQE GLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
149368-nt Full CAR	240	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAGCTGGTCCAGTCGGGCGCCGAGGTCAA GAAGCCCGGGAGCTCTGTGAAAGTGTCCTGCAAGGCCTCCGGGGGCACC TTTAGCTCCTACGCCATCTCCTGGGTCCGCCAAGCACCGGGTCAAGGCC TGGAGTGGATGGGGGGAATTATCCCTATCTTCGGCACTGCCAACTACGC CCAGAAGTTCCAGGGACGCGTGACCATTACCGCGGACGAATCCACCTCC ACCGCTTATATGGAGCTGTCCAGCTTGCGCTCGGAAGATACCGCCGTGT ACTACTGCGCCCGGAGGGGTGGATACCAGCTGCTGAGATGGGACGTGGG CCTCCTGCGGTCGGCGTTCGACATCTGGGGCCAGGGCACTATGGTCACT GTGTCCAGCGGAGGAGGCGGATCGGGAGGCGGCGGATCAGGGGGAGGCG GTTCCAGCTACGTGCTTACTCAACCCCCTTCGGTGTCCGTGGCCCCGGG ACAGACCGCCAGAATCACTTGCGGAGGAAACAACATTGGGTCCAAGAGC GTGCATTGGTACCAGCAGAAGCCAGGACAGGCCCCTGTGCTGGTGCTCT ACGGGAAGAACAATCGGCCCAGCGGAGTGCCGGACAGGTTCTCGGGTTC ACGCTCCGGTACAACCGCTTCACTGACTATCACCGGGGCCCAGGCAGAG GATGAAGCGGACTACTACTGTTCCTCCCGGGATTCATCCGGCGACCACC TCCGGGTGTTCGGAACCGGAACGAAGGTCACCGTGCTGACCACTACCCC AGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTG TCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATA CCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGC TGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGT AAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGA GGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCC AGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGC GCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAAC TCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGG ACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAG GGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCG AGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGACT GTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCAC ATGCAGGCCCTGCCGCCTCGG
149369		
149369-aa ScFv domain	136	EVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLEW LGRTYYRSKWYSFYAISLKSRIIINPDTSKNQFSLQLKSVTPEDTAVYY CARSSPEGLFLYWFDPWGQGTLVTVSSGGDGSGGGGSGGGGSSSELTQD PAVSVALGQTIRITCQGDSLGNYYATWYQQKPGQAPVLVIYGTNNRPSG IPDRFSASSSGNTASLTITGAQAEDEADYYCNSRDSSGHHLLFGTGTKV TVL

149369-nt ScFv domain	157	GAAGTGCAGCTCCAACAGTCAGGACCGGGGCTCGTGAAGCCATCCCAGA CCCTGTCCCTGACTTGTGCCATCTCGGGAGATAGCGTGTCATCGAACTC CGCCGCCTGGAACTGGATTCGGCAGAGCCCGTCCCGCGGACTGGAGTGG CTTGGAAGGACCTACTACCGGTCCAAGTGGTACTCTTTCTACGCGATCT CGCTGAAGTCCCGCATTATCATTAACCCTGATACCTCCAAGAATCAGTT CTCCCTCCAACTGAAATCCGTCACCCCCGAGGACACAGCAGTGTATTAC TGCGCACGGAGCAGCCCCGAAGGACTGTTCCTGTATTGGTTTGACCCCT GGGGCCAGGGGACTCTTGTGACCGTGTCGAGCGGCGGAGATGGGTCCGG TGGCGGTGGTTCGGGGGGCGGCGGATCATCATCCGAACTGACCCAGGAC CCGGCTGTGTCCGTGGCGCTGGGACAAACCATCCGCATTACGTGCCAGG GAGACTCCCTGGGCAACTACTACGCCACTTGGTACCAGCAGAAGCCGGG CCAAGCCCCTGTGTTGGTCATCTACGGGACCAACAACAGACCTTCCGGC ATCCCCGACCGGTTCAGCGCTTCGTCCTCCGGCAACACTGCCAGCCTGA CCATCACTGGAGCGCAGGCCGAAGATGAGGCCGACTACTACTGCAACAG CAGAGACTCCTCGGGTCATCACCTCTTGTTCGGAACTGGAACCAAGGTC ACCGTGCTG
149369-aa VH	178	EVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPSRGLEW LGRTYYRSKWYSFYAISLKSRIIINPDTSKNQFSLQLKSVTPEDTAVYY CARSSPEGLFLYWFDPWGQGTLVTVSS
149369-aa VL	199	SSELTQDPAVSVALGQTIRITCQGDSLGNYYATWYQQKPGQAPVLVIYG TNNRPSGIPDRFSASSSGNTASLTITGAQAEDEADYYCNSRDSSGHHLL FGTGTKVTVL
149369-aa Full CAR	220	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSLTCAISGDS VSSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYSFYAISLKSRIIINPDT SKNQFSLQLKSVTPEDTAVYYCARSSPEGLFLYWFDPWGQGTLVTVSSG GDGSGGGGSGGGGSSSELTQDPAVSVALGQTIRITCQGDSLGNYYATWY QQKPGQAPVLVIYGTNNRPSGIPDRFSASSSGNTASLTITGAQAEDEAD YYCNSRDSSGHHLLFGTGTKVTVLTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPA YKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNE LQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALP PR
149369-nt Full CAR	241	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTCCAACAGTCAGGACCGGGGCTCGT GAAGCCATCCCAGACCCTGTCCCTGACTTGTGCCATCTCGGGAGATAGC GTGTCATCGAACTCCGCCGCCTGGAACTGGATTCGGCAGAGCCCGTCCC GCGGACTGGAGTGGCTTGGAAGGACCTACTACCGGTCCAAGTGGTACTC TTTCTACGCGATCTCGCTGAAGTCCCGCATTATCATTAACCCTGATACC TCCAAGAATCAGTTCTCCCTCCAACTGAAATCCGTCACCCCCGAGGACA CAGCAGTGTATTACTGCGCACGGAGCAGCCCCGAAGGACTGTTCCTGTA TTGGTTTGACCCCTGGGGCCAGGGGACTCTTGTGACCGTGTCGAGCGGC GGAGATGGGTCCGGTGGCGGTGGTTCGGGGGGCGGCGGATCATCATCCG AACTGACCCAGGACCCGGCTGTGTCCGTGGCGCTGGGACAAACCATCCG CATTACGTGCCAGGGAGACTCCCTGGGCAACTACTACGCCACTTGGTAC CAGCAGAAGCCGGGCCAAGCCCCTGTGTTGGTCATCTACGGGACCAACA ACAGACCTTCCGGCATCCCCGACCGGTTCAGCGCTTCGTCCTCCGGCAA CACTGCCAGCCTGACCATCACTGGAGCGCAGGCCGAAGATGAGGCCGAC TACTACTGCAACAGCAGAGACTCCTCGGGTCATCACCTCTTGTTCGGAA CTGGAACCAAGGTCACCGTGCTGACCACTACCCCAGCACCGAGGCCACC CACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACT

		TCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGT CCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAG AAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTA CTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGG CGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCC TACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGA GAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAAT GGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAG CTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAG GGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAG CACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCG CCTCGG
BCMA_EBB-C1978-A4		
BCMA_EBB-C1978-A4 - aa ScFv domain	137	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK VEGSGSLDYWGQGTLVTVSSGGGGSGGGGSGGGGSEIVMTQSPGTLSLS PGERATLSCRASQSVSSAYLAWYQQKPGQPPRLLISGASTRATGIPDRF GGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSFNGSSLFTFGQGTRLEI K
BCMA_EBB-C1978-A4 - nt ScFv domain	158	GAAGTGCAGCTCGTGGAGTCAGGAGGCGGCCTGGTCCAGCCGGGAGGGT CCCTTAGACTGTCATGCGCCGCAAGCGGATTCACTTTCTCCTCCTATGC CATGAGCTGGGTCCGCCAAGCCCCCGGAAAGGGACTGGAATGGGTGTCC GCCATCTCGGGGTCTGGAGGCTCAACTTACTACGCTGACTCCGTGAAGG GACGGTTCACCATTAGCCGCGACAACTCCAAGAACACCCTCTACCTCCA AATGAACTCCCTGCGGGCCGAGGATACCGCCGTCTACTACTGCGCCAAA GTGGAAGGTTCAGGATCGCTGGACTACTGGGGACAGGGTACTCTCGTGA CCGTGTCATCGGGCGGAGGAGGTTCCGGCGGTGGCGGCTCCGGCGGCGG AGGGTCGGAGATCGTGATGACCCAGAGCCCTGGTACTCTGAGCCTTTCG CCGGGAGAAAGGGCCACCCTGTCCTGCCGCGCTTCCCAATCCGTGTCCT CCGCGTACTTGGCGTGGTACCAGCAGAAGCCGGGACAGCCCCCTCGGCT GCTGATCAGCGGGGCCAGCACCCGGGCAACCGGAATCCCAGACAGATTC GGGGGTTCCGGCAGCGGCACAGATTTCACCCTGACTATTTCGAGGTTGG AGCCCGAGGACTTTGCGGTGTATTACTGTCAGCACTACGGGTCGTCCTT TAATGGCTCCAGCCTGTTCACGTTCGGACAGGGGACCCGCCTGGAAATC AAG
BCMA_EBB-C1978-A4 - aa VH	179	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK VEGSGSLDYWGQGTLVTVSS
BCMA_EBB-C1978-A4 - aa VL	200	EIVMTQSPGTLSLSPGERATLSCRASQSVSSAYLAWYQQKPGQPPRLLI SGASTRATGIPDRFGGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSFNG SSLFTFGQGTRLEIK
BCMA_EBB-C1978-A4 - aa Full CART	221	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCAKVEGSGSLDYWGQGTLVTVSSGGGGSGGG GSGGGGSEIVMTQSPGTLSLSPGERATLSCRASQSVSSAYLAWYQQKPG QPPRLLISGASTRATGIPDRFGGSGSGTDFTLTISRLEPEDFAVYYCQH YGSSFNGSSLFTFGQGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK

		QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-A4 - nt Full CART	242	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTCGTGGAGTCAGGAGGCGGCCTGGT CCAGCCGGGAGGGTCCCTTAGACTGTCATGCGCCGCAAGCGGATTCACT TTCTCCTCCTATGCCATGAGCTGGGTCCGCCAAGCCCCCGGAAAGGGAC TGGAATGGGTGTCCGCCATCTCGGGGTCTGGAGGCTCAACTTACTACGC TGACTCCGTGAAGGGACGGTTCACCATTAGCCGCGACAACTCCAAGAAC ACCCTCTACCTCCAAATGAACTCCCTGCGGGCCGAGGATACCGCCGTCT ACTACTGCGCCAAAGTGGAAGGTTCAGGATCGCTGGACTACTGGGGACA GGGTACTCTCGTGACCGTGTCATCGGGCGGAGGAGGTTCCGGCGGTGGC GGCTCCGGCGGCGGAGGGTCGGAGATCGTGATGACCCAGAGCCCTGGTA CTCTGAGCCTTTCGCCGGGAGAAAGGGCCACCCTGTCCTGCCGCGCTTC CCAATCCGTGTCCTCCGCGTACTTGGCGTGGTACCAGCAGAAGCCGGGA CAGCCCCCTCGGCTGCTGATCAGCGGGGCCAGCACCCGGGCAACCGGAA TCCCAGACAGATTCGGGGGTTCCGGCAGCGGCACAGATTTCACCCTGAC TATTTCGAGGTTGGAGCCCGAGGACTTTGCGGTGTATTACTGTCAGCAC TACGGGTCGTCCTTTAATGGCTCCAGCCTGTTCACGTTCGGACAGGGGA CCCGCCTGGAAATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-G1		
BCMA_EBB-C1978-G1 - aa ScFv domain	138	EVQLVETGGGLVQPGGSLRLSCAASGITFSRYPMSWVRQAPGKGL EWVSGISDSGVSTYYADSAKGRFTISRDNSKNTLFLQMSSLRDEDT AVYYCVTRAGSEASDIWGQGTMVTVSSGGGGSGGGGSGGGGSEI VLTQSPATLSLSPGERATLSCRASQSVSNSLAWYQQKPGQAPRLLI YDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAIYYCQQFGTSSG LTFGGGTKLEIK
BCMA_EBB-C1978-G1 - nt ScFv domain	159	GAAGTGCAACTGGTGGAAACCGGTGGCGGCCTGGTGCAGCCTGGAGGAT CATTGAGGCTGTCATGCGCGGCCAGCGGTATTACCTTCTCCCGGTACCC CATGTCCTGGGTCAGACAGGCCCCGGGGAAAGGGCTTGAATGGGTGTCC GGGATCTCGGACTCCGGTGTCAGCACTTACTACGCCGACTCCGCCAAGG GACGCTTCACCATTTCCCGGGACAACTCGAAGAACACCCTGTTCCTCCA AATGAGCTCCCTCCGGGACGAGGATACTGCAGTGTACTACTGCGTGACC CGCGCCGGGTCCGAGGCGTCTGACATTTGGGGACAGGGCACTATGGTCA CCGTGTCGTCCGGCGGAGGGGGCTCGGGAGGCGGTGGCAGCGGAGGAGG AGGGTCCGAGATCGTGCTGACCCAATCCCCGGCCACCCTCTCGCTGAGC CCTGGAGAAAGGGCAACCTTGTCCTGTCGCGCGAGCCAGTCCGTGAGCA ACTCCCTGGCCTGGTACCAGCAGAAGCCCGGACAGGCTCCGAGACTTCT GATCTACGACGCTTCGAGCCGGGCCACTGGAATCCCCGACCGCTTTTCG GGGTCCGGCTCAGGAACCGATTTCACCCTGACAATCTCACGGCTGGAGC

		CAGAGGATTTCGCCATCTATTACTGCCAGCAGTTCGGTACTTCCTCCGG CCTGACTTTCGGAGGCGGCACGAAGCTCGAAATCAAG
BCMA_EBB-C1978-G1 - aa VH	180	EVQLVETGGGLVQPGGSLRLSCAASGITFSRYPMSWVRQAPGKGLEWVS GISDSGVSTYYADSAKGRFTISRDNSKNTLFLQMSSLRDEDTAVYYCVT RAGSEASDIWGQGTMVTVSS
BCMA_EBB-C1978-G1 - aa VL	201	EIVLTQSPATLSLSPGERATLSCRASQSVSNSLAWYQQKPGQAPRLLIY DASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAIYYCQQFGTSSGLT FGGGTKLEIK
BCMA_EBB-C1978-G1 - aa Full CART	222	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAA SGITFSRYPMSWVRQAPGKGLEWVSGISDSGVSTYYADSAKGRFTI SRDNSKNTLFLQMSSLRDEDTAVYYCVTRAGSEASDIWGQGTMV TVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQ SVSNSLAWYQQKPGQAPRLLIYDASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAIYYCQQFGTSSGLTFGGGTKLEIKTTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVL LLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRR GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRG KGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-G1 - nt Full CART	243	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAACTGGTGGAAACCGGTGGCGGCCTGGT GCAGCCTGGAGGATCATTGAGGCTGTCATGCGCGGCCAGCGGTATTACC TTCTCCCGGTACCCCATGTCCTGGGTCAGACAGGCCCCGGGGAAAGGGC TTGAATGGGTGTCCGGGATCTCGGACTCCGGTGTCAGCACTTACTACGC CGACTCCGCCAAGGGACGCTTCACCATTTCCCGGGACAACTCGAAGAAC ACCCTGTTCCTCCAAATGAGCTCCCTCCGGGACGAGGATACTGCAGTGT ACTACTGCGTGACCCGCGCCGGGTCCGAGGCGTCTGACATTTGGGGACA GGGCACTATGGTCACCGTGTCGTCCGGCGGAGGGGGCTCGGGAGGCGGT GGCAGCGGAGGAGGAGGGTCCGAGATCGTGCTGACCCAATCCCCGGCCA CCCTCTCGCTGAGCCCTGGAGAAAGGGCAACCTTGTCCTGTCGCGCGAG CCAGTCCGTGAGCAACTCCCTGGCCTGGTACCAGCAGAAGCCCGGACAG GCTCCGAGACTTCTGATCTACGACGCTTCGAGCCGGGCCACTGGAATCC CCGACCGCTTTTCGGGGTCCGGCTCAGGAACCGATTTCACCCTGACAAT CTCACGGCTGGAGCCAGAGGATTTCGCCATCTATTACTGCCAGCAGTTC GGTACTTCCTCCGGCCTGACTTTCGGAGGCGGCACGAAGCTCGAAATCA AGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGC CTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGT GGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTT GGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAG CAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTT CATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAA ATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGG ACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAA GAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCA GAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAG GCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTA TGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG

BCMA_EBB-C1979-C1		
BCMA_EBB-C1979-C1 - aa ScFv domain	139	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAIYYCAR ATYKRELRYYYGMDVWGQGTMVTVSSGGGGSGGGGSGGGGSEIVMTQSP GTVSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLIYGASSRAT GIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSWTFGQGTRL EIK
BCMA_EBB-C1979-C1 - nt ScFv domain	160	CAAGTGCAGCTCGTGGAATCGGGTGGCGGACTGGTGCAGCCGGGGGGCT CACTTAGACTGTCCTGCGCGGCCAGCGGATTCACTTTCTCCTCCTACGC CATGTCCTGGGTCAGACAGGCCCCTGGAAAGGGCCTGGAATGGGTGTCC GCAATCAGCGGCAGCGGCGGCTCGACCTATTACGCGGATTCAGTGAAGG GCAGATTCACCATTTCCCGGGACAACGCCAAGAACTCCTTGTACCTTCA AATGAACTCCCTCCGCGCGGAAGATACCGCAATCTACTACTGCGCTCGG GCCACTTACAAGAGGGAACTGCGCTACTACTACGGGATGGACGTCTGGG GCCAGGGAACCATGGTCACCGTGTCCAGCGGAGGAGGAGGATCGGGAGG AGGCGGTAGCGGGGGTGGAGGGTCGGAGATCGTGATGACCCAGTCCCCC GGCACTGTGTCGCTGTCCCCCGGCGAACGGGCCACCCTGTCATGTCGGG CCAGCCAGTCAGTGTCGTCAAGCTTCCTCGCCTGGTACCAGCAGAAACC GGGACAAGCTCCCCGCCTGCTGATCTACGGAGCCAGCAGCCGGGCCACC GGTATTCCTGACCGGTTCTCCGGTTCGGGGTCCGGGACCGACTTTACTC TGACTATCTCTCGCCTCGAGCCAGAGGACTCCGCCGTGTATTACTGCCA GCAGTACCACTCCTCCCCGTCCTGGACGTTCGGACAGGGCACAAGGCTG GAGATTAAG
BCMA_EBB-C1979-C1 - aa VH	181	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAIYYCAR ATYKRELRYYYGMDVWGQGTMVTVSS
BCMA_EBB-C1979-C1 - aa VL	202	EIVMTQSPGTVSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLLI YGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYHSSPSW TFGQGTRLEIK
BCMA_EBB-C1979-C1 - aa Full CART	223	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNAKN SLYLQMNSLRAEDTAIYYCARATYKRELRYYYGMDVWGQGTMVTVSSGG GGSGGGGSGGGGSEIVMTQSPGTVSLSPGERATLSCRASQSVSSSFLAW YQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDSA VYYCQQYHSSPSWTFGQGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPA YKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNE LQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALP PR
BCMA_EBB-C1979-C1 - nt Full CART	244	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAGCTCGTGGAATCGGGTGGCGGACTGGT GCAGCCGGGGGGCTCACTTAGACTGTCCTGCGCGGCCAGCGGATTCACT TTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGCCCCTGGAAAGGGCC TGGAATGGGTGTCCGCAATCAGCGGCAGCGGCGGCTCGACCTATTACGC GGATTCAGTGAAGGGCAGATTCACCATTTCCCGGGACAACGCCAAGAAC TCCTTGTACCTTCAAATGAACTCCCTCCGCGCGGAAGATACCGCAATCT ACTACTGCGCTCGGGCCACTTACAAGAGGGAACTGCGCTACTACTACGG GATGGACGTCTGGGGCCAGGGAACCATGGTCACCGTGTCCAGCGGAGGA

		GGAGGATCGGGAGGAGGCGGTAGCGGGGGTGGAGGGTCGGAGATCGTGA TGACCCAGTCCCCCGGCACTGTGTCGCTGTCCCCCGGCGAACGGGCCAC CCTGTCATGTCGGGCCAGCCAGTCAGTGTCGTCAAGCTTCCTCGCCTGG TACCAGCAGAAACCGGGACAAGCTCCCCGCCTGCTGATCTACGGAGCCA GCAGCCGGGCCACCGGTATTCCTGACCGGTTCTCCGGTTCGGGGTCCGG GACCGACTTTACTCTGACTATCTCTCGCCTCGAGCCAGAGGACTCCGCC GTGTATTACTGCCAGCAGTACCACTCCTCCCCGTCCTGGACGTTCGGAC AGGGCACAAGGCTGGAGATTAAGACCACTACCCCAGCACCGAGGCCACC CACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACT TCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGT CCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAG AAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTA CTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGG CGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCC TACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGA GAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAAT GGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAG CTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAG GGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAG CACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCG CCTCGG
BCMA_EBB-C1978-C7		
BCMA_EBB-C1978-C7 - aa ScFv domain	140	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNTLKAEDTAVYYCAR ATYKRELRYYYGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSP STLSLSPGESATLSCRASQSVSTTFLAWYQQKPGQAPRLLIYGSSNRAT GIPDRFSGSGSGTDFTLTIRRLEPEDFAVYYCQQYHSSPSWTFGQGTKV EIK
BCMA_EBB-C1978-C7 - nt ScFv domain	161	GAGGTGCAGCTTGTGGAAACCGGTGGCGGACTGGTGCAGCCCGGAGGAA GCCTCAGGCTGTCCTGCGCCGCGTCCGGCTTCACCTTCTCCTCGTACGC CATGTCCTGGGTCCGCCAGGCCCCCGGAAAGGGCCTGGAATGGGTGTCC GCCATCTCTGGAAGCGGAGGTTCCACGTACTACGCGGACAGCGTCAAGG GAAGGTTCACAATCTCCCGCGATAATTCGAAGAACACTCTGTACCTTCA AATGAACACCCTGAAGGCCGAGGACACTGCTGTGTACTACTGCGCACGG GCCACCTACAAGAGAGAGCTCCGGTACTACTACGGAATGGACGTCTGGG GCCAGGGAACTACTGTGACCGTGTCCTCGGGAGGGGGTGGCTCCGGGGG GGGCGGCTCCGGCGGAGGCGGTTCCGAGATTGTGCTGACCCAGTCACCT TCAACTCTGTCGCTGTCCCCGGGAGAGAGCGCTACTCTGAGCTGCCGGG CCAGCCAGTCCGTGTCCACCACCTTCCTCGCCTGGTATCAGCAGAAGCC GGGGCAGGCACCACGGCTCTTGATCTACGGGTCAAGCAACAGAGCGACC GGAATTCCTGACCGCTTCTCGGGGAGCGGTTCAGGCACCGACTTCACCC TGACTATCCGGCGCCTGGAACCCGAAGATTTCGCCGTGTATTACTGTCA ACAGTACCACTCCTCGCCGTCCTGGACCTTTGGCCAAGGAACCAAAGTG GAAATCAAG
BCMA_EBB-C1978-C7 - aa VH	182	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNTLKAEDTAVYYCAR ATYKRELRYYYGMDVWGQGTTVTVSS

BCMA_EBB-C1978-C7 - aa VL	203	EIVLTQSPSTLSLSPGESATLSCRASQSVSTTFLAWYQQKPGQAPRLLI YGSSNRATGIPDRFSGSGSGTDFTLTIRRLEPEDFAVYYCQQYHSSPSW TFGQGTKVEIK
BCMA_EBB-C1978-C7 - aa Full CART	224	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNTLKAEDTAVYYCARATYKRELRYYYGMDVWGQGTTVTVSSGG GGSGGGGSGGGGSEIVLTQSPSTLSLSPGESATLSCRASQSVSTTFLAW YQQKPGQAPRLLIYGSSNRATGIPDRFSGSGSGTDFTLTIRRLEPEDFA VYYCQQYHSSPSWTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPA YKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNE LQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALP PR
BCMA_EBB-C1978-C7 - nt Full CART	245	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAGGTGCAGCTTGTGGAAACCGGTGGCGGACTGGT GCAGCCCGGAGGAAGCCTCAGGCTGTCCTGCGCCGCGTCCGGCTTCACC TTCTCCTCGTACGCCATGTCCTGGGTCCGCCAGGCCCCCGGAAAGGGCC TGGAATGGGTGTCCGCCATCTCTGGAAGCGGAGGTTCCACGTACTACGC GGACAGCGTCAAGGGAAGGTTCACAATCTCCCGCGATAATTCGAAGAAC ACTCTGTACCTTCAAATGAACACCCTGAAGGCCGAGGACACTGCTGTGT ACTACTGCGCACGGGCCACCTACAAGAGAGAGCTCCGGTACTACTACGG AATGGACGTCTGGGGCCAGGGAACTACTGTGACCGTGTCCTCGGGAGGG GGTGGCTCCGGGGGGGGCGGCTCCGGCGGAGGCGGTTCCGAGATTGTGC TGACCCAGTCACCTTCAACTCTGTCGCTGTCCCCGGGAGAGAGCGCTAC TCTGAGCTGCCGGGCCAGCCAGTCCGTGTCCACCACCTTCCTCGCCTGG TATCAGCAGAAGCCGGGGCAGGCACCACGGCTCTTGATCTACGGGTCAA GCAACAGAGCGACCGGAATTCCTGACCGCTTCTCGGGGAGCGGTTCAGG CACCGACTTCACCCTGACTATCCGGCGCCTGGAACCCGAAGATTTCGCC GTGTATTACTGTCAACAGTACCACTCCTCGCCGTCCTGGACCTTTGGCC AAGGAACCAAAGTGGAAATCAAGACCACTACCCCAGCACCGAGGCCACC CACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACT TCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGT CCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAG AAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTA CTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGG CGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCC TACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGA GAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAAT GGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAG CTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAG GGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAG CACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCG CCTCGG
BCMA_EBB-C1978-D10		
BCMA_EBB-C1978-D10 - aa ScFv domain	141	EVQLVETGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVS GISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRDEDTAVYYCAR VGKAVPDVWGQGTTVTVSSGGGGSGGGGSGGGGSDIVMTQTPSSLSASV GDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYSTPYSFGQGTRLEIK

BCMA_EBB-C1978-D10-nt ScFv domain	162	GAAGTGCAGCTCGTGGAAACTGGAGGTGGACTCGTGCAGCCTGGACGGT CGCTGCGGCTGAGCTGCGCTGCATCCGGCTTCACCTTCGACGATTATGC CATGCACTGGGTCAGACAGGCGCCAGGGAAGGGACTTGAGTGGGTGTCC GGTATCAGCTGGAATAGCGGCTCAATCGGATACGCGGACTCCGTGAAGG GAAGGTTCACCATTTCCCGCGACAACGCCAAGAACTCCCTGTACTTGCA AATGAACAGCCTCCGGGATGAGGACACTGCCGTGTACTACTGCGCCCGC GTCGGAAAAGCTGTGCCCGACGTCTGGGGCCAGGGAACCACTGTGACCG TGTCCAGCGGCGGGGGTGGATCGGGCGGTGGAGGGTCCGGTGGAGGGGG CTCAGATATTGTGATGACCCAGACCCCCTCGTCCCTGTCCGCCTCGGTC GGCGACCGCGTGACTATCACATGTAGAGCCTCGCAGAGCATCTCCAGCT ACCTGAACTGGTATCAGCAGAAGCCGGGGAAGGCCCCGAAGCTCCTGAT CTACGCGGCATCATCACTGCAATCGGGAGTGCCGAGCCGGTTTTCCGGG TCCGGCTCCGGCACCGACTTCACGCTGACCATTTCTTCCCTGCAACCCG AGGACTTCGCCACTTACTACTGCCAGCAGTCCTACTCCACCCCTTACTC CTTCGGCCAAGGAACCAGGCTGGAAATCAAG
BCMA_EBB-C1978-D10 - aa VH	183	EVQLVETGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVS GISWNSGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRDEDTAVYYCAR VGKAVPDVWGQGTTVTVSS
BCMA_EBB-C1978-D10-aa VL	204	DIVMTQTPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIY AASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPYSF GQGTRLEIK
BCMA_EBB-C1978-D10 - aa Full CART	225	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGRSLRLSCAASGFT FDDYAMHWVRQAPGKGLEWVSGISWNSGSIGYADSVKGRFTISRDNAKN SLYLQMNSLRDEDTAVYYCARVGKAVPDVWGQGTTVTVSSGGGGSGGGG SGGGGSDIVMTQTPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSY STPYSFGQGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLY NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-D10 - nt Full CART	246	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTCGTGGAAACTGGAGGTGGACTCGT GCAGCCTGGACGGTCGCTGCGGCTGAGCTGCGCTGCATCCGGCTTCACC TTCGACGATTATGCCATGCACTGGGTCAGACAGGCGCCAGGGAAGGGAC TTGAGTGGGTGTCCGGTATCAGCTGGAATAGCGGCTCAATCGGATACGC GGACTCCGTGAAGGGAAGGTTCACCATTTCCCGCGACAACGCCAAGAAC TCCCTGTACTTGCAAATGAACAGCCTCCGGGATGAGGACACTGCCGTGT ACTACTGCGCCCGCGTCGGAAAAGCTGTGCCCGACGTCTGGGGCCAGGG AACCACTGTGACCGTGTCCAGCGGCGGGGGTGGATCGGGCGGTGGAGGG TCCGGTGGAGGGGGCTCAGATATTGTGATGACCCAGACCCCCTCGTCCC TGTCCGCCTCGGTCGGCGACCGCGTGACTATCACATGTAGAGCCTCGCA GAGCATCTCCAGCTACCTGAACTGGTATCAGCAGAAGCCGGGGAAGGCC CCGAAGCTCCTGATCTACGCGGCATCATCACTGCAATCGGGAGTGCCGA GCCGGTTTTCCGGGTCCGGCTCCGGCACCGACTTCACGCTGACCATTTC TTCCCTGCAACCCGAGGACTTCGCCACTTACTACTGCCAGCAGTCCTAC TCCACCCCTTACTCCTTCGGCCAAGGAACCAGGCTGGAAATCAAGACCA CTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCA GCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCC GTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCC

		CTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCT TTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCC TTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCC GGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAG CCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTAC AACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGC GGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCC CCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCC TATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACG ACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTATGACGC TCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1979-C12		
BCMA_EBB-C1979-C12-aa ScFv domain	142	EVQLVESGGGLVQPGRSLRLSCTASGFTFDDYAMHWVRQRPGKGLEWVA SINWKGNSLAYGDSVKGRFAISRDNAKNTVFLQMNSLRTEDTAVYYCAS HQGVAYYNYAMDVWGRGTLVTVSSGGGGSGGGGSGGGGSEIVLTQSPGT LSLSPGERATLSCRATQSIGSSFLAWYQQRPGQAPRLLIYGASQRATGI PDRFSGRGSGTDFTLTISRVEPEDSAVYYCQHYESSPSWTFGQGTKVEI K
BCMA_EBB-C1979-C12 - nt ScFv domain	163	GAAGTGCAGCTCGTGGAGAGCGGGGGAGGATTGGTGCAGCCCGGAAGGT CCCTGCGGCTCTCCTGCACTGCGTCTGGCTTCACCTTCGACGACTACGC GATGCACTGGGTCAGACAGCGCCCGGGAAAGGGCCTGGAATGGGTCGCC TCAATCAACTGGAAGGGAAACTCCCTGGCCTATGGCGACAGCGTGAAGG GCCGCTTCGCCATTTCGCGCGACAACGCCAAGAACACCGTGTTTCTGCA AATGAATTCCCTGCGGACCGAGGATACCGCTGTGTACTACTGCGCCAGC CACCAGGGCGTGGCATACTATAACTACGCCATGGACGTGTGGGGAAGAG GGACGCTCGTCACCGTGTCCTCCGGGGGCGGTGGATCGGGTGGAGGAGG AAGCGGTGGCGGGGGCAGCGAAATCGTGCTGACTCAGAGCCCGGGAACT CTTTCACTGTCCCCGGGAGAACGGGCCACTCTCTCGTGCCGGGCCACCC AGTCCATCGGCTCCTCCTTCCTTGCCTGGTACCAGCAGAGGCCAGGACA GGCGCCCCGCCTGCTGATCTACGGTGCTTCCCAACGCGCCACTGGCATT CCTGACCGGTTCAGCGGCAGAGGGTCGGGAACCGATTTCACACTGACCA TTTCCCGGGTGGAGCCCGAAGATTCGGCAGTCTACTACTGTCAGCATTA CGAGTCCTCCCCTTCATGGACCTTCGGTCAAGGGACCAAAGTGGAGATC AAG
BCMA_EBB-C1979-C12 - aa VH	184	EVQLVESGGGLVQPGRSLRLSCTASGFTFDDYAMHWVRQRPGKGLEWVA SINWKGNSLAYGDSVKGRFAISRDNAKNTVFLQMNSLRTEDTAVYYCAS HQGVAYYNYAMDVWGRGTLVTVSS
BCMA_EBB-C1979-C12 - aa VL	205	EIVLTQSPGTLSLSPGERATLSCRATQSIGSSFLAWYQQRPGQAPRLLI YGASQRATGIPDRFSGRGSGTDFTLTISRVEPEDSAVYYCQHYESSPSW TFGQGTKVEIK
BCMA_EBB-C1979-C12 - aa Full CART	226	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGRSLRLSCTASGFT FDDYAMHWVRQRPGKGLEWVASINWKGNSLAYGDSVKGRFAISRDNAKN TVFLQMNSLRTEDTAVYYCASHQGVAYYNYAMDVWGRGTLVTVSSGGGG SGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRATQSIGSSFLAWYQ QRPGQAPRLLIYGASQRATGIPDRFSGRGSGTDFTLTISRVEPEDSAVY YCQHYESSPSWTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

BCMA_EBB-C1979-C12 - nt Full CART	247	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTCGTGGAGAGCGGGGGAGGATTGGT GCAGCCCGGAAGGTCCCTGCGGCTCTCCTGCACTGCGTCTGGCTTCACC TTCGACGACTACGCGATGCACTGGGTCAGACAGCGCCCGGGAAAGGGCC TGGAATGGGTCGCCTCAATCAACTGGAAGGGAAACTCCCTGGCCTATGG CGACAGCGTGAAGGGCCGCTTCGCCATTTCGCGCGACAACGCCAAGAAC ACCGTGTTTCTGCAAATGAATTCCCTGCGGACCGAGGATACCGCTGTGT ACTACTGCGCCAGCCACCAGGGCGTGGCATACTATAACTACGCCATGGA CGTGTGGGGAAGAGGGACGCTCGTCACCGTGTCCTCCGGGGGCGGTGGA TCGGGTGGAGGAGGAAGCGGTGGCGGGGGCAGCGAAATCGTGCTGACTC AGAGCCCGGGAACTCTTTCACTGTCCCCGGGAGAACGGGCCACTCTCTC GTGCCGGGCCACCCAGTCCATCGGCTCCTCCTTCCTTGCCTGGTACCAG CAGAGGCCAGGACAGGCGCCCCGCCTGCTGATCTACGGTGCTTCCCAAC GCGCCACTGGCATTCCTGACCGGTTCAGCGGCAGAGGGTCGGGAACCGA TTTCACACTGACCATTTCCCGGGTGGAGCCCGAAGATTCGGCAGTCTAC TACTGTCAGCATTACGAGTCCTCCCCTTCATGGACCTTCGGTCAAGGGA CCAAAGTGGAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1980-G4		
BCMA_EBB-C1980-G4- aa ScFv domain	143	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL EWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAED TAVYYCAKVVRDGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSE IVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRL LIYGASSRATGIPDRFSGNGSGTDFTLTISRLEPEDFAVYYCQQYGS PPRFTFGPGTKVDIK
BCMA_EBB-C1980-G4- nt ScFv domain	164	GAGGTGCAGTTGGTCGAAAGCGGGGGCGGGCTTGTGCAGCCTGGCGGAT CACTGCGGCTGTCCTGCGCGGCATCAGGCTTCACGTTTTCTTCCTACGC CATGTCCTGGGTGCGCCAGGCCCCTGGAAAGGGACTGGAATGGGTGTCC GCGATTTCGGGGTCCGGCGGGAGCACCTACTACGCCGATTCCGTGAAGG GCCGCTTCACTATCTCGCGGGACAACTCCAAGAACACCCTCTACCTCCA AATGAATAGCCTGCGGGCCGAGGATACCGCCGTCTACTATTGCGCTAAG GTCGTGCGCGACGGAATGGACGTGTGGGGACAGGGTACCACCGTGACAG TGTCCTCGGGGGGAGGCGGTAGCGGCGGAGGAGGAAGCGGTGGTGGAGG TTCCGAGATTGTGCTGACTCAATCACCCGCGACCCTGAGCCTGTCCCCC GGCGAAAGGGCCACTCTGTCCTGTCGGGCCAGCCAATCAGTCTCCTCCT CGTACCTGGCCTGGTACCAGCAGAAGCCAGGACAGGCTCCGAGACTCCT TATCTATGGCGCATCCTCCCGCGCCACCGGAATCCCGGATAGGTTCTCG GGAAACGGATCGGGGACCGACTTCACTCTCACCATCTCCCGGCTGGAAC CGGAGGACTTCGCCGTGTACTACTGCCAGCAGTACGGCAGCCCGCCTAG ATTCACTTTCGGCCCCGGCACCAAAGTGGACATCAAG

BCMA_EBB-C1980-G4- aa VH	185	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK VVRDGMDVWGQGTTVTVSS
BCMA_EBB-C1980-G4- aa VL	206	EIVLTQSPATLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLI YGASSRATGIPDRFSGNGSGTDFTLTISRLEPEDFAVYYCQQYGSPPRF TFGPGTKVDIK
BCMA_EBB-C1980-G4- aa Full CART	227	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAA SGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFT ISRDNSKNTLYLQMNSLRAEDTAVYYCAKVVRDGMDVWGQGTT VTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRAS QSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGNGSGTDF TLTISRLEPEDFAVYYCQQYGSPPRFTFGPGTKVDIKTTTPAPRPPT PAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTC GVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP EEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKG ERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1980-G4- nt Full CART	248	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAGGTGCAGTTGGTCGAAAGCGGGGGCGGGCTTGT GCAGCCTGGCGGATCACTGCGGCTGTCCTGCGCGGCATCAGGCTTCACG TTTTCTTCCTACGCCATGTCCTGGGTGCGCCAGGCCCCTGGAAAGGGAC TGGAATGGGTGTCCGCGATTTCGGGGTCCGGCGGGAGCACCTACTACGC CGATTCCGTGAAGGGCCGCTTCACTATCTCGCGGGACAACTCCAAGAAC ACCCTCTACCTCCAAATGAATAGCCTGCGGGCCGAGGATACCGCCGTCT ACTATTGCGCTAAGGTCGTGCGCGACGGAATGGACGTGTGGGGACAGGG TACCACCGTGACAGTGTCCTCGGGGGGAGGCGGTAGCGGCGGAGGAGGA AGCGGTGGTGGAGGTTCCGAGATTGTGCTGACTCAATCACCCGCGACCC TGAGCCTGTCCCCCGGCGAAAGGGCCACTCTGTCCTGTCGGGCCAGCCA ATCAGTCTCCTCCTCGTACCTGGCCTGGTACCAGCAGAAGCCAGGACAG GCTCCGAGACTCCTTATCTATGGCGCATCCTCCCGCGCCACCGGAATCC CGGATAGGTTCTCGGGAAACGGATCGGGGACCGACTTCACTCTCACCAT CTCCCGGCTGGAACCGGAGGACTTCGCCGTGTACTACTGCCAGCAGTAC GGCAGCCCGCCTAGATTCACTTTCGGCCCCGGCACCAAAGTGGACATCA AGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGC CTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGT GGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACATTT GGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTAAG CAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTGTT CATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAA ATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAACCAG CTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGCTGG ACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGAAA GAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCA GAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAG GCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACACCTA TGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1980-D2		
BCMA_EBB-C1980-D2- aa ScFv domain	144	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK IPQTGTFDYWGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQSPGTLSLS

		PGERATLSCRASQSVSSSYLAWYQQRPGQAPRLLIYGASSRATGIPDRF SGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSPSWTFGQGTRLEIK
BCMA_EBB-C1980-D2- nt ScFv domain	165	GAAGTGCAGCTGCTGGAGTCCGGCGGTGGATTGGTGCAACCGGGGGGAT CGCTCAGACTGTCCTGTGCGGCGTCAGGCTTCACCTTCTCGAGCTACGC CATGTCATGGGTCAGACAGGCCCCTGGAAAGGGTCTGGAATGGGTGTCC GCCATTTCCGGGAGCGGGGGATCTACATACTACGCCGATAGCGTGAAGG GCCGCTTCACCATTTCCCGGGACAACTCCAAGAACACTCTCTATCTGCA AATGAACTCCCTCCGCGCTGAGGACACTGCCGTGTACTACTGCGCCAAA ATCCCTCAGACCGGCACCTTCGACTACTGGGGACAGGGGACTCTGGTCA CCGTCAGCAGCGGTGGCGGAGGTTCGGGGGGAGGAGGAAGCGGCGGCGG AGGGTCCGAGATTGTGCTGACCCAGTCACCCGGCACTTTGTCCCTGTCG CCTGGAGAAAGGGCCACCCTTTCCTGCCGGGCATCCCAATCCGTGTCCT CCTCGTACCTGGCCTGGTACCAGCAGAGGCCCGGACAGGCCCCACGGCT TCTGATCTACGGAGCAAGCAGCCGCGCGACCGGTATCCCGGACCGGTTT TCGGGCTCGGGCTCAGGAACTGACTTCACCCTCACCATCTCCCGCCTGG AACCCGAAGATTTCGCTGTGTATTACTGCCAGCACTACGGCAGCTCCCC GTCCTGGACGTTCGGCCAGGGAACTCGGCTGGAGATCAAG
BCMA_EBB-C1980-D2- aa VH	186	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK IPQTGTFDYWGQGTLVTVSS
BCMA_EBB-C1980-D2- aa VL	207	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQRPGQAPRLLI YGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSPSW TFGQGTRLEIK
BCMA_EBB-C1980-D2- aa Full CART	228	MALPVTALLLPLALLLHAARPEVQLLESGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCAKIPQTGTFDYWGQGTLVTVSSGGGGSGGG GSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQRPG QAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQH YGSSPSWTFGQGTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIF KQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQN QLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKM AEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1980-D2- nt Full CART	249	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTGCTGGAGTCCGGCGGTGGATTGGT GCAACCGGGGGGATCGCTCAGACTGTCCTGTGCGGCGTCAGGCTTCACC TTCTCGAGCTACGCCATGTCATGGGTCAGACAGGCCCCTGGAAAGGGTC TGGAATGGGTGTCCGCCATTTCCGGGAGCGGGGGATCTACATACTACGC CGATAGCGTGAAGGGCCGCTTCACCATTTCCCGGGACAACTCCAAGAAC ACTCTCTATCTGCAAATGAACTCCCTCCGCGCTGAGGACACTGCCGTGT ACTACTGCGCCAAAATCCCTCAGACCGGCACCTTCGACTACTGGGGACA GGGGACTCTGGTCACCGTCAGCAGCGGTGGCGGAGGTTCGGGGGGAGGA GGAAGCGGCGGCGGAGGGTCCGAGATTGTGCTGACCCAGTCACCCGGCA CTTTGTCCCTGTCGCCTGGAGAAAGGGCCACCCTTTCCTGCCGGGCATC CCAATCCGTGTCCTCCTCGTACCTGGCCTGGTACCAGCAGAGGCCCGGA CAGGCCCCACGGCTTCTGATCTACGGAGCAAGCAGCCGCGCGACCGGTA TCCCGGACCGGTTTTCGGGCTCGGGCTCAGGAACTGACTTCACCCTCAC CATCTCCCGCCTGGAACCCGAAGATTTCGCTGTGTATTACTGCCAGCAC TACGGCAGCTCCCCGTCCTGGACGTTCGGCCAGGGAACTCGGCTGGAGA TCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCAT CGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCT GGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACA

		TTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGT GATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTT AAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCT GTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACTGCGCGT GAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGGCAGAAC CAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGC TGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAG AAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGATAAGATG GCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCA AAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACAC CTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1978-A10		
BCMA_EBB-C1978-A10-aa ScFv domain	145	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKG LEWVSAISGSGGSTYYADSVKGRFTMSRENDKNSVFLQMNSLRVE DTGVYYCARANYKRELRYYYGMDVWGQGTMVTVSSGGGGSGG GGSGGGGSEIVMTQSPGTLSLSPGESATLSCRASQRVASNYLAWY QHKPGQAPSLLISGASSRATGVPDRFSGSGSGTDFTLAISRLEPEDS AVYYCQHYDSSPSWTFGQGTKVEIK
BCMA_EBB-C1978-A10-nt ScFv domain	166	GAAGTGCAACTGGTGGAAACCGGTGGAGGACTCGTGCAGCCTGGCGGCA GCCTCCGGCTGAGCTGCGCCGCTTCGGGATTCACCTTTTCCTCCTACGC GATGTCTTGGGTCAGACAGGCCCCCGGAAAGGGGCTGGAATGGGTGTCA GCCATCTCCGGCTCCGGCGGATCAACGTACTACGCCGACTCCGTGAAAG GCCGGTTCACCATGTCGCGCGAGAATGACAAGAACTCCGTGTTCCTGCA AATGAACTCCCTGAGGGTGGAGGACACCGGAGTGTACTATTGTGCGCGC GCCAACTACAAGAGAGAGCTGCGGTACTACTACGGAATGGACGTCTGGG GACAGGGAACTATGGTGACCGTGTCATCCGGTGGAGGGGGAAGCGGCGG TGGAGGCAGCGGGGGCGGGGGTTCAGAAATTGTCATGACCCAGTCCCCG GGAACTCTTTCCCTCTCCCCCGGGGAATCCGCGACTTTGTCCTGCCGGG CCAGCCAGCGCGTGGCCTCGAACTACCTCGCATGGTACCAGCATAAGCC AGGCCAAGCCCCTTCCCTGCTGATTTCCGGGGCTAGCAGCCGCGCCACT GGCGTGCCGGATAGGTTCTCGGGAAGCGGCTCGGGTACCGATTTCACCC TGGCAATCTCGCGGCTGGAACCGGAGGATTCGGCCGTGTACTACTGCCA GCACTATGACTCATCCCCCTCCTGGACATTCGGACAGGGCACCAAGGTC GAGATCAAG
BCMA_EBB-C1978-A10-aa VH	187	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTMSRENDKNSVFLQMNSLRVEDTGVYYCAR ANYKRELRYYYGMDVWGQGTMVTVSS
BCMA_EBB-C1978-A10-aa VL	208	EIVMTQSPGTLSLSPGESATLSCRASQRVASNYLAWYQHKPGQAPSLLI SGASSRATGVPDRFSGSGSGTDFTLAISRLEPEDSAVYYCQHYDSSPSW TFGQGTKVEIK
BCMA_EBB-C1978-A10-aa Full CART	229	MALPVTALLLPLALLLHAARPEVQLVETGGGLVQPGGSLRLSCAA SGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFT MSRENDKNSVFLQMNSLRVEDTGVYYCARANYKRELRYYYGMD VWGQGTMVTVSSGGGGSGGGGSGGGGSEIVMTQSPGTLSLSPGES ATLSCRASQRVASNYLAWYQHKPGQAPSLLISGASSRATGVPDRF SGSGSGTDFTLAISRLEPEDSAVYYCQHYDSSPSWTFGQGTKVEIK TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIY IWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQE EDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLYNELNLG

		RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-A10-nt Full CART	250	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAACTGGTGGAAACCGGTGGAGGACTCGT GCAGCCTGGCGGCAGCCTCCGGCTGAGCTGCGCCGCTTCGGGATTCACC TTTTCCTCCTACGCGATGTCTTGGGTCAGACAGGCCCCCGGAAAGGGGC TGGAATGGGTGTCAGCCATCTCCGGCTCCGGCGGATCAACGTACTACGC CGACTCCGTGAAAGGCCGGTTCACCATGTCGCGCGAGAATGACAAGAAC TCCGTGTTCCTGCAAATGAACTCCCTGAGGGTGGAGGACACCGGAGTGT ACTATTGTGCGCGCGCCAACTACAAGAGAGAGCTGCGGTACTACTACGG AATGGACGTCTGGGGACAGGGAACTATGGTGACCGTGTCATCCGGTGGA GGGGGAAGCGGCGGTGGAGGCAGCGGGGGCGGGGGTTCAGAAATTGTCA TGACCCAGTCCCCGGGAACTCTTTCCCTCTCCCCCGGGGAATCCGCGAC TTTGTCCTGCCGGGCCAGCCAGCGCGTGGCCTCGAACTACCTCGCATGG TACCAGCATAAGCCAGGCCAAGCCCCTTCCCTGCTGATTTCCGGGGCTA GCAGCCGCGCCACTGGCGTGCCGGATAGGTTCTCGGGAAGCGGCTCGGG TACCGATTTCACCCTGGCAATCTCGCGGCTGGAACCGGAGGATTCGGCC GTGTACTACTGCCAGCACTATGACTCATCCCCCTCCTGGACATTCGGAC AGGGCACCAAGGTCGAGATCAAGACCACTACCCCAGCACCGAGGCCACC CACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACT TCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGT CCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAG AAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTA CTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGG CGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCC TACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGA GAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAAT GGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAG CTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAG GGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAG CACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCG CCTCGG
BCMA_EBB-C1978-D4		
BCMA_EBB-C1978-D4- aa ScFv domain	146	EVQLLETGGGLVQPGGSLRLSCAASGFSFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK ALVGATGAFDIWGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQSPGTLS LSPGERATLSCRASQSLSSNFLAWYQQKPGQAPGLLIYGASNWATGTPD RFSGSGSGTDFTLTITRLEPEDFAVYYCQYYGTSPMYTFGQGTKVEIK
BCMA_EBB-C1978-D4- nt ScFv domain	167	GAAGTGCAGCTGCTCGAAACCGGTGGAGGGCTGGTGCAGCCAGGGGGCT CCCTGAGGCTTTCATGCGCCGCTAGCGGATTCTCCTTCTCCTCTTACGC CATGTCGTGGGTCCGCCAAGCCCCTGGAAAAGGCCTGGAATGGGTGTCC GCGATTTCCGGGAGCGGAGGTTCGACCTATTACGCCGACTCCGTGAAGG GCCGCTTTACCATCTCCCGGGATAACTCCAAGAACACTCTGTACCTCCA AATGAACTCGCTGAGAGCCGAGGACACCGCCGTGTATTACTGCGCGAAG GCGCTGGTCGGCGCGACTGGGGCATTCGACATCTGGGGACAGGGAACTC TTGTGACCGTGTCGAGCGGAGGCGGCGGCTCCGGCGGAGGAGGGAGCGG GGGCGGTGGTTCCGAAATCGTGTTGACTCAGTCCCCGGGAACCCTGAGC TTGTCACCCGGGGAGCGGGCCACTCTCTCCTGTCGCGCCTCCCAATCGC TCTCATCCAATTTCCTGGCCTGGTACCAGCAGAAGCCCGGACAGGCCCC GGGCCTGCTCATCTACGGCGCTTCAAACTGGGCAACGGGAACCCCTGAT CGGTTCAGCGGAAGCGGATCGGGTACTGACTTTACCCTGACCATCACCA

		GACTGGAACCGGAGGACTTCGCCGTGTACTACTGCCAGTACTACGGCAC CTCCCCCATGTACACATTCGGACAGGGTACCAAGGTCGAGATTAAG
BCMA_EBB-C1978-D4- aa VH	188	EVQLLETGGGLVQPGGSLRLSCAASGFSFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK ALVGATGAFDIWGQGTLVTVSS
BCMA_EBB-C1978-D4- aa VL	209	EIVLTQSPGTLSLSPGERATLSCRASQSLSSNFLAWYQQKPGQAPGLLI YGASNWATGTPDRFSGSGSGTDFTLTITRLEPEDFAVYYCQYYGTSPMY TFGQGTKVEIK
BCMA_EBB-C1978-D4- aa Full CART	230	MALPVTALLLPLALLLHAARPEVQLLETGGGLVQPGGSLRLSCAASGFS FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCAKALVGATGAFDIWGQGTLVTVSSGGGGSG GGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSLSSNFLAWYQQK PGQAPGLLIYGASNWATGTPDRFSGSGSGTDFTLTITRLEPEDFAVYYC QYYGTSPMYTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRP AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLY IFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQG QNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKD KMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-D4- nt Full CART	251	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTGCTCGAAACCGGTGGAGGGCTGGT GCAGCCAGGGGGCTCCCTGAGGCTTTCATGCGCCGCTAGCGGATTCTCC TTCTCCTCTTACGCCATGTCGTGGGTCCGCCAAGCCCCTGGAAAAGGCC TGGAATGGGTGTCCGCGATTTCCGGGAGCGGAGGTTCGACCTATTACGC CGACTCCGTGAAGGGCCGCTTTACCATCTCCCGGGATAACTCCAAGAAC ACTCTGTACCTCCAAATGAACTCGCTGAGAGCCGAGGACACCGCCGTGT ATTACTGCGCGAAGGCGCTGGTCGGCGCGACTGGGGCATTCGACATCTG GGGACAGGGAACTCTTGTGACCGTGTCGAGCGGAGGCGGCGGCTCCGGC GGAGGAGGGAGCGGGGGCGGTGGTTCCGAAATCGTGTTGACTCAGTCCC CGGGAACCCTGAGCTTGTCACCCGGGGAGCGGGCCACTCTCTCCTGTCG CGCCTCCCAATCGCTCTCATCCAATTTCCTGGCCTGGTACCAGCAGAAG CCCGGACAGGCCCCGGGCCTGCTCATCTACGGCGCTTCAAACTGGGCAA CGGGAACCCCTGATCGGTTCAGCGGAAGCGGATCGGGTACTGACTTTAC CCTGACCATCACCAGACTGGAACCGGAGGACTTCGCCGTGTACTACTGC CAGTACTACGGCACCTCCCCCATGTACACATTCGGACAGGGTACCAAGG TCGAGATTAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCC TACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATA TCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTC ACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGG ACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACT GCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGG CAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCC GCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGAT AAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAA GAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAA GGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1980-A2		

BCMA_EBB-C1980-A2- aa ScFv domain	147	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCVL WFGEGFDPWGQGTLVTVSSGGGGSGGGGSGGGGSDIVLTQSPLSLPVTP GEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVDIK
BCMA_EBB-C1980-A2- nt ScFv domain	168	GAAGTGCAGCTGCTTGAGAGCGGTGGAGGTCTGGTGCAGCCCGGGGGAT CACTGCGCCTGTCCTGTGCCGCGTCCGGTTTCACTTTCTCCTCGTACGC CATGTCGTGGGTCAGACAGGCACCGGGAAAGGGACTGGAATGGGTGTCA GCCATTTCGGGTTCGGGGGGCAGCACCTACTACGCTGACTCCGTGAAGG GCCGGTTCACCATTTCCCGCGACAACTCCAAGAACACCTTGTACCTCCA AATGAACTCCCTGCGGGCCGAAGATACCGCCGTGTATTACTGCGTGCTG TGGTTCGGAGAGGGATTCGACCCGTGGGGACAAGGAACACTCGTGACTG TGTCATCCGGCGGAGGCGGCAGCGGTGGCGGCGGTTCCGGCGGCGGCGG ATCTGACATCGTGTTGACCCAGTCCCCTCTGAGCCTGCCGGTCACTCCT GGCGAACCAGCCAGCATCTCCTGCCGGTCGAGCCAGTCCCTCCTGCACT CCAATGGGTACAACTACCTCGATTGGTATCTGCAAAAGCCGGGCCAGAG CCCCCAGCTGCTGATCTACCTTGGGTCAAACCGCGCTTCCGGGGTGCCT GATAGATTCTCCGGGTCCGGGAGCGGAACCGACTTTACCCTGAAAATCT CGAGGGTGGAGGCCGAGGACGTCGGAGTGTACTACTGCATGCAGGCGCT CCAGACTCCCCTGACCTTCGGAGGAGGAACGAAGGTCGACATCAAGA
BCMA_EBB-C1980-A2- aa VH	189	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCVL WFGEGFDPWGQGTLVTVSS
BCMA_EBB-C1980-A2- aa VL	210	DIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSP QLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQ TPLTFGGGTKVDIK
BCMA_EBB-C1980-A2- aa Full CART	231	MALPVTALLLPLALLLHAARPEVQLLESGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCVLWFGEGFDPWGQGTLVTVSSGGGGSGGGG SGGGGSDIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQ KPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYY CMQALQTPLTFGGGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEACRP AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLY IFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQG QNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKD KMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1980-A2- nt Full CART	252	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTGCAGCTGCTTGAGAGCGGTGGAGGTCTGGT GCAGCCCGGGGGATCACTGCGCCTGTCCTGTGCCGCGTCCGGTTTCACT TTCTCCTCGTACGCCATGTCGTGGGTCAGACAGGCACCGGGAAAGGGAC TGGAATGGGTGTCAGCCATTTCGGGTTCGGGGGGCAGCACCTACTACGC TGACTCCGTGAAGGGCCGGTTCACCATTTCCCGCGACAACTCCAAGAAC ACCTTGTACCTCCAAATGAACTCCCTGCGGGCCGAAGATACCGCCGTGT ATTACTGCGTGCTGTGGTTCGGAGAGGGATTCGACCCGTGGGGACAAGG AACACTCGTGACTGTGTCATCCGGCGGAGGCGGCAGCGGTGGCGGCGGT TCCGGCGGCGGCGGATCTGACATCGTGTTGACCCAGTCCCCTCTGAGCC TGCCGGTCACTCCTGGCGAACCAGCCAGCATCTCCTGCCGGTCGAGCCA GTCCCTCCTGCACTCCAATGGGTACAACTACCTCGATTGGTATCTGCAA AAGCCGGGCCAGAGCCCCCAGCTGCTGATCTACCTTGGGTCAAACCGCG CTTCCGGGGTGCCTGATAGATTCTCCGGGTCCGGGAGCGGAACCGACTT TACCCTGAAAATCTCGAGGGTGGAGGCCGAGGACGTCGGAGTGTACTAC TGCATGCAGGCGCTCCAGACTCCCCTGACCTTCGGAGGAGGAACGAAGG

		TCGACATCAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGCTCC TACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCC GCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATA TCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTC ACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGGAGG ACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGAACT GCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAGCAGGGG CAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGGAAGCC GCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAGGAT AAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAA GAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAA GGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
BCMA_EBB-C1981-C3		
BCMA_EBB-C1981-C3- aa ScFv domain	148	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK VGYDSSGYYRDYYGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQ SPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGTSSR ATGISDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGNSPPKFTFGPG TKLEIK
BCMA_EBB-C1981-C3- nt ScFv domain	169	CAAGTGCAGCTCGTGGAGTCAGGCGGAGGACTGGTGCAGCCCGGGGGCT CCCTGAGACTTTCCTGCGCGGCATCGGGTTTTACCTTCTCCTCCTATGC TATGTCCTGGGTGCGCCAGGCCCCGGGAAAGGGACTGGAATGGGTGTCC GCAATCAGCGGTAGCGGGGGCTCAACATACTACGCCGACTCCGTCAAGG GTCGCTTCACTATTTCCCGGGACAACTCCAAGAATACCCTGTACCTCCA AATGAACAGCCTCAGGGCCGAGGATACTGCCGTGTACTACTGCGCCAAA GTCGGATACGATAGCTCCGGTTACTACCGGGACTACTACGGAATGGACG TGTGGGGACAGGGCACCACCGTGACCGTGTCAAGCGGCGGAGGCGGTTC AGGAGGGGGAGGCTCCGGCGGTGGAGGGTCCGAAATCGTCCTGACTCAG TCGCCTGGCACTCTGTCGTTGTCCCCGGGGGAGCGCGCTACCCTGTCGT GTCGGGCGTCGCAGTCCGTGTCGAGCTCCTACCTCGCGTGGTACCAGCA GAAGCCCGGACAGGCCCCTAGACTTCTGATCTACGGCACTTCTTCACGC GCCACCGGGATCAGCGACAGGTTCAGCGGCTCCGGCTCCGGGACCGACT TCACCCTGACCATTAGCCGGCTGGAGCCTGAAGATTTCGCCGTGTATTA CTGCCAACACTACGGAAACTCGCCGCCAAAGTTCACGTTCGGACCCGGA ACCAAGCTGGAAATCAAG
BCMA_EBB-C1981-C3- aa VH	190	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK VGYDSSGYYRDYYGMDVWGQGTTVTVSS
BCMA_EBB-C1981-C3- aa VL	211	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLI YGTSSRATGISDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGNSPPK FTFGPGTKLEIK

BCMA_EBB-C1981-C3- aa Full CART	232	MALPVTALLLPLALLLHAARPQVQLVESGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCAKVGYDSSGYYRDYYGMDVWGQGTTVTVSS GGGGSGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYL AWYQQKPGQAPRLLIYGTSSRATGISDRFSGSGSGTDFTLTISRLEPED FAVYYCQHYGNSPPKFTFGPGTKLEIKTTTPAPRPPTPAPTIASQPLSL RPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSAD APAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQ ALPPR
BCMA_EBB-C1981-C3- nt Full CART	253	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCCAAGTGCAGCTCGTGGAGTCAGGCGGAGGACTGGT GCAGCCCGGGGGCTCCCTGAGACTTTCCTGCGCGGCATCGGGTTTTACC TTCTCCTCCTATGCTATGTCCTGGGTGCGCCAGGCCCCGGGAAAGGGAC TGGAATGGGTGTCCGCAATCAGCGGTAGCGGGGGCTCAACATACTACGC CGACTCCGTCAAGGGTCGCTTCACTATTTCCCGGGACAACTCCAAGAAT ACCCTGTACCTCCAAATGAACAGCCTCAGGGCCGAGGATACTGCCGTGT ACTACTGCGCCAAAGTCGGATACGATAGCTCCGGTTACTACCGGGACTA CTACGGAATGGACGTGTGGGGACAGGGCACCACCGTGACCGTGTCAAGC GGCGGAGGCGGTTCAGGAGGGGGAGGCTCCGGCGGTGGAGGGTCCGAAA TCGTCCTGACTCAGTCGCCTGGCACTCTGTCGTTGTCCCCGGGGGAGCG CGCTACCCTGTCGTGTCGGGCGTCGCAGTCCGTGTCGAGCTCCTACCTC GCGTGGTACCAGCAGAAGCCCGGACAGGCCCCTAGACTTCTGATCTACG GCACTTCTTCACGCGCCACCGGGATCAGCGACAGGTTCAGCGGCTCCGG CTCCGGGACCGACTTCACCCTGACCATTAGCCGGCTGGAGCCTGAAGAT TTCGCCGTGTATTACTGCCAACACTACGGAAACTCGCCGCCAAAGTTCA CGTTCGGACCCGGAACCAAGCTGGAAATCAAGACCACTACCCCAGCACC GAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTG CGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGGG GTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGTAC TTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGCGC GGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTG TGCAGACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGA GGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAGAT GCTCCAGCCTACAAGCAGGGGCAGAACCAGCTCTACAACGAACTCAATC TTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGGAGAGGACGGGA CCCAGAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTG TACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAGATTG GTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTACCA GGGACTCAGCACCGCCACCAAGGACACCTATGACGCTCTTCACATGCAG GCCCTGCCGCCTCGG
BCMA_EBB-C1978-G4		
BCMA_EBB-C1978-G4- aa ScFv domain	149	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK MGWSSGYLGAFDIWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPGT LSLSPGERATLSCRASQSVASSFLAWYQQKPGQAPRLLIYGASGRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGGSPRLTFGGGTKVDI K
BCMA_EBB-C1978-G4- nt ScFv domain	170	GAAGTCCAACTGGTGGAGTCCGGGGGAGGGCTCGTGCAGCCCGGAGGCA GCCTTCGGCTGTCGTGCGCCGCCTCCGGGTTCACGTTCTCATCCTACGC GATGTCGTGGGTCAGACAGGCACCAGGAAAGGGACTGGAATGGGTGTCC

		GCCATTAGCGGCTCCGGCGGTAGCACCTACTATGCCGACTCAGTGAAGG GAAGGTTCACTATCTCCCGCGACAACAGCAAGAACACCCTGTACCTCCA AATGAACTCTCTGCGGGCCGAGGATACCGCGGTGTACTATTGCGCCAAG ATGGGTTGGTCCAGCGGATACTTGGGAGCCTTCGACATTTGGGGACAGG GCACTACTGTGACCGTGTCCTCCGGGGGTGGCGGATCGGGAGGCGGCGG CTCGGGTGGAGGGGGTTCCGAAATCGTGTTGACCCAGTCACCGGGAACC CTCTCGCTGTCCCCGGGAGAACGGGCTACACTGTCATGTAGAGCGTCCC AGTCCGTGGCTTCCTCGTTCCTGGCCTGGTACCAGCAGAAGCCGGGACA GGCACCCCGCCTGCTCATCTACGGAGCCAGCGGCCGGGCGACCGGCATC CCTGACCGCTTCTCCGGTTCCGGCTCGGGCACCGACTTTACTCTGACCA TTAGCAGGCTTGAGCCCGAGGATTTTGCCGTGTACTACTGCCAACACTA CGGGGGGAGCCCTCGCCTGACCTTCGGAGGCGGAACTAAGGTCGATATC AAAA
BCMA_EBB-C1978-G4- aa VH	191	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK MGWSSGYLGAFDIWGQGTTVTVSS
BCMA_EBB-C1978-G4- aa VL	212	EIVLTQSPGTLSLSPGERATLSCRASQSVASSFLAWYQQKPGQAPRLLI YGASGRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHYGGSPRL TFGGGTKVDIK
BCMA_EBB-C1978-G4- aa Full CART	233	MALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFT FSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCAKMGWSSGYLGAFDIWGQGTTVTVSSGGGG SGGGGSGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVASSFLAWYQ QKPGQAPRLLIYGASGRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVY YCQHYGGSPRLTFGGGTKVDIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYK QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
BCMA_EBB-C1978-G4- nt Full CART	254	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCC ACGCCGCTCGGCCCGAAGTCCAACTGGTGGAGTCCGGGGGAGGGCTCGT GCAGCCCGGAGGCAGCCTTCGGCTGTCGTGCGCCGCCTCCGGGTTCACG TTCTCATCCTACGCGATGTCGTGGGTCAGACAGGCACCAGGAAAGGGAC TGGAATGGGTGTCCGCCATTAGCGGCTCCGGCGGTAGCACCTACTATGC CGACTCAGTGAAGGGAAGGTTCACTATCTCCCGCGACAACAGCAAGAAC ACCCTGTACCTCCAAATGAACTCTCTGCGGGCCGAGGATACCGCGGTGT ACTATTGCGCCAAGATGGGTTGGTCCAGCGGATACTTGGGAGCCTTCGA CATTTGGGGACAGGGCACTACTGTGACCGTGTCCTCCGGGGGTGGCGGA TCGGGAGGCGGCGGCTCGGGTGGAGGGGGTTCCGAAATCGTGTTGACCC AGTCACCGGGAACCCTCTCGCTGTCCCCGGGAGAACGGGCTACACTGTC ATGTAGAGCGTCCCAGTCCGTGGCTTCCTCGTTCCTGGCCTGGTACCAG CAGAAGCCGGGACAGGCACCCCGCCTGCTCATCTACGGAGCCAGCGGCC GGGCGACCGGCATCCCTGACCGCTTCTCCGGTTCCGGCTCGGGCACCGA CTTTACTCTGACCATTAGCAGGCTTGAGCCCGAGGATTTTGCCGTGTAC TACTGCCAACACTACGGGGGGAGCCCTCGCCTGACCTTCGGAGGCGGAA CTAAGGTCGATATCAAAACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGT AGACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCCT GCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCT GCTTTCACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAG AGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTG

		CGAACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCCTACAAG CAGGGGCAGAACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGG GAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAA AAGGATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAAGGGGAAC GCAGAAGAGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCACCGC CACCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG

Table 3. Heavy Chain Variable Domain CDRs according to the Kabat numbering scheme (Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD)

Candidate	HCDR1	SEQ ID NO	HCDR2	SEQ ID NO	HCDR3	SEQ ID NO
139109	NHGMS	1051	GIVYSGSTYYAA SVKG	1091	HGGESDV	1131
139103	NYAMS	1052	GISRSGENTYYA DSVKG	1092	SPAHYYGGMDV	1132
139105	DYAMH	1053	GISWNSGSIGYA DSVKG	1093	HSFLAY	1133
139111	NHGMS	1054	GIVYSGSTYYAA SVKG	1094	HGGESDV	1134
139100	NFGIN	1055	WINPKNNNTNYA QKFQG	1095	GPYYYQSYMDV	1135
139101	SDAMT	1056	VISGSGGTTYYA DSVKG	1096	LDSSGYYYARG PRY	1136
139102	NYGIT	1057	WISAYNGNTNYA QKFQG	1097	GPYYYYMDV	1137
139104	NHGMS	1058	GIVYSGSTYYAA SVKG	1098	HGGESDV	1138
139106	NHGMS	1059	GIVYSGSTYYAA SVKG	1099	HGGESDV	1139
139107	NHGMS	1060	GIVYSGSTYYAA SVKG	1100	HGGESDV	1140
139108	DYYMS	1061	YISSSGSTIYYAD SVKG	1101	ESGDGMDV	1141
139110	DYYMS	1062	YISSSGNTIYYAD SVKG	1102	STMVREDY	1142
139112	NHGMS	1063	GIVYSGSTYYAA SVKG	1103	HGGESDV	1143
139113	NHGMS	1064	GIVYSGSTYYAA SVKG	1104	HGGESDV	1144
139114	NHGMS	1065	GIVYSGSTYYAA SVKG	1105	HGGESDV	1145
149362	SSYYYW G	1066	SIYYSGSAYYNPS LKS	1106	HWQEWPDAFDI	1146
149363	TSGMCVS	1067	RIDWDEDKFYST SLKT	1107	SGAGGTSATAF DI	1147
149364	SYSMN	1068	SISSSSSYIYYADS VKG	1108	TIAAVYAFDI	1148
149365	DYYMS	1069	YISSSGSTIYYAD SVKG	1109	DLRGAFDI	1149
149366	SHYIH	1070	MINPSGGVTAYS QTLQG	1110	EGSGSGWYFDF	1150

149367	SGGYYWS	1071	YIYYSGSTYYNPSLKS	1111	AGIAARLRGAFDI	1151
149368	SYAIS	1072	GIIPIFGTANYAQKFQG	1112	RGGYQLLRWDVGLLRSAFDI	1152
149369	SNSAAWN	1073	RTYYRSKWYSFYAISLKS	1113	SSPEGLFLYWFDP	1153
BCMA_EBB-C1978-A4	SYAMS	1074	AISGSGGSTYYADSVKG	1114	VEGSGSLDY	1154
BCMA_EBB-C1978-G1	RYPMS	1075	GISDSGVSTYYADSAKG	1115	RAGSEASDI	1155
BCMA_EBB-C1979-C1	SYAMS	1076	AISGSGGSTYYADSVKG	1116	ATYKRELRYYYGMDV	1156
BCMA_EBB-C1978-C7	SYAMS	1077	AISGSGGSTYYADSVKG	1117	ATYKRELRYYYGMDV	1157
BCMA_EBB-C1978-D10	DYAMH	1078	GISWNSGSIGYADSVKG	1118	VGKAVPDV	1158
BCMA_EBB-C1979-C12	DYAMH	1079	SINWKGNSLAYGDSVKG	1119	HQGVAYYNYAMDV	1159
BCMA_EBB-C1980-G4	SYAMS	1080	AISGSGGSTYYADSVKG	1120	VVRDGMDV	1160
BCMA_EBB-C1980-D2	SYAMS	1081	AISGSGGSTYYADSVKG	1121	IPQTGTFDY	1161
BCMA_EBB-C1978-A10	SYAMS	1082	AISGSGGSTYYADSVKG	1122	ANYKRELRYYYGMDV	1162
BCMA_EBB-C1978-D4	SYAMS	1083	AISGSGGSTYYADSVKG	1123	ALVGATGAFDI	1163
BCMA_EBB-C1980-A2	SYAMS	1084	AISGSGGSTYYADSVKG	1124	WFGEGFDP	1164
BCMA_EBB-C1981-C3	SYAMS	1085	AISGSGGSTYYADSVKG	1125	VGYDSSGYYRDYYGMDV	1165
BCMA_EBB-C1978-G4	SYAMS	1086	AISGSGGSTYYADSVKG	1126	MGWSSGYLGAFDI	1166
A7D12.2	NFGMN	1087	WINTYTGESYFADDFKG	1127	GEIYYGYDGGFAY	1167
C11D5.3	DYSIN	1088	WINTETREPAYAYDFRG	1128	DYSYAMDY	1168
C12A3.2	HYSMN	1089	RINTESGVPIYADDFKG	1129	DYLYSLDF	1169
C13F12.1	HYSMN	1090	RINTETGEPLYADDFKG	1130	DYLYSCDY	1170

5

Table 4. Light Chain Variable Domain CDRs according to the Kabat numbering scheme (Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD)

Candidate	**LCDR1**	**SEQ ID NO**	**LCDR2**	**SEQ ID NO**	**LCDR3**	**SEQ ID NO**
139109	RASQSISSYLN	1171	AASSLQS	1211	QQSYSTPYT	1251
139103	RASQSISSSFLA	1172	GASRRAT	1212	QQYHSSPSWT	1252

139105	RSSQSLLHSNGYNYLD	1173	LGSNRAS	1213	MQALQTPYT	1253
139111	KSSQSLLRNDGKTPLY	1174	EVSNRFS	1214	MQNIQFPS	1254
139100	RSSQSLLHSNGYNYLN	1175	LGSKRAS	1215	MQALQTPYT	1255
139101	RASQSISSYLN	1176	GASTLAS	1216	QQSYKRAS	1256
139102	RSSQSLLYSNGYNYVD	1177	LGSNRAS	1217	MQGRQFPYS	1257
139104	RASQSVSSNLA	1178	GASTRAS	1218	QQYGSSLT	1258
139106	RASQSVSSKLA	1179	GASIRAT	1219	QQYGSSSWT	1259
139107	RASQSVGSTNLA	1180	DASNRAT	1220	QQYGSSPPWT	1260
139108	RASQSISSYLN	1181	AASSLQS	1221	QQSYTLA	1261
139110	KSSESLVHNSGKTYLN	1182	EVSNRDS	1222	MQGTHWPGT	1262
139112	QASEDINKFLN	1183	DASTLQT	1223	QQYESLPLT	1263
139113	RASQSVGSNLA	1184	GASTRAT	1224	QQYNDWLPVT	1264
139114	RASQSIGSSSLA	1185	GASSRAS	1225	QQYAGSPPFT	1265
149362	KASQDIDDAMN	1186	SATSPVP	1226	LQHDNFPLT	1266
149363	RASQDIYNNLA	1187	AANKSQS	1227	QHYYRFPYS	1267
149364	RSSQSLLHSNGYNYLD	1188	LGSNRAS	1228	MQALQTPYT	1268
149365	GGNNIGTKSVH	1189	DDSVRPS	1229	QVWDSDSEHVV	1269
149366	SGDGLSKKYVS	1190	RDKERPS	1230	QAWDDTTVV	1270
149367	RASQGIRNWLA	1191	AASNLQS	1231	QKYNSAPFT	1271
149368	GGNNIGSKSVH	1192	GKNNRPS	1232	SSRDSSGDHLRV	1272
149369	QGDSLGNYYAT	1193	GTNNRPS	1233	NSRDSSGHHLL	1273
BCMA_EBB-C1978-A4	RASQSVSSAYLA	1194	GASTRAT	1234	QHYGSSFNGSSLFT	1274
BCMA_EBB-C1978-G1	RASQSVSNSLA	1195	DASSRAT	1235	QQFGTSSGLT	1275
BCMA_EBB-C1979-C1	RASQSVSSSFLA	1196	GASSRAT	1236	QQYHSSPSWT	1276
BCMA_EBB-C1978-C7	RASQSVSTTFLA	1197	GSSNRAT	1237	QQYHSSPSWT	1277
BCMA_EBB-C1978-D10	RASQSISSYLN	1198	AASSLQS	1238	QQSYSTPYS	1278
BCMA_EBB-C1979-C12	RATQSIGSSFLA	1199	GASQRAT	1239	QHYESSPSWT	1279
BCMA_EBB-C1980-G4	RASQSVSSSYLA	1200	GASSRAT	1240	QQYGSPPRFT	1280
BCMA_EBB-C1980-D2	RASQSVSSSYLA	1201	GASSRAT	1241	QHYGSSPSWT	1281
BCMA_EBB-C1978-A10	RASQRVASNYLA	1202	GASSRAT	1242	QHYDSSPSWT	1282
BCMA_EBB-C1978-D4	RASQSLSSNFLA	1203	GASNWAT	1243	QYYGTSPMYT	1283
BCMA_EBB-C1980-A2	RSSQSLLHSNGYNYLD	1204	LGSNRAS	1244	MQALQTPLT	1284

BCMA_EBB-C1981-C3	RASQSVSSSYLA	1205	GTSSRAT	1245	QHYGNSPPKFT	1285
BCMA_EBB-C1978-G4	RASQSVASSFLA	1206	GASGRAT	1246	QHYGGSPRLT	1286
A7D12.2	RASQDVNTAVS	1207	SASYRYT	1247	QQHYSTPWT	1287
C11D5.3	RASESVSVIGAHLIH	1208	LASNLET	1248	LQSRIFPRT	1288
C12A3.2	RASESVTILGSHLIY	1209	LASNVQT	1249	LQSRTIPRT	1289
C13F12.1	RASESVTILGSHLIY	1210	LASNVQT	1250	LQSRTIPRT	1290

Table 5. Additional exemplary BCMA CAR sequences

Name	SEQ ID NO:
A7D12.2 VH	255
A7D12.2 VL	259
A7D12.2 scFv domain	263
A7D12.2 Full CART	267
C11D5.3 VH	256
C11D5.3 VL	260
C11D5.3 scFv domain	264
C11D5.3 Full CART	268
C12A3.2 VH	257
C12A3.2 VL	261
C12A3.2 scFv domain	265
C12A3.2 Full CART	269
C13F12.1 VH	258
C13F12.1 VL	262
C13F12.1 scFv domain	266
C13F12.1 Full CART	270

RNA Transfection

Disclosed herein are methods for producing an in vitro transcribed RNA CAR. The present invention also includes a CAR encoding RNA construct that can be directly transfected into a cell. A method for generating mRNA for use in transfection can involve in vitro transcription (IVT) of a template with specially designed primers, followed by polyA addition, to produce a construct containing 3' and 5' untranslated sequence ("UTR"), a 5' cap and/or Internal Ribosome Entry Site (IRES), the nucleic acid to be expressed, and a polyA tail, typically 50-2000 bases (SEQ ID NO: 2025) in length. RNA so produced can efficiently transfect different kinds of cells. In one aspect, the template includes sequences for the CAR.

In one aspect the anti-BCMA CAR is encoded by a messenger RNA (mRNA). In one aspect the mRNA encoding the anti-BCMA CAR is introduced into an immune effector cell, e.g., a T cell or a NK cell, for production of a CAR-expressing cell (e.g., CART cell or CAR-expressing NK cell).

In one embodiment, the in vitro transcribed RNA CAR can be introduced to a cell as a form of transient transfection. The RNA is produced by in vitro transcription using a polymerase chain reaction (PCR)-generated template. DNA of interest from any source can be directly converted by PCR into a template for in vitro mRNA synthesis using appropriate primers and RNA polymerase. The source of the DNA can be, for example, genomic DNA, plasmid DNA, phage DNA, cDNA, synthetic DNA sequence or any other appropriate source of DNA. The desired temple for in vitro transcription is a CAR of the present invention. For example, the template for the RNA CAR comprises an extracellular region comprising a single chain variable domain of an anti-tumor antibody; a hinge region, a transmembrane domain (e.g., a transmembrane domain of CD8a); and a cytoplasmic region that includes an intracellular signaling domain, e.g., comprising the signaling domain of CD3-zeta and the signaling domain of 4-1BB.

In one embodiment, the DNA to be used for PCR contains an open reading frame. The DNA can be from a naturally occurring DNA sequence from the genome of an organism. In one embodiment, the nucleic acid can include some or all of the 5' and/or 3' untranslated regions (UTRs). The nucleic acid can include exons and introns. In one embodiment, the DNA to be used for PCR is a human nucleic acid sequence. In another embodiment, the DNA to be used for PCR is a human nucleic acid sequence including the 5' and 3' UTRs. The DNA can alternatively be an artificial DNA sequence that is not normally expressed in a naturally occurring organism. An exemplary artificial DNA sequence is one that contains portions of genes that are ligated together to form an open reading frame that encodes a fusion protein. The portions of DNA that are ligated together can be from a single organism or from more than one organism.

PCR is used to generate a template for in vitro transcription of mRNA which is used for transfection. Methods for performing PCR are well known in the art. Primers for use in PCR are designed to have regions that are substantially complementary to regions of the DNA to be used as a template for the PCR. "Substantially complementary," as used herein, refers to sequences of nucleotides where a majority or all of the bases in the primer sequence are complementary, or one or more bases are non-complementary, or mismatched. Substantially complementary sequences are able to anneal or hybridize with the intended DNA target under annealing conditions used for PCR. The primers can be designed to be substantially complementary to any portion of the DNA template. For example, the primers can be designed to amplify the portion of a nucleic acid that is normally transcribed in cells (the open reading frame), including 5' and 3' UTRs. The primers can also be designed to amplify a portion of a nucleic acid that encodes a particular domain of interest. In one embodiment, the primers are designed to amplify the coding region of a human cDNA, including all or portions of the 5' and 3' UTRs. Primers useful for PCR can be generated by synthetic methods that are well known in the art. "Forward primers"

are primers that contain a region of nucleotides that are substantially complementary to nucleotides on the DNA template that are upstream of the DNA sequence that is to be amplified. "Upstream" is used herein to refer to a location 5, to the DNA sequence to be amplified relative to the coding strand. "Reverse primers" are primers that contain a region of nucleotides that are substantially complementary to a double-stranded DNA template that are downstream of the DNA sequence that is to be amplified. "Downstream" is used herein to refer to a location 3' to the DNA sequence to be amplified relative to the coding strand.

Any DNA polymerase useful for PCR can be used in the methods disclosed herein. The reagents and polymerase are commercially available from a number of sources.

Chemical structures with the ability to promote stability and/or translation efficiency may also be used. The RNA preferably has 5' and 3' UTRs. In one embodiment, the 5' UTR is between one and 3000 nucleotides in length. The length of 5' and 3' UTR sequences to be added to the coding region can be altered by different methods, including, but not limited to, designing primers for PCR that anneal to different regions of the UTRs. Using this approach, one of ordinary skill in the art can modify the 5' and 3' UTR lengths required to achieve optimal translation efficiency following transfection of the transcribed RNA.

The 5' and 3' UTRs can be the naturally occurring, endogenous 5' and 3' UTRs for the nucleic acid of interest. Alternatively, UTR sequences that are not endogenous to the nucleic acid of interest can be added by incorporating the UTR sequences into the forward and reverse primers or by any other modifications of the template. The use of UTR sequences that are not endogenous to the nucleic acid of interest can be useful for modifying the stability and/or translation efficiency of the RNA. For example, it is known that AU-rich elements in 3' UTR sequences can decrease the stability of mRNA. Therefore, 3' UTRs can be selected or designed to increase the stability of the transcribed RNA based on properties of UTRs that are well known in the art.

In one embodiment, the 5' UTR can contain the Kozak sequence of the endogenous nucleic acid. Alternatively, when a 5' UTR that is not endogenous to the nucleic acid of interest is being added by PCR as described above, a consensus Kozak sequence can be redesigned by adding the 5' UTR sequence. Kozak sequences can increase the efficiency of translation of some RNA transcripts, but does not appear to be required for all RNAs to enable efficient translation. The requirement for Kozak sequences for many mRNAs is known in the art. In other embodiments the 5' UTR can be 5'UTR of an RNA virus whose RNA genome is stable in cells. In other embodiments various nucleotide analogues can be used in the 3' or 5' UTR to impede exonuclease degradation of the mRNA.

To enable synthesis of RNA from a DNA template without the need for gene cloning, a promoter of transcription should be attached to the DNA template upstream of the sequence to be transcribed. When a sequence that functions as a promoter for an RNA polymerase is added to the 5' end of the forward primer, the RNA polymerase promoter becomes incorporated into the PCR product upstream of the open reading frame that is to be transcribed. In one preferred embodiment, the promoter is a T7 polymerase promoter, as described elsewhere herein. Other useful promoters include, but are not limited to, T3 and SP6 RNA polymerase promoters. Consensus nucleotide sequences for T7, T3 and SP6 promoters are known in the art.

In a preferred embodiment, the mRNA has both a cap on the 5' end and a 3' poly(A) tail which determine ribosome binding, initiation of translation and stability mRNA in the cell. On a circular DNA template, for instance, plasmid DNA, RNA polymerase produces a long concatameric product which is not suitable for expression in eukaryotic cells. The transcription of plasmid DNA linearized at the end of the 3' UTR results in normal sized mRNA which is not effective in eukaryotic transfection even if it is polyadenylated after transcription.

On a linear DNA template, phage T7 RNA polymerase can extend the 3' end of the transcript beyond the last base of the template (Schenborn and Mierendorf, Nuc Acids Res., 13:6223-36 (1985); Nacheva and Berzal-Herranz, Eur. J. Biochem., 270:1485-65 (2003).

The conventional method of integration of polyA/T stretches into a DNA template is molecular cloning. However polyA/T sequence integrated into plasmid DNA can cause plasmid instability, which is why plasmid DNA templates obtained from bacterial cells are often highly contaminated with deletions and other aberrations. This makes cloning procedures not only laborious and time consuming but often not reliable. That is why a method which allows construction of DNA templates with polyA/T 3' stretch without cloning highly desirable.

The polyA/T segment of the transcriptional DNA template can be produced during PCR by using a reverse primer containing a polyT tail, such as 100T tail (SEQ ID NO: 2026) (size can be 50-5000 T (SEQ ID NO: 2027)), or after PCR by any other method, including, but not limited to, DNA ligation or in vitro recombination. Poly(A) tails also provide stability to RNAs and reduce their degradation. Generally, the length of a poly(A) tail positively correlates with the stability of the transcribed RNA. In one embodiment, the poly(A) tail is between 100 and 5000 adenosines (SEQ ID NO: 2028).

Poly(A) tails of RNAs can be further extended following in vitro transcription with the use of a poly(A) polymerase, such as E. coli polyA polymerase (E-PAP). In one embodiment, increasing the length of a poly(A) tail from 100 nucleotides to between 300 and 400 nucleotides (SEQ ID NO: 2024)

results in about a two-fold increase in the translation efficiency of the RNA. Additionally, the attachment of different chemical groups to the 3' end can increase mRNA stability. Such attachment can contain modified/artificial nucleotides, aptamers and other compounds. For example, ATP analogs can be incorporated into the poly(A) tail using poly(A) polymerase. ATP analogs can further increase the stability of the RNA.

5' caps on also provide stability to RNA molecules. In a preferred embodiment, RNAs produced by the methods disclosed herein include a 5' cap. The 5' cap is provided using techniques known in the art and described herein (Cougot, et al., Trends in Biochem. Sci., 29:436-444 (2001); Stepinski, et al., RNA, 7:1468-95 (2001); Elango, et al., Biochim. Biophys. Res. Commun., 330:958-966 (2005)).

The RNAs produced by the methods disclosed herein can also contain an internal ribosome entry site (IRES) sequence. The IRES sequence may be any viral, chromosomal or artificially designed sequence which initiates cap-independent ribosome binding to mRNA and facilitates the initiation of translation. Any solutes suitable for cell electroporation, which can contain factors facilitating cellular permeability and viability such as sugars, peptides, lipids, proteins, antioxidants, and surfactants can be included.

RNA can be introduced into target cells using any of a number of different methods, for instance, commercially available methods which include, but are not limited to, electroporation (Amaxa Nucleofector-II (Amaxa Biosystems, Cologne, Germany)), (ECM 830 (BTX) (Harvard Instruments, Boston, Mass.) or the Gene Pulser II (BioRad, Denver, Colo.), Multiporator (Eppendort, Hamburg Germany), cationic liposome mediated transfection using lipofection, polymer encapsulation, peptide mediated transfection, or biolistic particle delivery systems such as “gene guns” (see, for example, Nishikawa, et al. Hum Gene Ther., 12(8):861-70 (2001).

Non-viral delivery methods

In some aspects, non-viral methods can be used to deliver a nucleic acid encoding a CAR described herein into a cell or tissue or a subject.

In some embodiments, the non-viral method includes the use of a transposon (also called a transposable element). In some embodiments, a transposon is a piece of DNA that can insert itself at a location in a genome, for example, a piece of DNA that is capable of self-replicating and inserting its copy into a genome, or a piece of DNA that can be spliced out of a longer nucleic acid and inserted into another place in a genome. For example, a transposon comprises a DNA sequence made up of inverted repeats flanking genes for transposition.

Exemplary methods of nucleic acid delivery using a transposon include a Sleeping Beauty

transposon system (SBTS) and a piggyBac (PB) transposon system. See, e.g., Aronovich et al. Hum. Mol. Genet. 20.R1(2011):R14-20; Singh et al. Cancer Res. 15(2008):2961–2971; Huang et al. Mol. Ther. 16(2008):580–589; Grabundzija et al. Mol. Ther. 18(2010):1200–1209; Kebriaei et al. Blood. 122.21(2013):166; Williams. Molecular Therapy 16.9(2008):1515–16; Bell et al. Nat. Protoc. 2.12(2007):3153-65; and Ding et al. Cell. 122.3(2005):473-83, all of which are incorporated herein by reference.

The SBTS includes two components: 1) a transposon containing a transgene and 2) a source of transposase enzyme. The transposase can transpose the transposon from a carrier plasmid (or other donor DNA) to a target DNA, such as a host cell chromosome/genome. For example, the transposase binds to the carrier plasmid/donor DNA, cuts the transposon (including transgene(s)) out of the plasmid, and inserts it into the genome of the host cell. See, e.g., Aronovich et al. *supra.*

Exemplary transposons include a pT2-based transposon. See, e.g., Grabundzija et al. Nucleic Acids Res. 41.3(2013):1829-47; and Singh et al. Cancer Res. 68.8(2008): 2961–2971, all of which are incorporated herein by reference. Exemplary transposases include a Tc1/mariner-type transposase, e.g., the SB10 transposase or the SB11 transposase (a hyperactive transposase which can be expressed, e.g., from a cytomegalovirus promoter). See, e.g., Aronovich et al.; Kebriaei et al.; and Grabundzija et al., all of which are incorporated herein by reference.

Use of the SBTS permits efficient integration and expression of a transgene, e.g., a nucleic acid encoding a CAR described herein. Provided herein are methods of generating a cell, e.g., T cell or NK cell, that stably expresses a CAR described herein, e.g., using a transposon system such as SBTS.

In accordance with methods described herein, in some embodiments, one or more nucleic acids, e.g., plasmids, containing the SBTS components are delivered to a cell (e.g., T or NK cell). For example, the nucleic acid(s) are delivered by standard methods of nucleic acid (e.g., plasmid DNA) delivery, e.g., methods described herein, e.g., electroporation, transfection, or lipofection. In some embodiments, the nucleic acid contains a transposon comprising a transgene, e.g., a nucleic acid encoding a CAR described herein. In some embodiments, the nucleic acid contains a transposon comprising a transgene (e.g., a nucleic acid encoding a CAR described herein) as well as a nucleic acid sequence encoding a transposase enzyme. In other embodiments, a system with two nucleic acids is provided, e.g., a dual-plasmid system, e.g., where a first plasmid contains a transposon comprising a transgene, and a second plasmid contains a nucleic acid sequence encoding a transposase enzyme. For example, the first and the second nucleic acids are co-delivered into a host cell.

In some embodiments, cells, e.g., T or NK cells, are generated that express a CAR described herein by using a combination of gene insertion using the SBTS and genetic editing using a nuclease (e.g.,

Zinc finger nucleases (ZFNs), Transcription Activator-Like Effector Nucleases (TALENs), the CRISPR/Cas system, or engineered meganuclease re-engineered homing endonucleases).

In some embodiments, use of a non-viral method of delivery permits reprogramming of cells, e.g., T or NK cells, and direct infusion of the cells into a subject. Advantages of non-viral vectors include but are not limited to the ease and relatively low cost of producing sufficient amounts required to meet a patient population, stability during storage, and lack of immunogenicity.

Nucleic Acid Constructs Encoding a CAR

The present invention also provides nucleic acid molecules encoding one or more CAR constructs described herein. In one aspect, the nucleic acid molecule is provided as a messenger RNA transcript. In one aspect, the nucleic acid molecule is provided as a DNA construct.

Accordingly, in one aspect, the invention pertains to an isolated nucleic acid molecule encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain, a transmembrane domain, and an intracellular signaling domain comprising a stimulatory domain, e.g., a costimulatory signaling domain and/or a primary signaling domain, e.g., zeta chain.

The nucleic acid sequences coding for the desired molecules can be obtained using recombinant methods known in the art, such as, for example by screening libraries from cells expressing the gene, by deriving the gene from a vector known to include the same, or by isolating directly from cells and tissues containing the same, using standard techniques. Alternatively, the gene of interest can be produced synthetically, rather than cloned.

The present invention also provides vectors in which a DNA of the present invention is inserted. Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. A retroviral vector may also be, e.g., a gammaretroviral vector. A gammaretroviral vector may include, e.g., a promoter, a packaging signal (ψ), a primer binding site (PBS), one or more (e.g., two) long terminal repeats (LTR), and a transgene of interest, e.g., a gene encoding a CAR. A gammaretroviral vector may lack viral structural gens such as gag, pol, and env. Exemplary gammaretroviral vectors include Murine Leukemia Virus (MLV), Spleen-Focus Forming Virus (SFFV), and Myeloproliferative Sarcoma Virus (MPSV), and vectors derived therefrom. Other gammaretroviral vectors are described, e.g., in Tobias Maetzig et al., "Gammaretroviral Vectors: Biology, Technology and Application" Viruses. 2011 Jun; 3(6): 677–713.

In another embodiment, the vector comprising the nucleic acid encoding the desired CAR of the invention is an adenoviral vector (A5/35). In another embodiment, the expression of nucleic acids encoding CARs can be accomplished using of transposons such as sleeping beauty, CRISPR, CAS9, and zinc finger nucleases. See below June et al. 2009*Nature Reviews Immunology* 9.10: 704-716, is incorporated herein by reference.

In brief summary, the expression of natural or synthetic nucleic acids encoding CARs is typically achieved by operably linking a nucleic acid encoding the CAR polypeptide or portions thereof to a promoter, and incorporating the construct into an expression vector. The vectors can be suitable for replication and integration eukaryotes. Typical cloning vectors contain transcription and translation terminators, initiation sequences, and promoters useful for regulation of the expression of the desired nucleic acid sequence.

The expression constructs of the present invention may also be used for nucleic acid immunization and gene therapy, using standard gene delivery protocols. Methods for gene delivery are known in the art. See, e.g., U.S. Pat. Nos. 5,399,346, 5,580,859, 5,589,466, incorporated by reference herein in their entireties. In another embodiment, the invention provides a gene therapy vector.

The nucleic acid can be cloned into a number of types of vectors. For example, the nucleic acid can be cloned into a vector including, but not limited to a plasmid, a phagemid, a phage derivative, an animal virus, and a cosmid. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors, and sequencing vectors.

Further, the expression vector may be provided to a cell in the form of a viral vector. Viral vector technology is well known in the art and is described, for example, in Sambrook et al., 2012, MOLECULAR CLONING: A LABORATORY MANUAL, volumes 1 -4, Cold Spring Harbor Press, NY), and in other virology and molecular biology manuals. Viruses, which are useful as vectors include, but are not limited to, retroviruses, adenoviruses, adeno- associated viruses, herpes viruses, and lentiviruses. In general, a suitable vector contains an origin of replication functional in at least one organism, a promoter sequence, convenient restriction endonuclease sites, and one or more selectable markers, (e.g., WO 01/96584; WO 01/29058; and U.S. Pat. No. 6,326,193).

A number of viral based systems have been developed for gene transfer into mammalian cells. For example, retroviruses provide a convenient platform for gene delivery systems. A selected gene can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to cells of the subject either in vivo or ex vivo. A number of retroviral systems are known in the art. In some embodiments, adenovirus vectors are used. A number of adenovirus vectors are known in the art. In one embodiment, lentivirus vectors are used.

Additional promoter elements, e.g., enhancers, regulate the frequency of transcriptional initiation. Typically, these are located in the region 30-110 bp upstream of the start site, although a number of promoters have been shown to contain functional elements downstream of the start site as well. The spacing between promoter elements frequently is flexible, so that promoter function is preserved when elements are inverted or moved relative to one another. In the thymidine kinase (tk) promoter, the spacing between promoter elements can be increased to 50 bp apart before activity begins to decline. Depending on the promoter, it appears that individual elements can function either cooperatively or independently to activate transcription.

An example of a promoter that is capable of expressing a CAR transgene in a mammalian T cell is the EF1a promoter. The native EF1a promoter drives expression of the alpha subunit of the elongation factor-1 complex, which is responsible for the enzymatic delivery of aminoacyl tRNAs to the ribosome. The EF1a promoter has been extensively used in mammalian expression plasmids and has been shown to be effective in driving CAR expression from transgenes cloned into a lentiviral vector. See, e.g., Milone et al., Mol. Ther. 17(8): 1453–1464 (2009).

Another example of a promoter is the immediate early cytomegalovirus (CMV) promoter sequence. This promoter sequence is a strong constitutive promoter sequence capable of driving high levels of expression of any polynucleotide sequence operatively linked thereto. However, other constitutive promoter sequences may also be used, including, but not limited to the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV), human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous sarcoma virus promoter, as well as human gene promoters such as, but not limited to, the actin promoter, the myosin promoter, the elongation factor-1α promoter, the hemoglobin promoter, and the creatine kinase promoter. Further, the invention should not be limited to the use of constitutive promoters. Inducible promoters are also contemplated as part of the invention. The use of an inducible promoter provides a molecular switch capable of turning on expression of the polynucleotide sequence which it is operatively linked when such expression is desired, or turning off the expression when expression is not desired. Examples of inducible promoters include, but are not limited to a metallothionine promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter.

Another example of a promoter is the phosphoglycerate kinase (PGK) promoter. In embodiments, a truncated PGK promoter (e.g., a PGK promoter with one or more, e.g., 1, 2, 5, 10, 100, 200, 300, or 400, nucleotide deletions when compared to the wild-type PGK promoter sequence) may be desired. The nucleotide sequences of exemplary PGK promoters are provided below.

WT PGK Promoter

ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACGCGAGGCCTCCGAACG
TCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGATGGCGGGGTGTGGGGCGGAGGGCGTG
GCGGGGAAGGGCCGGCGACGAGAGCCGCGCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCG
CCAGCCGCGCGACGGTAACGAGGGACCGCGACAGGCAGACGCTCCCATGATCACTCTGCACGCCGAA
GGCAAATAGTGCAGGCCGTGCGGCGCTTGGCGTTCCTTGGAAGGGCTGAATCCCCGCCTCGTCCTTC
GCAGCGGCCCCCCGGGTGTTCCCATCGCCGCTTCTAGGCCCACTGCGACGCTTGCCTGCACTTCTTA
CACGCTCTGGGTCCCAGCCGCGGCGACGCAAAGGGCCTTGGTGCGGGTCTCGTCGGCGCAGGGACGC
GTTTGGGTCCCGACGGAACCTTTTCCGCGTTGGGGTTGGGGCACCATAAGCT
(SEQ ID NO: 1291)

Exemplary truncated PGK Promoters:

PGK100:
ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACGCGAGGCCTCCGAACG
TCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGATGGCGGGGTG
(SEQ ID NO: 1292)

PGK200:
ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACGCGAGGCCTCCGAACG
TCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGATGGCGGGGTGTGGGGCGGAGGGCGTG
GCGGGGAAGGGCCGGCGACGAGAGCCGCGCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCG
CCAGCCGCGCGACGGTAACG
(SEQ ID NO: 1293)

PGK300:
ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACGCGAGGCCTCCGAACG
TCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGATGGCGGGGTGTGGGGCGGAGGGCGTG
GCGGGGAAGGGCCGGCGACGAGAGCCGCGCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCG
CCAGCCGCGCGACGGTAACGAGGGACCGCGACAGGCAGACGCTCCCATGATCACTCTGCACGCCGAA
GGCAAATAGTGCAGGCCGTGCGGCGCTTGGCGTTCCTTGGAAGGGCTGAATCCCCG
(SEQ ID NO: 1294)

PGK400:
ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACGCGAGGCCTCCGAACG
TCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGATGGCGGGGTGTGGGGCGGAGGGCGTG
GCGGGGAAGGGCCGGCGACGAGAGCCGCGCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCG
CCAGCCGCGCGACGGTAACGAGGGACCGCGACAGGCAGACGCTCCCATGATCACTCTGCACGCCGAA
GGCAAATAGTGCAGGCCGTGCGGCGCTTGGCGTTCCTTGGAAGGGCTGAATCCCCGCCTCGTCCTTC
GCAGCGGCCCCCCGGGTGTTCCCATCGCCGCTTCTAGGCCCACTGCGACGCTTGCCTGCACTTCTTA
CACGCTCTGGGTCCCAGCCG
(SEQ ID NO: 1295)

A vector may also include, e.g., a signal sequence to facilitate secretion, a polyadenylation signal and transcription terminator (e.g., from Bovine Growth Hormone (BGH) gene), an element allowing episomal replication and replication in prokaryotes (e.g. SV40 origin and ColE1 or others known in the art) and/or elements to allow selection (e.g., ampicillin resistance gene and/or zeocin marker).

In order to assess the expression of a CAR polypeptide or portions thereof, the expression vector to be introduced into a cell can also contain either a selectable marker gene or a reporter gene or both to facilitate identification and selection of expressing cells from the population of cells sought to be transfected or infected through viral vectors. In other aspects, the selectable marker may be carried on a separate piece of DNA and used in a co- transfection procedure. Both selectable markers and reporter genes may be flanked with appropriate regulatory sequences to enable expression in the host cells. Useful selectable markers include, for example, antibiotic-resistance genes, such as neo and the like.

Reporter genes are used for identifying potentially transfected cells and for evaluating the functionality of regulatory sequences. In general, a reporter gene is a gene that is not present in or expressed by the recipient organism or tissue and that encodes a polypeptide whose expression is manifested by some easily detectable property, e.g., enzymatic activity. Expression of the reporter gene is assayed at a suitable time after the DNA has been introduced into the recipient cells. Suitable reporter genes may include genes encoding luciferase, beta-galactosidase, chloramphenicol acetyl transferase, secreted alkaline phosphatase, or the green fluorescent protein gene (e.g., Ui-Tei et al., 2000 FEBS Letters 479: 79-82). Suitable expression systems are well known and may be prepared using known techniques or obtained commercially. In general, the construct with the minimal 5' flanking region showing the highest level of expression of reporter gene is identified as the promoter. Such promoter regions may be linked to a reporter gene and used to evaluate agents for the ability to modulate promoter- driven transcription.

In one embodiment, the vector can further comprise a nucleic acid encoding a second CAR. In one embodiment, the second CAR includes an antigen binding domain to a target expressed on acute myeloid leukemia cells, such as, e.g., CD123, CD34, CLL-1, folate receptor beta, or FLT3; or a target expressed on a B cell, e.g., CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a. In one embodiment, the vector comprises a nucleic acid sequence encoding a first CAR that specifically binds a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a nucleic acid encoding a second CAR that specifically binds a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. In one embodiment, the vector comprises a nucleic acid encoding a first BCMA CAR that includes a BCMA binding domain, a transmembrane domain and a costimulatory domain and a nucleic acid encoding a second CAR that targets an antigen other than BCMA (e.g., an antigen expressed on AML cells, e.g., CD123, CD34, CLL-1, folate receptor beta, or FLT3; or an antigen expressed on a B cell, e.g., CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another

embodiment, the vector comprises a nucleic acid encoding a first BCMA CAR that includes a BCMA binding domain, a transmembrane domain and a primary signaling domain and a nucleic acid encoding a second CAR that specifically binds an antigen other than BCMA (e.g., an antigen expressed on AML cells, e.g., CD123, CD34, CLL-1, folate receptor beta, or FLT3; or an antigen expressed on a B cell, e.g., CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In one embodiment, the vector comprises a nucleic acid encoding a BCMA CAR described herein and a nucleic acid encoding an inhibitory CAR. In one embodiment, the inhibitory CAR comprises an antigen binding domain that binds an antigen found on normal cells but not cancer cells, e.g., normal cells that also express BCMA. In one embodiment, the inhibitory CAR comprises the antigen binding domain, a transmembrane domain and an intracellular domain of an inhibitory molecule. For example, the intracellular domain of the inhibitory CAR can be an intracellular domain of PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGFR beta.

In embodiments, the vector may comprise two or more nucleic acid sequences encoding a CAR, e.g., a BCMA CAR described herein and a second CAR, e.g., an inhibitory CAR or a CAR that specifically binds to an antigen other than BCMA (e.g., an antigen expressed on AML cells, e.g., CD123, CLL-1, CD34, FLT3, or folate receptor beta; or antigen expresson B cells, e.g., CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a). In such embodiments, the two or more nucleic acid sequences encoding the CAR are encoded by a single nucleic molecule in the same frame and as a single polypeptide chain. In this aspect, the two or more CARs, can, e.g., be separated by one or more peptide cleavage sites. (e.g., an auto-cleavage site or a substrate for an intracellular protease). Examples of peptide cleavage sites include the following, wherein the GSG residues are optional:

T2A: (GSG) E G R G S L L T C G D V E E N P G P (SEQ ID NO: 1296)

P2A: (GSG) A T N F S L L K Q A G D V E E N P G P (SEQ ID NO: 1297)

E2A: (GSG) Q C T N Y A L L K L A G D V E S N P G P (SEQ ID NO: 1298)

F2A: (GSG) V K Q T L N F D L L K L A G D V E S N P G P (SEQ ID NO: 1299)

Methods of introducing and expressing genes into a cell are known in the art. In the context of an expression vector, the vector can be readily introduced into a host cell, e.g., mammalian, bacterial,

yeast, or insect cell by any method in the art. For example, the expression vector can be transferred into a host cell by physical, chemical, or biological means.

Physical methods for introducing a polynucleotide into a host cell include calcium phosphate precipitation, lipofection, particle bombardment, microinjection, electroporation, and the like. Methods for producing cells comprising vectors and/or exogenous nucleic acids are well-known in the art. See, for example, Sambrook et al., 2012, MOLECULAR CLONING: A LABORATORY MANUAL, volumes 1 -4, Cold Spring Harbor Press, NY). A preferred method for the introduction of a polynucleotide into a host cell is calcium phosphate transfection

Biological methods for introducing a polynucleotide of interest into a host cell include the use of DNA and RNA vectors. Viral vectors, and especially retroviral vectors, have become the most widely used method for inserting genes into mammalian, e.g., human cells. Other viral vectors can be derived from lentivirus, poxviruses, herpes simplex virus I, adenoviruses and adeno-associated viruses, and the like. See, for example, U.S. Pat. Nos. 5,350,674 and 5,585,362.

Chemical means for introducing a polynucleotide into a host cell include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. An exemplary colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (e.g., an artificial membrane vesicle). Other methods of state-of-the-art targeted delivery of nucleic acids are available, such as delivery of polynucleotides with targeted nanoparticles or other suitable sub-micron sized delivery system.

In the case where a non-viral delivery system is utilized, an exemplary delivery vehicle is a liposome. The use of lipid formulations is contemplated for the introduction of the nucleic acids into a host cell (in vitro, ex vivo or in vivo). In another aspect, the nucleic acid may be associated with a lipid. The nucleic acid associated with a lipid may be encapsulated in the aqueous interior of a liposome, interspersed within the lipid bilayer of a liposome, attached to a liposome via a linking molecule that is associated with both the liposome and the oligonucleotide, entrapped in a liposome, complexed with a liposome, dispersed in a solution containing a lipid, mixed with a lipid, combined with a lipid, contained as a suspension in a lipid, contained or complexed with a micelle, or otherwise associated with a lipid. Lipid, lipid/DNA or lipid/expression vector associated compositions are not limited to any particular structure in solution. For example, they may be present in a bilayer structure, as micelles, or with a "collapsed" structure. They may also simply be interspersed in a solution, possibly forming aggregates that are not uniform in size or shape. Lipids are fatty substances which may be naturally occurring or synthetic lipids. For example, lipids include the fatty droplets that naturally occur in the cytoplasm as

well as the class of compounds which contain long-chain aliphatic hydrocarbons and their derivatives, such as fatty acids, alcohols, amines, amino alcohols, and aldehydes.

Lipids suitable for use can be obtained from commercial sources. For example, dimyristyl phosphatidylcholine ("DMPC") can be obtained from Sigma, St. Louis, MO; dicetyl phosphate ("DCP") can be obtained from K & K Laboratories (Plainview, NY); cholesterol ("Choi") can be obtained from Calbiochem-Behring; dimyristyl phosphatidylglycerol ("DMPG") and other lipids may be obtained from Avanti Polar Lipids, Inc. (Birmingham, AL.). Stock solutions of lipids in chloroform or chloroform/methanol can be stored at about -20°C. Chloroform is used as the only solvent since it is more readily evaporated than methanol. "Liposome" is a generic term encompassing a variety of single and multilamellar lipid vehicles formed by the generation of enclosed lipid bilayers or aggregates. Liposomes can be characterized as having vesicular structures with a phospholipid bilayer membrane and an inner aqueous medium. Multilamellar liposomes have multiple lipid layers separated by aqueous medium. They form spontaneously when phospholipids are suspended in an excess of aqueous solution. The lipid components undergo self-rearrangement before the formation of closed structures and entrap water and dissolved solutes between the lipid bilayers (Ghosh et al., 1991 Glycobiology 5: 505-10). However, compositions that have different structures in solution than the normal vesicular structure are also encompassed. For example, the lipids may assume a micellar structure or merely exist as nonuniform aggregates of lipid molecules. Also contemplated are lipofectamine-nucleic acid complexes.

Regardless of the method used to introduce exogenous nucleic acids into a host cell or otherwise expose a cell to the inhibitor of the present invention, in order to confirm the presence of the recombinant DNA sequence in the host cell, a variety of assays may be performed. Such assays include, for example, "molecular biological" assays well known to those of skill in the art, such as Southern and Northern blotting, RT-PCR and PCR; "biochemical" assays, such as detecting the presence or absence of a particular peptide, e.g., by immunological means (ELISAs and Western blots) or by assays described herein to identify agents falling within the scope of the invention.

The present invention further provides a vector comprising a CAR encoding nucleic acid molecule. In one aspect, a CAR vector can be directly transduced into a cell, *e.g.,* a T cell or NK cell. In one aspect, the vector is a cloning or expression vector, *e.g.,* a vector including, but not limited to, one or more plasmids (*e.g.*, expression plasmids, cloning vectors, minicircles, minivectors, double minute chromosomes), retroviral and lentiviral vector constructs. In one aspect, the vector is capable of expressing the CAR construct in mammalian T cells or NK cells. In one aspect, the mammalian T cell is a human T cell. In one aspect, the mammalian NK cell is a human NK cell.

Sources of cells

Prior to expansion and genetic modification, a source of cells, e.g., immune effector cells (e.g., T cells or NK cells), is obtained from a subject. The term "subject" is intended to include living organisms in which an immune response can be elicited (e.g., mammals). Examples of subjects include humans, dogs, cats, mice, rats, and transgenic species thereof. T cells can be obtained from a number of sources, including peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors.

In certain aspects of the present invention, any number of immune effector cell (e.g., T cell or NK cell) lines available in the art, may be used. In certain aspects of the present invention, T cells can be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as Ficoll™ separation. In one preferred aspect, cells from the circulating blood of an individual are obtained by apheresis. The apheresis product typically contains lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and platelets. In one aspect, the cells collected by apheresis may be washed to remove the plasma fraction and to place the cells in an appropriate buffer or media for subsequent processing steps. In one aspect of the invention, the cells are washed with phosphate buffered saline (PBS). In an alternative aspect, the wash solution lacks calcium and may lack magnesium or may lack many if not all divalent cations.

Initial activation steps in the absence of calcium can lead to magnified activation. As those of ordinary skill in the art would readily appreciate a washing step may be accomplished by methods known to those in the art, such as by using a semi-automated "flow-through" centrifuge (for example, the Cobe 2991 cell processor, the Baxter CytoMate, or the Haemonetics Cell Saver 5) according to the manufacturer's instructions. After washing, the cells may be resuspended in a variety of biocompatible buffers, such as, for example, Ca-free, Mg-free PBS, PlasmaLyte A, or other saline solution with or without buffer. Alternatively, the undesirable components of the apheresis sample may be removed and the cells directly resuspended in culture media.

It is recognized that the methods of the application can utilize culture media conditions comprising 5% or less, for example 2%, human AB serum, and employ known culture media conditions and compositions, for example those described in Smith *et al.*, "Ex vivo expansion of human T cells for adoptive immunotherapy using the novel Xeno-free CTS Immune Cell Serum Replacement" *Clinical & Translational Immunology* (2015) 4, e31; doi:10.1038/cti.2014.31.

In one aspect, T cells are isolated from peripheral blood lymphocytes by lysing the red blood cells and depleting the monocytes, for example, by centrifugation through a PERCOLLTM gradient or

by counterflow centrifugal elutriation. A specific subpopulation of T cells, such as CD3+, CD4+, CD8+, CD45RA+, and/or CD45RO+T cells, can be further isolated by positive or negative selection techniques. For example, in one aspect, T cells are isolated by incubation with anti-CD3/anti-CD28 (e.g., 3x28)-conjugated beads, such as DYNABEADS® M-450 CD3/CD28 T, for a time period sufficient for positive selection of the desired T cells. In one aspect, the time period is about 30 minutes. In a further aspect, the time period ranges from 30 minutes to 36 hours or longer and all integer values there between. In a further aspect, the time period is at least 1, 2, 3, 4, 5, or 6 hours. In yet another preferred aspect, the time period is 10 to 24 hours. In one aspect, the incubation time period is 24 hours. Longer incubation times may be used to isolate T cells in any situation where there are few T cells as compared to other cell types, such in isolating tumor infiltrating lymphocytes (TIL) from tumor tissue or from immunocompromised individuals. Further, use of longer incubation times can increase the efficiency of capture of CD8+ T cells. Thus, by simply shortening or lengthening the time T cells are allowed to bind to the CD3/CD28 beads and/or by increasing or decreasing the ratio of beads to T cells (as described further herein), subpopulations of T cells can be preferentially selected for or against at culture initiation or at other time points during the process. Additionally, by increasing or decreasing the ratio of anti-CD3 and/or anti-CD28 antibodies on the beads or other surface, subpopulations of T cells can be preferentially selected for or against at culture initiation or at other desired time points. The skilled artisan would recognize that multiple rounds of selection can also be used in the context of this invention. In certain aspects, it may be desirable to perform the selection procedure and use the "unselected" cells in the activation and expansion process. "Unselected" cells can also be subjected to further rounds of selection.

Enrichment of a T cell population by negative selection can be accomplished with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immunoadherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4+ cells by negative selection, a monoclonal antibody cocktail typically includes antibodies to CD14, CD20, CD11b, CD16, HLA-DR, and CD8. In certain aspects, it may be desirable to enrich for or positively select for regulatory T cells which typically express CD4+, CD25+, CD62Lhi, GITR+, and FoxP3+. In certain aspects, it may be desirable to enrich for cells that are CD127low. Alternatively, in certain aspects, T regulatory cells are depleted by anti-C25 conjugated beads or other similar method of selection.

The methods described herein can include, e.g., selection of a specific subpopulation of immune effector cells, e.g., T cells, that are a T regulatory cell-depleted population, CD25+ depleted cells, using,

e.g., a negative selection technique, e.g., described herein. Preferably, the population of T regulatory depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells.

In one embodiment, T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, IL-2. In one embodiment, the anti-CD25 antibody, or fragment thereof, or CD25-binding ligand is conjugated to a substrate, e.g., a bead, or is otherwise coated on a substrate, e.g., a bead. In one embodiment, the anti-CD25 antibody, or fragment thereof, is conjugated to a substrate as described herein.

In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using CD25 depletion reagent from Miltenyi™. In one embodiment, the ratio of cells to CD25 depletion reagent is 1e7 cells to 20 uL, or 1e7 cells to15 uL, or 1e7 cells to 10 uL, or 1e7 cells to 5 uL, or 1e7 cells to 2.5 uL, or 1e7 cells to 1.25 uL. In one embodiment, e.g., for T regulatory cells, e.g., CD25+ depletion, greater than 500 million cells/ml is used. In a further aspect, a concentration of cells of 600, 700, 800, or 900 million cells/ml is used.

In one embodiment, the population of immune effector cells to be depleted includes about 6 x 10^9 CD25+ T cells. In other aspects, the population of immune effector cells to be depleted include about 1 x 10^9 to 1x 10^{10} CD25+ T cell, and any integer value in between. In one embodiment, the resulting population T regulatory depleted cells has 2 x 10^9 T regulatory cells, e.g., CD25+ cells, or less (e.g., 1 x 10^9, 5 x 10^8, 1 x 10^8, 5 x 10^7, 1 x 10^7, or less CD25+ cells).

In one embodiment, the T regulatory cells, e.g., CD25+ cells, are removed from the population using the CliniMAC system with a depletion tubing set, such as, e.g., tubing 162-01. In one embodiment, the CliniMAC system is run on a depletion setting such as, e.g., DEPLETION2.1.

Without wishing to be bound by a particular theory, decreasing the level of negative regulators of immune cells (e.g., decreasing the number of unwanted immune cells, e.g., T_{REG} cells), in a subject prior to apheresis or during manufacturing of a CAR-expressing cell product can reduce the risk of subject relapse. For example, methods of depleting T_{REG} cells are known in the art. Methods of decreasing T_{REG} cells include, but are not limited to, cyclophosphamide, anti-GITR antibody (an anti-GITR antibody described herein), CD25-depletion, and combinations thereof.

In some embodiments, the manufacturing methods comprise reducing the number of (e.g., depleting) T_{REG} cells prior to manufacturing of the CAR-expressing cell. For example, manufacturing methods comprise contacting the sample, e.g., the apheresis sample, with an anti-GITR antibody and/or an anti-CD25 antibody (or fragment thereof, or a CD25-binding ligand), e.g., to deplete T_{REG} cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product.

In an embodiment, a subject is pre-treated with one or more therapies that reduce T_{REG} cells prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In an embodiment, methods of decreasing T_{REG} cells include, but are not limited to, administration to the subject of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof. Administration of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof, can occur before, during or after an infusion of the CAR-expressing cell product.

In an embodiment, a subject is pre-treated with cyclophosphamide prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In an embodiment, a subject is pre-treated with an anti-GITR antibody prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment.

In one embodiment, the population of cells to be removed are neither the regulatory T cells or tumor cells, but cells that otherwise negatively affect the expansion and/or function of CART cells, e.g. cells expressing CD14, CD11b, CD33, CD15, or other markers expressed by potentially immune suppressive cells. In one embodiment, such cells are envisioned to be removed concurrently with regulatory T cells and/or tumor cells, or following said depletion, or in another order.

The methods described herein can include more than one selection step, e.g., more than one depletion step. Enrichment of a T cell population by negative selection can be accomplished, e.g., with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immunoadherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4+ cells by negative selection, a monoclonal antibody cocktail can include antibodies to CD14, CD20, CD11b, CD16, HLA-DR, and CD8.

The methods described herein can further include removing cells from the population which express a tumor antigen, e.g., a tumor antigen that does not comprise CD25, e.g., CD19, CD30, CD38, CD123, CD20, CD14 or CD11b, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted, and tumor antigen depleted cells that are suitable for expression of a CAR, e.g., a CAR described herein. In one embodiment, tumor antigen expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-tumor antigen antibody, or fragment thereof, can be attached to the same substrate, e.g., bead, which can be used to remove the cells or an anti-CD25 antibody, or fragment thereof, or the anti-tumor antigen antibody, or fragment thereof, can be attached to separate beads, a mixture of which can be used

to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the tumor antigen expressing cells is sequential, and can occur, e.g., in either order.

Also provided are methods that include removing cells from the population which express a check point inhibitor, e.g., a check point inhibitor described herein, e.g., one or more of PD1+ cells, LAG3+ cells, and TIM3+ cells, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted cells, and check point inhibitor depleted cells, e.g., PD1+, LAG3+ and/or TIM3+ depleted cells. Exemplary check point inhibitors include PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGFR beta. In embodiments, the checkpoint inhibitor is PD1 or PD-L1. In one embodiment, check point inhibitor expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-check point inhibitor antibody, or fragment thereof, can be attached to the same bead which can be used to remove the cells, or an anti-CD25 antibody, or fragment thereof, and the anti-check point inhibitor antibody, or fragment there, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the check point inhibitor expressing cells is sequential, and can occur, e.g., in either order.

In one embodiment, a T cell population can be selected that expresses one or more of IFN-γ, TNFα, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, granzyme B, and perforin, or other appropriate molecules, e.g., other cytokines. Methods for screening for cell expression can be determined, e.g., by the methods described in PCT Publication No.: WO 2013/126712.

For isolation of a desired population of cells by positive or negative selection, the concentration of cells and surface (e.g., particles such as beads) can be varied. In certain aspects, it may be desirable to significantly decrease the volume in which beads and cells are mixed together (e.g., increase the concentration of cells), to ensure maximum contact of cells and beads. For example, in one aspect, a concentration of 2 billion cells/ml is used. In one aspect, a concentration of 1 billion cells/ml is used. In a further aspect, greater than 100 million cells/ml is used. In a further aspect, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet one aspect, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used. Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells, or from samples where there are many tumor cells present (e.g., leukemic blood, tumor tissue, etc.). Such populations of cells

may have therapeutic value and would be desirable to obtain. For example, using high concentration of cells allows more efficient selection of CD8+ T cells that normally have weaker CD28 expression.

In a related aspect, it may be desirable to use lower concentrations of cells. By significantly diluting the mixture of T cells and surface (e.g., particles such as beads), interactions between the particles and cells is minimized. This selects for cells that express high amounts of desired antigens to be bound to the particles. For example, CD4+ T cells express higher levels of CD28 and are more efficiently captured than CD8+ T cells in dilute concentrations. In one aspect, the concentration of cells used is 5 X 10e6/ml. In other aspects, the concentration used can be from about 1 X 10^5/ml to 1 X 10^6/ml, and any integer value in between.

In other aspects, the cells may be incubated on a rotator for varying lengths of time at varying speeds at either 2-10°C or at room temperature.

T cells for stimulation can also be frozen after a washing step. Wishing not to be bound by theory, the freeze and subsequent thaw step provides a more uniform product by removing granulocytes and to some extent monocytes in the cell population. After the washing step that removes plasma and platelets, the cells may be suspended in a freezing solution. While many freezing solutions and parameters are known in the art and will be useful in this context, one method involves using PBS containing 20% DMSO and 8% human serum albumin, or culture media containing 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin and 7.5% DMSO, or 31.25% Plasmalyte-A, 31.25% Dextrose 5%, 0.45% NaCl, 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin, and 7.5% DMSO or other suitable cell freezing media containing for example, Hespan and PlasmaLyte A, the cells then are frozen to -80°C at a rate of 1° per minute and stored in the vapor phase of a liquid nitrogen storage tank. Other methods of controlled freezing may be used as well as uncontrolled freezing immediately at -20° C or in liquid nitrogen.

In certain aspects, cryopreserved cells are thawed and washed as described herein and allowed to rest for one hour at room temperature prior to activation using the methods of the present invention.

Also contemplated in the context of the invention is the collection of blood samples or apheresis product from a subject at a time period prior to when the expanded cells as described herein might be needed. As such, the source of the cells to be expanded can be collected at any time point necessary, and desired cells, such as immune effector cells, e.g., T cells or NK cells, isolated and frozen for later use in cell therapy, e.g., T cell therapy, for any number of diseases or conditions that would benefit from cell therapy, e.g., T cell therapy, such as those described herein. In one aspect a blood sample or an apheresis is taken from a generally healthy subject. In certain aspects, a blood sample or an apheresis is taken from a generally healthy subject who is at risk of developing a disease, but who has not yet

developed a disease, and the cells of interest are isolated and frozen for later use. In certain aspects, the immune effector cells (e.g., T cells or NK cells) may be expanded, frozen, and used at a later time. In certain aspects, samples are collected from a patient shortly after diagnosis of a particular disease as described herein but prior to any treatments. In a further aspect, the cells are isolated from a blood sample or an apheresis from a subject prior to any number of relevant treatment modalities, including but not limited to treatment with agents such as natalizumab, efalizumab, antiviral agents, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, and irradiation.

In a further aspect of the present invention, T cells are obtained from a patient directly following treatment that leaves the subject with functional T cells. In this regard, it has been observed that following certain cancer treatments, in particular treatments with drugs that damage the immune system, shortly after treatment during the period when patients would normally be recovering from the treatment, the quality of T cells obtained may be optimal or improved for their ability to expand ex vivo. Likewise, following ex vivo manipulation using the methods described herein, these cells may be in a preferred state for enhanced engraftment and in vivo expansion. Thus, it is contemplated within the context of the present invention to collect blood cells, including T cells, dendritic cells, or other cells of the hematopoietic lineage, during this recovery phase. Further, in certain aspects, mobilization (for example, mobilization with GM-CSF) and conditioning regimens can be used to create a condition in a subject wherein repopulation, recirculation, regeneration, and/or expansion of particular cell types is favored, especially during a defined window of time following therapy. Illustrative cell types include T cells, B cells, dendritic cells, and other cells of the immune system.

In one embodiment, the immune effector cells expressing a CAR molecule, e.g., a CAR molecule described herein, are obtained from a subject that has received a low, immune enhancing dose of an mTOR inhibitor. In an embodiment, the population of immune effector cells, e.g., T cells, to be engineered to express a CAR, are harvested after a sufficient time, or after sufficient dosing of the low, immune enhancing, dose of an mTOR inhibitor, such that the level of PD1 negative immune effector cells, e.g., T cells, or the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells, in the subject or harvested from the subject has been, at least transiently, increased.

In other embodiments, population of immune effector cells, e.g., T cells, which have, or will be engineered to express a CAR, can be treated ex vivo by contact with an amount of an mTOR inhibitor

that increases the number of PD1 negative immune effector cells, e.g., T cells or increases the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells.

In one embodiment, a T cell population is diaglycerol kinase (DGK)-deficient. DGK-deficient cells include cells that do not express DGK RNA or protein, or have reduced or inhibited DGK activity. DGK-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent DGK expression. Alternatively, DGK-deficient cells can be generated by treatment with DGK inhibitors described herein.

In one embodiment, a T cell population is Ikaros-deficient. Ikaros-deficient cells include cells that do not express Ikaros RNA or protein, or have reduced or inhibited Ikaros activity, Ikaros-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent Ikaros expression. Alternatively, Ikaros-deficient cells can be generated by treatment with Ikaros inhibitors, e.g., lenalidomide.

In embodiments, a T cell population is DGK-deficient and Ikaros-deficient, e.g., does not express DGK and Ikaros, or has reduced or inhibited DGK and Ikaros activity. Such DGK and Ikaros-deficient cells can be generated by any of the methods described herein.

In an embodiment, the NK cells are obtained from the subject. In another embodiment, the NK cells are an NK cell line, e.g., NK-92 cell line (Conkwest).

Modifications of CAR cells, including allogeneic CAR cells

In embodiments described herein, the immune effector cell can be an allogeneic immune effector cell, e.g., T cell or NK cell. For example, the cell can be an allogeneic T cell, e.g., an allogeneic T cell lacking expression of a functional T cell receptor (TCR) and/or human leukocyte antigen (HLA), e.g., HLA class I and/or HLA class II, and/or beta-2 microglobulin (β_2m). Compositions of allogeneic CAR and methods thereof have been described in, e.g., pages 227-237 of WO 2016/014565, incorporated herein by reference in its entirety.

In some embodiments, a cell, e.g., a T cell or a NK cell, is modified to reduce the expression of a TCR, and/or HLA, and/or β_2m, and/or an inhibitory molecule described herein (e.g., PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGFR beta), using, e.g., a method described herein, e.g., siRNA, shRNA, clustered regularly interspaced short palindromic repeats (CRISPR) transcription-activator like effector nuclease (TALEN), or zinc finger endonuclease (ZFN).

In some embodiments, a cell, e.g., a T cell or a NK cell is engineered to express a telomerase subunit, e.g., the catalytic subunit of telomerase, e.g., TERT, e.g., hTERT. In one embodiment, such modification improves persistence of the cell in a patient.

Activation and Expansion of T Cells

T cells may be activated and expanded generally using methods as described, for example, in U.S. Patents 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466; 6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publication No. 20060121005.

Generally, the T cells of the invention may be expanded by contact with a surface having attached thereto an agent that stimulates a CD3/TCR complex associated signal and a ligand that stimulates a costimulatory molecule on the surface of the T cells. In particular, T cell populations may be stimulated as described herein, such as by contact with an anti-CD3 antibody, or antigen-binding fragment thereof, or an anti-CD2 antibody immobilized on a surface, or by contact with a protein kinase C activator (e.g., bryostatin) in conjunction with a calcium ionophore. For co-stimulation of an accessory molecule on the surface of the T cells, a ligand that binds the accessory molecule is used. For example, a population of T cells can be contacted with an anti-CD3 antibody and an anti-CD28 antibody, under conditions appropriate for stimulating proliferation of the T cells. To stimulate proliferation of either CD4+ T cells or CD8+ T cells, an anti-CD3 antibody and an anti-CD28 antibody can be used. Examples of an anti-CD28 antibody include 9.3, B-T3, XR-CD28 (Diaclone, Besançon, France) can be used as can other methods commonly known in the art (Berg et al., Transplant Proc. 30(8):3975-3977, 1998; Haanen et al., J. Exp. Med. 190(9):13191328, 1999; Garland et al., J. Immunol Meth. 227(1-2):53-63, 1999).

In certain aspects, the primary stimulatory signal and the costimulatory signal for the T cell may be provided by different protocols. For example, the agents providing each signal may be in solution or coupled to a surface. When coupled to a surface, the agents may be coupled to the same surface (i.e., in "cis" formation) or to separate surfaces (i.e., in "trans" formation). Alternatively, one agent may be coupled to a surface and the other agent in solution. In one aspect, the agent providing the costimulatory signal is bound to a cell surface and the agent providing the primary activation signal is in solution or coupled to a surface. In certain aspects, both agents can be in solution. In one aspect, the agents may be in soluble form, and then cross-linked to a surface, such as a cell expressing Fc receptors or an antibody or other binding agent which will bind to the agents. In this regard, see for example, U.S. Patent

Application Publication Nos. 20040101519 and 20060034810 for artificial antigen presenting cells (aAPCs) that are contemplated for use in activating and expanding T cells in the present invention.

In one aspect, the two agents are immobilized on beads, either on the same bead, i.e., "cis," or to separate beads, i.e., "trans." By way of example, the agent providing the primary activation signal is an anti-CD3 antibody or an antigen-binding fragment thereof and the agent providing the costimulatory signal is an anti-CD28 antibody or antigen-binding fragment thereof; and both agents are co-immobilized to the same bead in equivalent molecular amounts. In one aspect, a 1:1 ratio of each antibody bound to the beads for CD4+ T cell expansion and T cell growth is used. In certain aspects of the present invention, a ratio of anti CD3:CD28 antibodies bound to the beads is used such that an increase in T cell expansion is observed as compared to the expansion observed using a ratio of 1:1. In one particular aspect an increase of from about 1 to about 3 fold is observed as compared to the expansion observed using a ratio of 1:1. In one aspect, the ratio of CD3:CD28 antibody bound to the beads ranges from 100:1 to 1:100 and all integer values there between. In one aspect of the present invention, more anti-CD28 antibody is bound to the particles than anti-CD3 antibody, i.e., the ratio of CD3:CD28 is less than one. In certain aspects of the invention, the ratio of anti CD28 antibody to anti CD3 antibody bound to the beads is greater than 2:1. In one particular aspect, a 1:100 CD3:CD28 ratio of antibody bound to beads is used. In one aspect, a 1:75 CD3:CD28 ratio of antibody bound to beads is used. In a further aspect, a 1:50 CD3:CD28 ratio of antibody bound to beads is used. In one aspect, a 1:30 CD3:CD28 ratio of antibody bound to beads is used. In one preferred aspect, a 1:10 CD3:CD28 ratio of antibody bound to beads is used. In one aspect, a 1:3 CD3:CD28 ratio of antibody bound to the beads is used. In yet one aspect, a 3:1 CD3:CD28 ratio of antibody bound to the beads is used.

Ratios of particles to cells from 1:500 to 500:1 and any integer values in between may be used to stimulate T cells or other target cells. As those of ordinary skill in the art can readily appreciate, the ratio of particles to cells may depend on particle size relative to the target cell. For example, small sized beads could only bind a few cells, while larger beads could bind many. In certain aspects the ratio of cells to particles ranges from 1:100 to 100:1 and any integer values in-between and in further aspects the ratio comprises 1:9 to 9:1 and any integer values in between, can also be used to stimulate T cells. The ratio of anti-CD3- and anti-CD28-coupled particles to T cells that result in T cell stimulation can vary as noted above, however certain preferred values include 1:100, 1:50, 1:40, 1:30, 1:20, 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, and 15:1 with one preferred ratio being at least 1:1 particles per T cell. In one aspect, a ratio of particles to cells of 1:1 or less is used. In one particular aspect, a preferred particle: cell ratio is 1:5. In further aspects, the ratio of particles to cells can be varied depending on the day of stimulation. For example, in one aspect, the ratio of particles to cells is from 1:1 to 10:1 on the first day and additional particles are added to the cells every day or

every other day thereafter for up to 10 days, at final ratios of from 1:1 to 1:10 (based on cell counts on the day of addition). In one particular aspect, the ratio of particles to cells is 1:1 on the first day of stimulation and adjusted to 1:5 on the third and fifth days of stimulation. In one aspect, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:5 on the third and fifth days of stimulation. In one aspect, the ratio of particles to cells is 2:1 on the first day of stimulation and adjusted to 1:10 on the third and fifth days of stimulation. In one aspect, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:10 on the third and fifth days of stimulation. One of skill in the art will appreciate that a variety of other ratios may be suitable for use in the present invention. In particular, ratios will vary depending on particle size and on cell size and type. In one aspect, the most typical ratios for use are in the neighborhood of 1:1, 2:1 and 3:1 on the first day.

In further aspects of the present invention, the cells, such as T cells, are combined with agent-coated beads, the beads and the cells are subsequently separated, and then the cells are cultured. In an alternative aspect, prior to culture, the agent-coated beads and cells are not separated but are cultured together. In a further aspect, the beads and cells are first concentrated by application of a force, such as a magnetic force, resulting in increased ligation of cell surface markers, thereby inducing cell stimulation.

By way of example, cell surface proteins may be ligated by allowing paramagnetic beads to which anti-CD3 and anti-CD28 are attached (3x28 beads) to contact the T cells. In one aspect the cells (for example, 10^4 to 10^9 T cells) and beads (for example, DYNABEADS® M-450 CD3/CD28 T paramagnetic beads at a ratio of 1:1) are combined in a buffer, for example PBS (without divalent cations such as, calcium and magnesium). Again, those of ordinary skill in the art can readily appreciate any cell concentration may be used. For example, the target cell may be very rare in the sample and comprise only 0.01% of the sample or the entire sample (i.e., 100%) may comprise the target cell of interest. Accordingly, any cell number is within the context of the present invention. In certain aspects, it may be desirable to significantly decrease the volume in which particles and cells are mixed together (i.e., increase the concentration of cells), to ensure maximum contact of cells and particles. For example, in one aspect, a concentration of about 10 billion cells/ml, 9 billion/ml, 8 billion/ml, 7 billion/ml, 6 billion/ml, 5 billion/ml, or 2 billion cells/ml is used. In one aspect, greater than 100 million cells/ml is used. In a further aspect, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet one aspect, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used. Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells. Such populations of cells may have therapeutic value and

would be desirable to obtain in certain aspects. For example, using high concentration of cells allows more efficient selection of CD8+ T cells that normally have weaker CD28 expression.

In one embodiment, cells transduced with a nucleic acid encoding a CAR, e.g., a CAR described herein, are expanded, e.g., by a method described herein. In one embodiment, the cells are expanded in culture for a period of several hours (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 14 days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days). In one embodiment, the cells are expanded for a period of 4 to 9 days. In one embodiment, the cells are expanded for a period of 8 days or less, e.g., 7, 6 or 5 days. In one embodiment, the cells, e.g., a BCMA CAR cell described herein, are expanded in culture for 5 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions. Potency can be defined, e.g., by various T cell functions, e.g. proliferation, target cell killing, cytokine production, activation, migration, or combinations thereof. In one embodiment, the cells, e.g., a BCMA CAR cell described herein, expanded for 5 days show at least a one, two, three or four fold increase in cells doublings upon antigen stimulation as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the cells, e.g., the cells expressing a BCMA CAR described herein, are expanded in culture for 5 days, and the resulting cells exhibit higher proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the cells, e.g., a BCMA CAR cell described herein, expanded for 5 days show at least a one, two, three, four, five, ten fold or more increase in pg/ml of proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions.

In one aspect of the present invention, the mixture may be cultured for several hours (about 3 hours) to about 14 days or any hourly integer value in between. In one aspect, the mixture may be cultured for 21 days. In one aspect of the invention the beads and the T cells are cultured together for about eight days. In one aspect, the beads and T cells are cultured together for 2-3 days. Several cycles of stimulation may also be desired such that culture time of T cells can be 60 days or more. Conditions appropriate for T cell culture include an appropriate media (e.g., Minimal Essential Media or RPMI Media 1640 or, X-vivo 15, (Lonza)) that may contain factors necessary for proliferation and viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, TGFβ, and TNF-α or any other additives for the growth of cells known to the skilled artisan. Other additives for the growth of cells include, but are not limited to, surfactant, plasmanate, and reducing agents such as N-acetyl-cysteine and 2-mercaptoethanol. Media can include RPMI 1640, AIM-V, DMEM, MEM, α-MEM, F-12, X-Vivo 15, and X-Vivo 20, Optimizer, with added amino acids, sodium pyruvate, and vitamins, either serum-free or supplemented with an appropriate

amount of serum (or plasma) or a defined set of hormones, and/or an amount of cytokine(s) sufficient for the growth and expansion of T cells. Antibiotics, e.g., penicillin and streptomycin, are included only in experimental cultures, not in cultures of cells that are to be infused into a subject. The target cells are maintained under conditions necessary to support growth, for example, an appropriate temperature (e.g., 37° C) and atmosphere (e.g., air plus 5% CO_2).

In one embodiment, the cells are expanded in an appropriate media (e.g., media described herein) that includes one or more interleukin that result in at least a 200-fold (e.g., 200-fold, 250-fold, 300-fold, 350-fold) increase in cells over a 14 day expansion period, e.g., as measured by a method described herein such as flow cytometry. In one embodiment, the cells are expanded in the presence of IL-15 and/or IL-7 (e.g., IL-15 and IL-7).

In embodiments, methods described herein, e.g., CAR-expressing cell manufacturing methods, comprise removing T regulatory cells, e.g., CD25+ T cells, from a cell population, e.g., using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, IL-2. Methods of removing T regulatory cells, e.g., CD25+ T cells, from a cell population are described herein. In embodiments, the methods, e.g., manufacturing methods, further comprise contacting a cell population (e.g., a cell population in which T regulatory cells, such as CD25+ T cells, have been depleted; or a cell population that has previously contacted an anti-CD25 antibody, fragment thereof, or CD25-binding ligand) with IL-15 and/or IL-7. For example, the cell population (e.g., that has previously contacted an anti-CD25 antibody, fragment thereof, or CD25-binding ligand) is expanded in the presence of IL-15 and/or IL-7.

In some embodiments a CAR-expressing cell described herein is contacted with a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide e.g., hetIL-15, during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a CAR-expressing cell described herein is contacted with a composition comprising a IL-15 polypeptide during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a CAR-expressing cell described herein is contacted with a composition comprising a combination of both a IL-15 polypeptide and a IL-15 Ra polypeptide during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a CAR-expressing cell described herein is contacted with a composition comprising hetIL-15 during the manufacturing of the CAR-expressing cell, e.g., ex vivo.

In one embodiment the CAR-expressing cell described herein is contacted with a composition comprising hetIL-15 during ex vivo expansion. In an embodiment, the CAR-expressing cell described herein is contacted with a composition comprising an IL-15 polypeptide during ex vivo expansion. In an embodiment, the CAR-expressing cell described herein is contacted with a composition comprising

both an IL-15 polypeptide and an IL-15Ra polypeptide during ex vivo expansion. In one embodiment the contacting results in the survival and proliferation of a lymphocyte subpopulation, e.g., CD8+ T cells.

T cells that have been exposed to varied stimulation times may exhibit different characteristics. For example, typical blood or apheresed peripheral blood mononuclear cell products have a helper T cell population (TH, CD4+) that is greater than the cytotoxic or suppressor T cell population. Ex vivo expansion of T cells by stimulating CD3 and CD28 receptors produces a population of T cells that prior to about days 8-9 consists predominately of TH cells, while after about days 8-9, the population of T cells comprises an increasingly greater population of TC cells. Accordingly, depending on the purpose of treatment, infusing a subject with a T cell population comprising predominately of TH cells may be advantageous. Similarly, if an antigen-specific subset of TC cells has been isolated it may be beneficial to expand this subset to a greater degree.

Further, in addition to CD4 and CD8 markers, other phenotypic markers vary significantly, but in large part, reproducibly during the course of the cell expansion process. Thus, such reproducibility enables the ability to tailor an activated T cell product for specific purposes.

Once a BCMA CAR is constructed, various assays can be used to evaluate the activity of the molecule, such as but not limited to, the ability to expand T cells following antigen stimulation, sustain T cell expansion in the absence of re-stimulation, and anti-cancer activities in appropriate in vitro and animal models. Assays to evaluate the effects of a BCMA CAR are described in further detail below

Western blot analysis of CAR expression in primary T cells can be used to detect the presence of monomers and dimers. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Very briefly, T cells (1:1 mixture of $CD4^+$ and $CD8^+$ T cells) expressing the CARs are expanded *in vitro* for more than 10 days followed by lysis and SDS-PAGE under reducing conditions. CARs containing the full length TCR-ζ cytoplasmic domain and the endogenous TCR-ζ chain are detected by western blotting using an antibody to the TCR-ζ chain. The same T cell subsets are used for SDS-PAGE analysis under non-reducing conditions to permit evaluation of covalent dimer formation.

In vitro expansion of CAR^+ T cells following antigen stimulation can be measured by flow cytometry. For example, a mixture of $CD4^+$ and $CD8^+$ T cells are stimulated with αCD3/αCD28 aAPCs followed by transduction with lentiviral vectors expressing GFP under the control of the promoters to be analyzed. Exemplary promoters include the CMV IE gene, EF-1α, ubiquitin C, or phosphoglycerokinase (PGK) promoters. GFP fluorescence is evaluated on day 6 of culture in the $CD4^+$ and/or $CD8^+$ T cell subsets by flow cytometry. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Alternatively, a mixture of $CD4^+$ and $CD8^+$ T cells are stimulated with αCD3/αCD28

coated magnetic beads on day 0, and transduced with CAR on day 1 using a bicistronic lentiviral vector expressing CAR along with eGFP using a 2A ribosomal skipping sequence. Cultures are re-stimulated with BCMA-expressing cells, such as multiple myeloma cell lines or K562-BCMA, following washing. Exogenous IL-2 is added to the cultures every other day at 100 IU/ml. GFP^+ T cells are enumerated by flow cytometry using bead-based counting. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009).

Sustained CAR^+ T cell expansion in the absence of re-stimulation can also be measured. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, mean T cell volume (fl) is measured on day 8 of culture using a Coulter Multisizer III particle counter, a Nexcelom Cellometer Vision or Millipore Scepter, following stimulation with αCD3/αCD28 coated magnetic beads on day 0, and transduction with the indicated CAR on day 1.

Animal models can also be used to measure a CART activity. For example, xenograft model using human BCMA-specific CAR^+ T cells to treat a primary human multiple myeloma in immunodeficient mice can be used. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Very briefly, after establishment of MM, mice are randomized as to treatment groups. Different numbers of BCMA CART cells can be injected into immunodeficient mice bearing MM. Animals are assessed for disease progression and tumor burden at weekly intervals. Survival curves for the groups are compared using the log-rank test. In addition, absolute peripheral blood $CD4^+$ and $CD8^+$ T cell counts 4 weeks following T cell injection in the immunodeficient mice can also be analyzed. Mice are injected with multiple myeloma cells and 3 weeks later are injected with T cells engineered to express BCMA CAR, e.g., by a bicistronic lentiviral vector that encodes the CAR linked to eGFP. T cells are normalized to 45–50% input GFP^+ T cells by mixing with mock-transduced cells prior to injection, and confirmed by flow cytometry. Animals are assessed for leukemia at 1-week intervals. Survival curves for the CAR^+ T cell groups are compared using the log-rank test.

Assessment of cell proliferation and cytokine production has been previously described, *e.g.*, at Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, assessment of CAR-mediated proliferation is performed in microtiter plates by mixing washed T cells with K562 cells expressing BCMA or other BCMA-expressing myeloma cells are irradiated with gamma-radiation prior to use. Anti-CD3 (clone OKT3) and anti- CD28 (clone 9.3) monoclonal antibodies are added to cultures with KT32-BBL cells to serve as a positive control for stimulating T-cell proliferation since these signals support long-term $CD8^+$ T cell expansion *ex vivo*. T cells are enumerated in cultures using CountBright™ fluorescent beads (Invitrogen, Carlsbad, CA) and flow cytometry as described by the manufacturer. CAR^+ T cells are identified by GFP expression using T cells that are engineered with eGFP-2A linked CAR-expressing lentiviral vectors. For CAR+ T cells not expressing GFP, the CAR+ T

cells are detected with biotinylated recombinant BCMA protein and a secondary avidin-PE conjugate. CD4+ and $CD8^+$ expression on T cells are also simultaneously detected with specific monoclonal antibodies (BD Biosciences). Cytokine measurements are performed on supernatants collected 24 hours following re-stimulation using the human TH1/TH2 cytokine cytometric bead array kit (BD Biosciences, San Diego, CA) according the manufacturer's instructions. Fluorescence is assessed using a FACScalibur flow cytometer, and data is analyzed according to the manufacturer's instructions.

Cytotoxicity can be assessed by a standard 51Cr-release assay. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, target cells (e.g., K562 lines expressing BCMA and primary multiple myeloma cells) are loaded with 51Cr (as NaCrO4, New England Nuclear, Boston, MA) at 37°C for 2 hours with frequent agitation, washed twice in complete RPMI and plated into microtiter plates. Effector T cells are mixed with target cells in the wells in complete RPMI at varying ratios of effector cell:target cell (E:T). Additional wells containing media only (spontaneous release, SR) or a 1% solution of triton-X 100 detergent (total release, TR) are also prepared. After 4 hours of incubation at 37°C, supernatant from each well is harvested. Released 51Cr is then measured using a gamma particle counter (Packard Instrument Co., Waltham, MA). Each condition is performed in at least triplicate, and the percentage of lysis is calculated using the formula: % Lysis = (ER– SR) / (TR – SR), where ER represents the average 51Cr released for each experimental condition. Alternatively, cytotoxicity can also be assessed using a Bright-Glo™ Luciferase Assay.

Imaging technologies can be used to evaluate specific trafficking and proliferation of CARs in tumor-bearing animal models. Such assays have been described, for example, in Barrett *et al.*, Human Gene Therapy 22:1575-1586 (2011). Briefly, NOD/SCID/$\gamma c^{-/-}$ (NSG) mice or other immunodeficient are injected IV with multiple myeloma cells followed 7 days later with BCMA CART cells 4 hour after electroporation with the CAR constructs. The T cells are stably transfected with a lentiviral construct to express firefly luciferase, and mice are imaged for bioluminescence. Alternatively, therapeutic efficacy and specificity of a single injection of CAR^+ T cells in a multiple myeloma xenograft model can be measured as the following: NSG mice are injected with multiple myeloma cells transduced to stably express firefly luciferase, followed by a single tail-vein injection of T cells electroporated with BCMA CAR construct days later. Animals are imaged at various time points post injection. For example, photon-density heat maps of firefly luciferasepositive tumors in representative mice at day 5 (2 days before treatment) and day 8 (24 hr post CAR^+ PBLs) can be generated.

Alternatively, or in combination to the methods disclosed herein, methods and compositions for one or more of: detection and/or quantification of CAR-expressing cells (*e.g.*, *in vitro* or *in vivo* (e.g., clinical monitoring)); immune cell expansion and/or activation; and/or CAR-specific selection, that involve the use of a CAR ligand, are disclosed. In one exemplary embodiment, the CAR ligand is an

antibody that binds to the CAR molecule, e.g., binds to the extracellular antigen binding domain of CAR (e.g., an antibody that binds to the antigen binding domain, e.g., an anti-idiotypic antibody; or an antibody that binds to a constant region of the extracellular binding domain). In other embodiments, the CAR ligand is a CAR antigen molecule (e.g., a CAR antigen molecule as described herein).

In one aspect, a method for detecting and/or quantifying CAR-expressing cells is disclosed. For example, the CAR ligand can be used to detect and/or quantify CAR-expressing cells *in vitro* or *in vivo* (e.g., clinical monitoring of CAR-expressing cells in a patient, or dosing a patient). The method includes:

providing the CAR ligand (optionally, a labelled CAR ligand, e.g., a CAR ligand that includes a tag, a bead, a radioactive or fluorescent label);

acquiring the CAR-expressing cell (e.g., acquiring a sample containing CAR-expressing cells, such as a manufacturing sample or a clinical sample);

contacting the CAR-expressing cell with the CAR ligand under conditions where binding occurs, thereby detecting the level (e.g., amount) of the CAR-expressing cells present. Binding of the CAR-expressing cell with the CAR ligand can be detected using standard techniques such as FACS, ELISA and the like.

In another aspect, a method of expanding and/or activating cells (e.g., immune effector cells) is disclosed. The method includes:

providing a CAR-expressing cell (e.g., a first CAR-expressing cell or a transiently expressing CAR cell);

contacting said CAR-expressing cell with a CAR ligand, e.g., a CAR ligand as described herein), under conditions where immune cell expansion and/or proliferation occurs, thereby producing the activated and/or expanded cell population.

In certain embodiments, the CAR ligand is present on (e.g., is immobilized or attached to a substrate, e.g., a non-naturally occurring substrate). In some embodiments, the substrate is a non-cellular substrate. The non-cellular substrate can be a solid support chosen from, e.g., a plate (e.g., a microtiter plate), a membrane (e.g., a nitrocellulose membrane), a matrix, a chip or a bead. In embodiments, the CAR ligand is present in the substrate (e.g., on the substrate surface). The CAR ligand can be immobilized, attached, or associated covalently or non-covalently (e.g., cross-linked) to the substrate. In one embodiment, the CAR ligand is attached (e.g., covalently attached) to a bead. In the aforesaid embodiments, the immune cell population can be expanded *in vitro* or *ex vivo*. The

method can further include culturing the population of immune cells in the presence of the ligand of the CAR molecule, e.g., using any of the methods described herein.

In other embodiments, the method of expanding and/or activating the cells further comprises addition of a second stimulatory molecule, e.g., CD28. For example, the CAR ligand and the second stimulatory molecule can be immobilized to a substrate, e.g., one or more beads, thereby providing increased cell expansion and/or activation.

In yet another aspect, a method for selecting or enriching for a CAR expressing cell is provided. The method includes contacting the CAR expressing cell with a CAR ligand as described herein; and selecting the cell on the basis of binding of the CAR ligand.

In yet other embodiments, a method for depleting, reducing and/or killing a CAR expressing cell is provided. The method includes contacting the CAR expressing cell with a CAR ligand as described herein; and targeting the cell on the basis of binding of the CAR ligand, thereby reducing the number, and/or killing, the CAR-expressing cell. In one embodiment, the CAR ligand is coupled to a toxic agent (e.g., a toxin or a cell ablative drug). In another embodiment, the anti-idiotypic antibody can cause effector cell activity, e.g., ADCC or ADC activities.

Exemplary anti-CAR antibodies that can be used in the methods disclosed herein are described, e.g., in WO 2014/190273 and by Jena et al., "Chimeric Antigen Receptor (CAR)-Specific Monoclonal Antibody to Detect CD19-Specific T cells in Clinical Trials", PLOS March 2013 8:3 e57838, the contents of which are incorporated by reference. In one embodiment, the anti-idiotypic antibody molecule recognizes an anti-CD19 antibody molecule, e.g., an anti-CD19 scFv. For instance, the anti-idiotypic antibody molecule can compete for binding with the CD19-specific CAR mAb clone no. 136.20.1 described in Jena et al., PLOS March 2013 8:3 e57838; may have the same CDRs (e.g., one or more of, e.g., all of, VH CDR1, VH CDR2, CH CDR3, VL CDR1, VL CDR2, and VL CDR3, using the Kabat definition, the Chothia definition, or a combination of tthe Kabat and Chothia definitions) as the CD19-specific CAR mAb clone no. 136.20.1; may have one or more (e.g., 2) variable regions as the CD19-specific CAR mAb clone no. 136.20.1, or may comprise the CD19-specific CAR mAb clone no. 136.20.1. In some embodiments, the anti-idiotypic antibody was made according to a method described in Jena et al. In another embodiment, the anti-idiotypic antibody molecule is an anti-idiotypic antibody molecule described in WO 2014/190273. In some embodiments, the anti-idiotypic antibody molecule has the same CDRs (e.g., one or more of, e.g., all of, VH CDR1, VH CDR2, CH CDR3, VL CDR1, VL CDR2, and VL CDR3) as an antibody molecule of WO 2014/190273 such as 136.20.1; may have one or more (e.g., 2) variable regions of an antibody molecule of WO 2014/190273, or may comprise an antibody molecule of WO 2014/190273 such as

136.20.1. In other embodiments, the anti-CAR antibody binds to a constant region of the extracellular binding domain of the CAR molecule, e.g., as described in WO 2014/190273. In some embodiments, the anti-CAR antibody binds to a constant region of the extracellular binding domain of the CAR molecule, e.g., a heavy chain constant region (e.g., a CH2-CH3 hinge region) or light chain constant region. For instance, in some embodiments the anti-CAR antibody competes for binding with the 2D3 monoclonal antibody described in WO 2014/190273, has the same CDRs (e.g., one or more of, e.g., all of, VH CDR1, VH CDR2, CH CDR3, VL CDR1, VL CDR2, and VL CDR3) as 2D3, or has one or more (e.g., 2) variable regions of 2D3, or comprises 2D3 as described in WO 2014/190273.

In some aspects and embodiments, the compositions and methods herein are optimized for a specific subset of T cells, e.g., as described in US Serial No. 62/031,699 filed July 31, 2014, the contents of which are incorporated herein by reference in their entirety. In some embodiments, the optimized subsets of T cells display an enhanced persistence compared to a control T cell, e.g., a T cell of a different type (e.g., $CD8^+$ or $CD4^+$) expressing the same construct.

In some embodiments, a $CD4^+$ T cell comprises a CAR described herein, which CAR comprises an intracellular signaling domain suitable for (e.g., optimized for, e.g., leading to enhanced persistence in) a $CD4^+$ T cell, e.g., an ICOS domain. In some embodiments, a $CD8^+$ T cell comprises a CAR described herein, which CAR comprises an intracellular signaling domain suitable for (e.g., optimized for, e.g., leading to enhanced persistence of) a $CD8^+$ T cell, e.g., a 4-1BB domain, a CD28 domain, or another costimulatory domain other than an ICOS domain. In some embodiments, the CAR described herein comprises an antigen binding domain described herein, e.g., a CAR comprising an antigen binding domain that targets BCMA).

In an aspect, described herein is a method of treating a subject, e.g., a subject having cancer. The method includes administering to said subject, an effective amount of:

1) a $CD4^+$ T cell comprising a CAR (the CAR^{CD4+})

comprising:

an antigen binding domain, e.g., an antigen binding domain described herein, e.g., an antigen binding domain that targets BCMA;

a transmembrane domain; and

an intracellular signaling domain, e.g., a first costimulatory domain, e.g., an ICOS domain; and

2) a $CD8^+$ T cell comprising a CAR (the CAR^{CD8+}) comprising:

an antigen binding domain, e.g., an antigen binding domain described herein, e.g., an antigen binding domain that targets BCMA;

a transmembrane domain; and

an intracellular signaling domain, e.g., a second costimulatory domain, e.g., a 4-1BB domain, a CD28 domain, or another costimulatory domain other than an ICOS domain;

wherein the CAR^{CD4+} and the CAR^{CD8+} differ from one another.

Optionally, the method further includes administering:

3) a second CD8+ T cell comprising a CAR (the second CAR^{CD8+}) comprising:

an antigen binding domain, e.g., an antigen binding domain described herein, e.g., an antigen binding domain that specifically binds BCMA;

a transmembrane domain; and

an intracellular signaling domain, wherein the second CAR^{CD8+} comprises an intracellular signaling domain, e.g., a costimulatory signaling domain, not present on the CAR^{CD8+}, and, optionally, does not comprise an ICOS signaling domain.

Other assays, including those that are known in the art can also be used to evaluate the BCMA CAR constructs of the invention.

Therapeutic Application

BCMA Associated Diseases and/or Disorders

In one aspect, the invention provides methods for treating a disease associated with BCMA expression. In one aspect, the invention provides methods for treating a disease wherein part of the tumor is negative for BCMA and part of the tumor is positive for BCMA For example, the CAR of the invention is useful for treating subjects that have undergone treatment for a disease associated with elevated expression of BCMA, wherein the subject that has undergone treatment for elevated levels of BCMA exhibits a disease associated with elevated levels of BCMA. In embodiments, the CAR of the invention is useful for treating subjects that have undergone treatment for a disease associated with expression of BCMA, wherein the subject that has undergone treatment related to expression of BCMA exhibits a disease associated with expression of BCMA.

In one embodiment, the invention provides methods for treating a disease wherein BCMA is expressed on both normal cells and cancers cells, but is expressed at lower levels on normal cells. In one embodiment, the method further comprises selecting a CAR that binds of the invention with an affinity that allows the BCMA CAR to bind and kill the cancer cells expressing BCMA but less than 30%, 25%, 20%, 15%, 10%, 5% or less of the normal cells expressing BCMA are killed, e.g., as determined by an assay described herein. For example, a killing assay such as flow cytometry based on

Cr51 CTL can be used. In one embodiment, the BCMA CAR has an antigen binding domain that has a binding affinity KD of 10^{-4} M to 10^{-8} M, e.g., 10^{-5} M to 10^{-7} M, e.g., 10^{-6} M or 10^{-7} M, for the target antigen. In one embodiment, the BCMA antigen binding domain has a binding affinity that is at least five-fold, 10-fold, 20-fold, 30-fold, 50-fold, 100-fold or 1,000-fold less than a reference antibody, e.g., an antibody described herein.

In one aspect, the invention pertains to a vector comprising BCMA CAR operably linked to promoter for expression in mammalian immune effector cells, e.g., T cells or NK cells. In one aspect, the invention provides a recombinant immune effector cell, e.g., T cell or NK cell, expressing the BCMA CAR for use in treating BCMA-expressing tumors, wherein the recombinant immune effector cell (e.g., T cell or NK cell) expressing the BCMA CAR is termed a BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell). In one aspect, the BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell)of the invention is capable of contacting a tumor cell with at least one BCMA CAR of the invention expressed on its surface such that the BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell)targets the tumor cell and growth of the tumor is inhibited.

In one aspect, the invention pertains to a method of inhibiting growth of a BCMA-expressing tumor cell, comprising contacting the tumor cell with a BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell) of the present invention such that the BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell) is activated in response to the antigen and targets the cancer cell, wherein the growth of the tumor is inhibited.

In one aspect, the invention pertains to a method of treating cancer in a subject. The method comprises administering to the subject a BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell) of the present invention such that the cancer is treated in the subject. An example of a cancer that is treatable by the BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell) of the invention is a cancer associated with expression of BCMA.

The invention includes a type of cellular therapy where immune effector cells (e.g., T cells or NK cells) are genetically modified to express a chimeric antigen receptor (CAR) and the BCMA CAR-expressing cell (e.g., BCMA CART or BCMA CAR-expressing NK cell) is infused to a recipient in need thereof. The infused cell is able to kill tumor cells in the recipient. Unlike antibody therapies, CAR-modified cells, e.g., T cells or NK cells, are able to replicate in vivo resulting in long-term persistence that can lead to sustained tumor control. In various aspects, the cells (e.g., T cells or NK cells) administered to the patient, or their progeny, persist in the patient for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve

months, thirteen months, fourteen month, fifteen months, sixteen months, seventeen months, eighteen months, nineteen months, twenty months, twenty-one months, twenty-two months, twenty-three months, two years, three years, four years, or five years after administration of the cell (e.g., T cell or NK cell) to the patient.

The invention also includes a type of cellular therapy where immune effector cells (e.g., T cells or NK cells) are modified, e.g., by in vitro transcribed RNA, to transiently express a chimeric antigen receptor (CAR) and the immune effector cell (e.g., T cell or NK cell) is infused to a recipient in need thereof. The infused cell is able to kill tumor cells in the recipient. Thus, in various aspects, the immune effector cells (e.g., T cells or NK cells) administered to the patient, is present for less than one month, e.g., three weeks, two weeks, one week, after administration of the immune effector cell (e.g., T cell or NK cell) to the patient.

Without wishing to be bound by any particular theory, the anti-tumor immunity response elicited by the CAR-modified immune effector cells (e.g., T cells or NK cells) may be an active or a passive immune response, or alternatively may be due to a direct vs indirect immune response. In one aspect, the CAR transduced immune effector cells (e.g., T cells or NK cells) exhibit specific proinflammatory cytokine secretion and potent cytolytic activity in response to human cancer cells expressing the BCMA, resist soluble BCMA inhibition, mediate bystander killing and mediate regression of an established human tumor. For example, antigen-less tumor cells within a heterogeneous field of BCMA-expressing tumor may be susceptible to indirect destruction by BCMA-redirected immune effector cells (e.g., T cells or NK cells) that has previously reacted against adjacent antigen-positive cancer cells.

In one aspect, the fully-human CAR-modified immune effector cells (e.g., T cells or NK cells) of the invention may be a type of vaccine for ex vivo immunization and/or in vivo therapy in a mammal. In one aspect, the mammal is a human.

With respect to ex vivo immunization, at least one of the following occurs in vitro prior to administering the cell into a mammal: i) expansion of the cells, ii) introducing a nucleic acid encoding a CAR to the cells or iii) cryopreservation of the cells.

Ex vivo procedures are well known in the art and are discussed more fully below. Briefly, cells are isolated from a mammal (e.g., a human) and genetically modified (i.e., transduced or transfected in vitro) with a vector expressing a CAR disclosed herein. The CAR-modified cell can be administered to a mammalian recipient to provide a therapeutic benefit. The mammalian recipient may be a human and the CAR-modified cell can be autologous with respect to the recipient. Alternatively, the cells can be allogeneic, syngeneic or xenogeneic with respect to the recipient.

The procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference, can be applied to the cells of the present invention. Other suitable methods are known in the art, therefore the present invention is not limited to any particular method of ex vivo expansion of the cells. Briefly, ex vivo culture and expansion of T cells comprises: (1) collecting CD34+ hematopoietic stem and progenitor cells from a mammal from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used for culturing and expansion of the cells.

In addition to using a cell-based vaccine in terms of ex vivo immunization, the present invention also provides compositions and methods for in vivo immunization to elicit an immune response directed against an antigen in a patient.

Generally, the cells activated and expanded as described herein may be utilized in the treatment and prevention of diseases that arise in individuals who are immunocompromised. In particular, the CAR-modified immune effector cells (e.g., T cells or NK cells) of the invention are used in the treatment of diseases, disorders and conditions associated with expression of BCMA. In certain aspects, the cells of the invention are used in the treatment of patients at risk for developing diseases, disorders and conditions associated with expression of BCMA. Thus, the present invention provides methods for the treatment or prevention of diseases, disorders and conditions associated with expression of BCMA comprising administering to a subject in need thereof, a therapeutically effective amount of the CAR-modified immune effector cells (e.g., T cells or NK cells) of the invention.

In one aspect the CAR-expressing cells (e.g., CART cells or CAR-expressing NK cells) of the inventions may be used to treat a proliferative disease such as a cancer or malignancy or is a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia. In one aspect, the cancer is a hematolical cancer. Hematological cancer conditions are the types of cancer such as leukemia and malignant lymphoproliferative conditions that affect blood, bone marrow and the lymphatic system.In one aspect, the hematological cancer is a leukemia or a hematological. An example of a disease or disorder associated with BCMA is multiple myeloma (also known as MM) (See Claudio et al., *Blood*. 2002, 100(6):2175-86; and Novak et al., *Blood*. 2004, 103(2):689-94). Multiple myeloma, also known as plasma cell myeloma or Kahler's disease, is a cancer characterized by an accumulation of abnormal or malignant plasma B-cells in the bone marrow. Frequently, the cancer cells invade adjacent bone, destroying skeletal structures and resulting in bone pain and fractures. Most cases of myeloma also features the production of a paraprotein (also known as M proteins or myeloma proteins), which is an abnormal immunoglobulin produced in excess by the clonal proliferation of the malignant plasma cells. Blood serum paraprotein levels of more than 30g/L is diagnostic of multiple myeloma, according

to the diagnostic criteria of the International Myeloma Working Group (IMWG) (*See* Kyle et al. (2009), Leukemia. 23:3-9). Other symptoms or signs of multiple myeloma include reduced kidney function or renal failure, bone lesions, anemia, hypercalcemia, and neurological symptoms.

Criteria for distinguishing multiple myeloma from other plasma cell proliferative disorders have been established by the International Myeloma Working Group (*See* Kyle et al. (2009), Leukemia. 23:3-9). All three of the following criteria must be met:

- Clonal bone marrow plasma cells ≥10%
- Present of serum and/or urinary monoclonal protein (except in patients with true non-secretory multiple myeloma)
- Evidence of end-organ damage attributable to the underlying plasma cell proliferative disorder, specifically:
    - Hypercalcemia: serum calcium ≥11.5 mg/100 ml
    - Renal insufficienty: serum creatinine > 1.73 mmol/l
    - Anemia: normochromic, normocytic with a hemoglobin value of >2g/100 ml below the lower limit of normal, or a hemoglobin value <10g/100ml
    - Bone lesions: lytic lesions, severe osteopenia, or pathologic fractures.

Other plasma cell proliferative disorders that can be treated by the compositions and methods described herein include, but are not limited to, asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammapathy of undetermined significance (MGUS), Waldenstrom's macroglobulinemia, plasmacytomas (e.g., plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, and POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome).

Two staging systems are used in the staging of multiple myeloma: the International Staging System (ISS) (*See* Greipp et al. (2005), J. Clin. Oncol. 23 (15):3412-3420, herein incorporated by reference in its entirety) and the Durie-Salmon Staging system (DSS) (*See* Durie et al. (1975), Cancer 36 (3): 842-854, herein incorporated by reference in its entirety). The two staging systems are summarized in the table below:

Table 6. Staging systems for the staging of multiple myeloma

Stage	International Staging System		Durie-Salmon Staging System	
	Criteria	Median survival	Criteria	Median survival*
I	β_2M <3.5 mg/l and serum albumin ≥3.5 g/dL	62 months	All of the following: Hemoglobin level >10g/dL	IA: 62 months

			Serum calcium, normal or <12 mg/dL Bone x-ray, normal or 1 plasmacytoma only Low monoclonal protein production (IgG <5g/dL, IgA<3g/dL, Bence Jones protein <4g/dL per 24 hours	IB: 22 months
II	Neither stage I or stage III	44 months	Neither stage I or stage III	IIA: 58 months IIB: 354 months
III	β_2M ≥5.5 mg/l	29 months	One or more of the following: Hemoglobin level <8.5g/dL Serum calcium, normal or >12 mg/dL Advanced osteolytic lesions High monoclonal protein production (IgG >7g/dL, IgA>5g/dL, Bence Jones protein >12g/dL per 24 hours	IIIA: 45 months IIIB: 24 months

*The Durie-Salmon Staging system also includes a subclassification that designates the status of renal function. The designation of "A" or "B" is added after the stage number, wherein "A" indicates relatively normal renal function (serum creatinine value <2.0 mg/dL), and B indicates abnormal renal function (serum creatinine value >2.0 mg/dL).

A third staging system for multiple myeloma is referred to as Revised International Staging System (R-ISS) (*see* Palumbo A, Avet-Loiseau H, Oliva S, et al. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2015;33:2863-9, herein incorporated by reference in its entirety). R-ISS stage I includes ISS stage I (serum β2-microglobulin level < 3.5 mg/L and serum albumin level ≥ 3.5 g/dL), no high-risk CA [del(17p) and/or t(4;14) and/or t(14;16)], and normal LDH level (less than the upper limit of normal range). R-ISS stage III includes ISS stage III (serum β2-microglobulin level > 5.5 mg/L) and high-risk CA or high LDH level. R-ISS stage II includes all the other possible combinations.

The response of patients can be determined based on IMWG 2016 criteria, as disclosed in Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. The Lancet Oncology;17(8):e328-e346 (2016), herein incorporated by reference in its entirety. Table 7 provides IMWG 2016 criteria for response assessment.

Table 7. IMWG criteria for response assessment including criteria for minimal residual disease (MRD)

	Response criteria*
IMWG MRD criteria (requires a complete response as defined below)	

Sustained MRD-negative	MRD negativity in the marrow (NGF or NGS, or both) and by imaging as defined below, confirmed minimum of 1 year apart. Subsequent evaluations can be used to further specify the duration of negativity (e.g., MRD-negative at 5 years)†
Flow MRD-negative	Absence of phenotypically aberrant clonal plasma cells by NGF‡ on bone marrow aspirates using the EuroFlow standard operation procedure for MRD detection in multiple myeloma (or validated equivalent method) with a minimum sensitivity of 1 in 10^5 nucleated cells or higher
Sequencing MRD-negative	Absence of clonal plasma cells by NGS on bone marrow aspirate in which presence of a clone is defined as less than two identical sequencing reads obtained after DNA sequencing of bone marrow aspirates using the LymphoSIGHT platform (or validated equivalent method) with a minimum sensitivity of 1 in 10^5 nucleated cells§ or higher
Imaging plus MRD-negative	MRD negativity as defined by NGF or NGS plus disappearance of every area of increased tracer uptake found at baseline or a preceding PET/CT or decrease to less mediastinal blood pool SUV or decrease to less than that of surrounding normal tissue¶
Standard IMWG response criteria‖	
Stringent complete response	Complete response as defined below plus normal FLC ratio** and absence of clonal cells in bone marrow biopsy by immunohistochemistry (κ/λ ratio ≤4:1 or ≥1:2 for κ and λ patients, respectively, after counting ≥100 plasma cells)††
Complete response	Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and <5% plasma cells in bone marrow aspirates
Very good partial response	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein plus urine M-protein level <100 mg per 24 h
Partial response	≥50% reduction of serum M-protein plus reduction in 24 h urinary M-protein by ≥90% or to <200 mg per 24 h; If the serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria; If serum and urine M-protein are unmeasurable, and serum-free light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma-cell percentage was ≥30%. In addition to these criteria, if present at baseline, a ≥50% reduction in the size (SPD)§§ of soft tissue plasmacytomas is also required
Minimal response	≥25% but ≤49% reduction of serum M-protein and reduction in 24-h urine M-protein by 50–89%. In addition to the above listed criteria, if present at baseline, a ≥50% reduction in the size (SPD)§§ of soft tissue plasmacytomas is also required
Stable disease	Not recommended for use as an indicator of response; stability of disease is best described by providing the time-to-progression estimates. Not meeting criteria for complete response, very good partial response, partial response, minimal response, or progressive disease
Progressive disease ¶¶,‖‖	Any one or more of the following criteria: Increase of 25% from lowest confi rmed response value in one or more of the following criteria: Serum M-protein (absolute increase must be ≥0.5 g/dL);

	Serum M-protein increase ≥1 g/dL, if the lowest M component was ≥5 g/dL; Urine M-protein (absolute increase must be ≥200 mg/24 h); In patients without measurable serum and urine M-protein levels, the difference between involved and uninvolved FLC levels (absolute increase must be >10 mg/dL); In patients without measurable serum and urine M-protein levels and without measurable involved FLC levels, bone marrow plasma-cell percentage irrespective of baseline status (absolute increase must be ≥10%); Appearance of a new lesion(s), ≥50% increase from nadir in SPD§§ of >1 lesion, or ≥50% increase in the longest diameter of a previous lesion >1 cm in short axis; ≥50% increase in circulating plasma cells (minimum of 200 cells per μL) if this is the only measure of disease
Clinical relapse	Clinical relapse requires one or more of the following criteria: Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) related to the underlying clonal plasma-cell proliferative disorder. It is not used in calculation of time to progression or progression-free survival but is listed as something that can be reported optionally or for use in clinical practice; Development of new soft tissue plasmacytomas or bone lesions (osteoporotic fractures do not constitute progression); Definite increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as a 50% (and ≥1 cm) increase as measured serially by the SPD§§ of the measurable lesion; Hypercalcaemia (>11 mg/dL); Decrease in haemoglobin of ≥2 g/dL not related to therapy or other non-myeloma-related conditions; Rise in serum creatinine by 2 mg/dL or more from the start of the therapy and attributable to myeloma; Hyperviscosity related to serum paraprotein
Relapse from complete response (to be used only if the end point is disease-free survival)	Any one or more of the following criteria: Reappearance of serum or urine M-protein by immunofixation or electrophoresis; Development of ≥5% plasma cells in the bone marrow; Appearance of any other sign of progression (i.e., new plasmacytoma, lytic bone lesion, or hypercalcaemia see above)
Relapse from MRD negative (to be used only if the end point is disease-free survival)	Any one or more of the following criteria: Loss of MRD negative state (evidence of clonal plasma cells on NGF or NGS, or positive imaging study for recurrence of myeloma); Reappearance of serum or urine M-protein by immunofixation or electrophoresis; Development of ≥5% clonal plasma cells in the bone marrow; Appearance of any other sign of progression (i.e., new plasmacytoma, lytic bone lesion, or hypercalcaemia)
For MRD assessment, the first bone marrow aspirate should be sent to MRD (not for morphology) and this sample should be taken in one draw with a volume of minimally 2 mL (to obtain sufficient cells), but maximally 4–5 mL to avoid haemodilution. IMWG=International Myeloma Working Group. MRD=minimal residual disease. NGF=next-generation flow. NGS=next-generation sequencing. FLC=free light chain. M-protein=myeloma protein. SPD=sum of the products	

of the maximal perpendicular diameters of measured lesions. CRAB features=calcium elevation, renal failure, anaemia, lytic bone lesions. FCM=fl ow cytometry. SUV_{max}=maximum standardised uptake value. MFC=multiparameter flow cytometry. ^{18}F-FDG PET=^{18}F-fluorodeoxyglucose PET. ASCT=autologous stem cell transplantation.

*All response categories require two consecutive assessments made any time before starting any new therapy; for MRD there is no need for two consecutive assessments, but information on MRD after each treatment stage is recommended (eg, after induction, high-dose therapy/ASCT, consolidation, maintenance). MRD tests should be initiated only at the time of suspected complete response.

All categories of response and MRD require no known evidence of progressive or new bone lesions if radiographic studies were performed. However, radiographic studies are not required to satisfy these response requirements except for the requirement of FDG PET if imaging MRD-negative status is reported. †Sustained MRD negativity when reported should also annotate the method used (eg, sustained flow MRD-negative, sustained sequencing MRD-negative). ‡Bone marrow MFC should follow NGF guidelines (Paiva B, Gutierrez NC, Rosinol L, et al, Blood 2012; 119: 687–91). The reference NGF method is an eight-colour two-tube approach, which has been extensively validated. The two-tube approach improves reliability, consistency, and sensitivity because of the acquisition of a greater number of cells. The eight-colour technology is widely available globally and the NGF method has already been adopted in many flow laboratories worldwide. The complete eight-colour method is most efficient using a lyophilised mixture of antibodies which reduces errors, time, and costs. 5 million cells should be assessed. The FCM method employed should have a sensitivity of detection of at least 1 in 10^5 plasma cells. §DNA sequencing assay on bone marrow aspirate should use a validated assay such as LymphoSIGHT (Sequenta). ¶Criteria used by Zamagni and colleagues (Zamagni E, Nanni C, Mancuso K, et al. Clin Cancer Res 2015; 21: 4384–90), and expert panel (IMPetUs; Italian Myeloma criteria for PET Use) (Usmani SZ, Mitchell A, Waheed S, et al. Blood 2013; 121: 1819–23; Nanni C, Zamagni E, Versari A, et al. Eur J Nucl Med Mol Imaging 2015; 43: 414–21.). Baseline positive lesions were identified by presence of focal areas of increased uptake within bones, with or without any underlying lesion identified by CT and present on at least two consecutive slices. Alternatively, an SUV_{max}=2.5 within osteolytic CT areas >1 cm in size, or SUV_{max}=1.5 within osteolytic CT areas ≤1 cm in size were considered positive. Imaging should be performed once MRD negativity is determined by MFC or NGS. ||Derived from international uniform response criteria for multiple myeloma (Durie BG, Harousseau JL, Miguel JS, et al, Leukemia 2006; 20: 1467–73). Minor response definition and clarifications derived from Rajkumar and colleagues (Rajkumar SV, Harousseau JL, Durie B, et al, Blood 2011; 117: 4691–95). When the only method to measure disease is by serum FLC levels: complete response can be defined as a normal FLC ratio of 0.26 to 1.65 in addition to the complete response criteria listed previously. Very good partial response in such patients requires a ≥90% decrease in the difference between involved and uninvolved FLC levels. All response categories require two consecutive assessments made at any time before the institution of any new therapy; all categories also require no known evidence of progressive or new bone lesions or extramedullary plasmacytomas if radiographic studies were performed. Radiographic studies are not required to satisfy these response requirements. Bone marrow assessments do not need to be confirmed. Each category, except for stable disease, will be considered unconfirmed until the confirmatory test is performed. The date of the initial test is considered as the date of response for evaluation of time dependent outcomes such as duration of response. **All recommendations regarding clinical uses relating to serum FLC levels or FLC ratio are based on results obtained with the validated Freelite test (Binding Site, Birmingham, UK). ††Presence/absence of clonal cells on immunohistochemistry is based upon the κ/λ/L ratio. An abnormal κ/λ ratio by immunohistochemistry requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting presence of an abnormal clone is κ/λ of >4:1 or <1:2. ‡‡Special attention should be given to the emergence of a different monoclonal protein following treatment, especially in the setting of patients having achieved a conventional complete response, often related to oligoclonal

reconstitution of the immune system. These bands typically disappear over time and in some studies have been associated with a better outcome. Also, appearance of monoclonal IgG κ in patients receiving monoclonal antibodies should be diff erentiated from the therapeutic antibody. §§Plasmacytoma measurements should be taken from the CT portion of the PET/CT, or MRI scans, or dedicated CT scans where applicable. For patients with only skin involvement, skin lesions should be measured with a ruler. Measurement of tumour size will be determined by the SPD. ¶¶Positive immunofi xation alone in a patient previously classifi ed as achieving a complete response will not be considered progression. For purposes of calculating time to progression and progression-free survival, patients who have achieved a complete response and are MRD-negative should be evaluated using criteria listed for progressive disease. Criteria for relapse from a complete response or relapse from MRD should be used only when calculating disease-free survival. ||||In the case where a value is felt to be a spurious result per physician discretion (eg, a possible laboratory error), that value will not be considered when determining the lowest value.

Standard treatment for multiple myeloma and associated diseases includes chemotherapy, stem cell transplant (autologous or allogeneic), radiation therapy, and other drug therapies. Frequently used anti-myeloma drugs include alkylating agents (e.g., bendamustine, cyclophosphamide and melphalan), proteasome inhibitors (e.g., bortezomib), corticosteroids (e.g., dexamethasone and prednisone), and immunomodulators (e.g., thalidomide and lenalidomide or Revlimid®), or any combination thereof. Biphosphonate drugs are also frequently administered in combination with the standard anti-MM treamtents to prevent bone loss. Patients older than 65-70 years of age are unlikely candidates for stem cell transplant. In some cases, double-autologous stem cell transplants are options for patients less than 60 years of age with suboptimal response to the first transplant. The compositions and methods of the present invention may be administered in combination with any of the currently prescribed treatments for multiple myeloma.

The first phase of treatment for multiple myeloma is induction therapy. The goal of induction therapy is to reduce the number of plasma cells in the bone marrow and the molecules (e.g., proteins) produced by the plasma cells. Induction therapy usually comprises a combination of 2 or 3 of the following types of drugs: targeted therapy, chemotherapy, or corticosteroids.

Induction therapy for patients who can have a stem cell transplant

Patients for a stem cell transplant are usually 70 years of age or younger and in generally good health. Patients can have induction therapy followed by high-dose chemotherapy and a stem cell transplant. Induction therapy is usually given for several cycles and may include one or more of the following drugs: CyBorD regimen – cyclophosphamide (Cytoxan, Procytox), bortezomib (Velcade) and dexamethasone (Decadron, Dexasone); VRD regimen – bortezomib, lenalidomide (Revlimid) and dexamethasone; thalidomide (Thalomid) and dexamethasone; lenalidomide and low-dose dexamethasone; bortezomib and dexamethasone; VTD regimen – bortezomib, thalidomide and dexamethasone; bortezomib, cyclophosphamide and prednisone; bortezomib, doxorubicin (Adriamycin)

and dexamethasone; dexamethasone; or liposomal doxorubicin (Caelyx, Doxil), vincristine (Oncovin) and dexamethasone

Induction therapy for patients who cannot have a stem cell transplant

Patients who cannot have a stem cell transplant may have induction therapy using one or more of the following drugs: CyBorD regimen – cyclophosphamide, bortezomib and dexamethasone; lenalidomide (Revlimid) and low-dose dexamethasone; MPT regimen – melphalan, prednisone and thalidomide; VMP regimen – bortezomib, melphalan and prednisone; MPL regimen – melphalan, prednisone and lenalidomide; melphalan and prednisone; bortezomib and dexamethasone; dexamethasone; liposomal doxorubicin, vincristine and dexamethasone; thalidomide and dexamethasone; VAD regimen – vincristine, doxorubicin and dexamethasone; or VRD regimen – bortezomib, lenalidomide and dexamethasone.

Another example of a disease or disorder associated with BCMA is Hodgkin's lymphoma and non-Hodgkin's lymphoma (*See* Chiu et al., *Blood*. 2007, 109(2):729-39; He et al., *J Immunol.* 2004, 172(5):3268-79).

Hodgkin's lymphoma (HL), also known as Hodgkin's disease, is a cancer of the lymphatic system that originates from white blood cells, or lymphocytes. The abnormal cells that comprise the lymphoma are called Reed-Sternberg cells. In Hodgkin's lymphoma, the cancer spreads from one lymph node group to another. Hodgkin's lymphoma can be subclassified into four pathologic subtypes based upon Reed-Sternberg cell morphology and the cell composition around the Reed-Sternberg cells (as determined through lymph node biopsy): nodular sclerosing HL, mixed-cellularity subtype, lymphocyte-rich or lymphocytic predominance, lymphocyte depleted. Some Hodgkin's lymphoma can also be nodular lymphocyte predominant Hodgkin's lymphoma, or can be unspecified. Symptoms and signs of Hodgkin's lymphoma include painless swelling in the lymph nodes in the neck, armpits, or groin, fever, night sweats, weight loss, fatigue, itching, or abdominal pain.

Non-Hodgkin's lymphoma (NHL) comprises a diverse group of blood cancers that include any kind of lymphoma other than Hodgkin's lymphoma. Subtypes of non-Hodgkin's lymphoma are classified primarily by cell morphology, chromosomal aberrations, and surface markers. NHL subtypes (or NHL-associated cancers) include B cell lymphomas such as, but not limited to, Burkitt's lymphoma, B-cell chronic lymphocytic leukemia (B-CLL), B-cell prolymphocytic leukemia (B-PLL), chronic lymphocytic leukemia (CLL), diffuse large B-cell lymphoma (DLBCL) (e.g., intravascular large B-cell lymphoma and primary mediastinal B-cell lymphoma), follicular lymphoma (e.g., follicle center lymphoma, follicular small cleaved cell), hair cell leukemia, high grade B-cell lymphoma (Burkitt's

like), lymphoplasmacytic lymphoma (Waldenstrom's macroglublinemia), mantle cell lymphoma, marginal zone B-cell lymphomas (e.g., extranodal marginal zone B-cell lymphoma or mucosa-associated lymphoid tissue (MALT) lymphoma, nodal marginal zone B-cell lymphoma, and splenic marginal zone B-cell lymphoma), plasmacytoma/myeloma, precursor B-lymphoblastic leukemia/lymphoma (PB-LBL/L), primary central nervous system (CNS) lymphoma, primary intraocular lymphoma, small lymphocytic lymphoma (SLL); and T cell lymphomas, such as, but not limited to, anaplastic large cell lymphoma (ALCL), adult T-cell lymphoma/leukemia (e.g., smoldering, chronic, acute and lymphomatous), angiocentric lymphoma, angioimmunoblastic T-cell lymphoma, cutaneous T-cell lymphomas (e.g., mycosis fungoides, Sezary syndrome, etc.), extranodal natural killer/T-cell lymphoma (nasal-type), enteropathy type intestinal T-cell lymphoma, large granular lymphocyte leukemia, precursor T-lymphoblastic lymphoma/leukemia (T-LBL/L), T-cell chronic lymphocytic leukemia/prolymphocytic leukemia (T-CLL/PLL), and unspecified peripheral T-cell lymphoma. Symptoms and signs of Hodgkin's lymphoma include painless swelling in the lymph nodes in the neck, armpits, or groin, fever, night sweats, weight loss, fatigue, itching, abdominal pain, coughing, or chest pain.

The staging is the same for both Hodgkin's and non-Hodgkin's lymphoma, and refers to the extent of spread of the cancer cells within the body. In stage I, the lymphoma cells are in one lymph node group. In stage II, lymphoma cells are present in at least two lymph node groups, but both groups are on the same side of the diaphragm, or in one part of a tissue or organ and the lymph nodes near that organ on the same side of the diaphragm. In stage III, lymphoma cells are in lymph nodes on both sides of the diaphragm, or in one part of a tissue or organ near these lymph node groups or in the spleen. In stage IV, lymphoma cells are found in several parts of at least one organ or tissue, or lymphoma cells are in an organ and in lymph nodes on the other side of the diaphragm. In addition to the Roman numeral staging designation, the stages of can also be described by letters A, B, E, and S, wherein A refers to patients without symptoms, B refers to patients with symptoms, E refers to patients in which lymphoma is found in tissues outside the lymph system, and S refers to patients in which lymphoma is found in the spleen.

Hodgkin's lymphoma is commonly treated with radiation therapy, chemotherapy, or hematopoietic stem cell transplantation. The most common therapy for non-Hodgkin's lymphoma is R-CHOP, which consists of four different chemotherapies (cyclophosphamide, doxorubicin, vincristine, and prenisolone) and rituximab (Rituxan®). Other therapies commonly used to treat NHL include other chemotherapeutic agents, radiation therapy, stem cell transplantation (autologous or allogeneic bone marrow transplantation), or biological therapy, such as immunotherapy. Other examples of biological therapeutic agents include, but are not limited to, rituximab (Rituxan®), tositumomab (Bexxar®),

epratuzumab (LymphoCide®), and alemtuzumab (MabCampath®). The compositions and methods of the present invention may be administered in combination with any of the currently prescribed treatments for Hodgkin's lymphoma or non-Hodgkin's lymphoma.

BCMA expression has also been associated Waldenstrom's macroglobulinemia (WM), also known as lymphoplasmacytic lymphoma (LPL). (See Elsawa et al., *Blood*. 2006, 107(7):2882-8). Waldenstrom's macroglobulinemia was previously considered to be related to multiple myeloma, but has more recently been classified as a subtype of non-Hodgkin's lymphoma. WM is characterized by uncontrolled B-cell lymphocyte proliferation, resulting in anemia and production of excess amounts of paraprotein, or immunoglobulin M (IgM), which thickens the blood and results in hyperviscosity syndrome. Other symptoms or signs of WM include fever, night sweats, fatigue, anemia, weight loss, lymphadenopathy or splenomegaly, blurred vision, dizziness, nose bleeds, bleeding gums, unusual bruises, renal impairment or failure, amyloidosis, or peripheral neuropathy.

Standard treatment for WM consists of chemotherapy, specifically with rituximab (Rituxan®). Other chemotherapeutic drugs can be used in combination, such as chlorambucil (Leukeran®), cyclophosphamide (Neosar®), fludarabine (Fludara®), cladribine (Leustatin®), vincristine, and/or thalidomide. Corticosteriods, such as prednisone, can also be administered in combination with the chemotherapy. Plasmapheresis, or plasma exchange, is commonly used throughout treatment of the patient to alleviate some symptoms by removing the paraprotein from the blood. In some cases, stem cell transplantation is an option for some patients.

Another example of a disease or disorder associated with BCMA is brain cancer. Specifically, expression of BCMA has been associated with astrocytoma or glioblastoma (*See* Deshayes et al, *Oncogene*. 2004, 23(17):3005-12, Pelekanou et al., *PLoS One*. 2013, 8(12):e83250). Astrocytomas are tumors that arise from astrocytes, which are a type of glial cell in the brain. Glioblastoma (also known as glioblastoma multiforme or GBM) is the most malignant form of astrocytoma, and is considered the most advanced stage of brain cancer (stage IV). There are two variants of glioblastoma: giant cell glioblastoma and gliosarcoma. Other astrocytomas include juvenile pilocytic astrocytoma (JPA), fibrillary astrocytoma, pleomorphic xantroastrocytoma (PXA), desembryoplastic neuroepithelial tumor (DNET), and anaplastic astrocytoma (AA).

Symptoms or signs associated with glioblastoma or astrocytoma include increased pressure in the brain, headaches, seizures, memory loss, changes in behavior, loss in movement or sensation on one side of the body, language dysfunction, cognitive impairments, visual impairment, nausea, vomiting, and weakness in the arms or legs.

Surgical removal of the tumor (or resection) is the standard treatment for removal of as much of the glioma as possible without damaging or with minimal damage to the normal, surrounding brain. Radiation therapy and/or chemotherapy are often used after surgery to suppress and slow recurrent disease from any remaining cancer cells or satellite lesions. Radiation therapy includes whole brain radiotherapy (conventional external beam radiation), targeted three-dimensional conformal radiotherapy, and targeted radionuclides. Chemotherapeutic agents commonly used to treat glioblastoma include temozolomide, gefitinib or erlotinib, and cisplatin. Angiogenesis inhibitors, such as Bevacizumab (Avastin®), are also commonly used in combination with chemotherapy and/or radiotherapy.

Supportive treatment is also frequently used to relieve neurological symptoms and improve neurologic function, and is administered in combination any of the cancer therapies described herein. The primary supportive agents include anticonvulsants and corticosteroids. Thus, the compositions and methods of the present invention may be used in combination with any of the standard or supportive treatments to treat a glioblastoma or astrocytoma.

Non-cancer related diseases and disorders associated with BCMA expression can also be treated by the compositions and methods disclosed herein. Examples of non-cancer related diseases and disorders associated with BCMA expression include, but are not limited to: viral infections; e.g., HIV, fungal invections, e.g.,*C. neoformans*; irritable bowel disease; ulcerative colitis, and disorders related to mucosal immunity.

The CAR-modified immune effector cells (e.g., T cells or NK cells) of the present invention may be administered either alone, or as a pharmaceutical composition in combination with diluents and/or with other components such as IL-2 or other cytokines or cell populations.

The present invention provides for compositions and methods for treating cancer. In one aspect, the cancer is a hematologic cancer including but is not limited to hematolical cancer is a leukemia or a lymphoma. In one aspect, the CAR-expressing cells (e.g., CART cells or CAR-expressing NK cells)of the invention may be used to treat cancers and malignancies such as, but not limited to, e.g., acute leukemias including but not limited to, e.g., B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, e.g., chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to, e.g., B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell

lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like. Further a disease associated with BCMA expression includes, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases expressing BCMA.

In embodiments, a composition described herein can be used to treat a disease including but not limited to a plasma cell proliferative disorder, e.g., asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammapathy of undetermined significance (MGUS), Waldenstrom's macroglobulinemia, plasmacytomas (e.g., plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, and POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome).

In embodiments, a composition described herein can be used to treat a disease including but not limited to a cancer, e.g., a cancer described herein, e.g., a prostate cancer (e.g., castrate-resistant or therapy-resistant prostate cancer, or metastatic prostate cancer), pancreatic cancer, or lung cancer.

The present invention also provides methods for inhibiting the proliferation or reducing a BCMA-expressing cell population, the methods comprising contacting a population of cells comprising a BMCA-expressing cell with an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention that binds to the BCMA-expressing cell. In a specific aspect, the present invention provides methods for inhibiting the proliferation or reducing the population of cancer cells expressing BCMA, the methods comprising contacting the BCMA-expressing cancer cell population with an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention that binds to the BCMA-expressing cell. In one aspect, the present invention provides methods for inhibiting the proliferation or reducing the population of cancer cells expressing BCMA, the methods comprising contacting the BMCA-expressing cancer cell population with an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention that binds to the BCMA-expressing cell. In certain aspects, the anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention reduces the quantity, number, amount or percentage of cells and/or cancer cells by at least 25%, at least 30%, at least 40%, at least 50%, at least 65%, at least 75%, at least 85%, at least 95%, or at least 99% in a subject with or animal model for myeloid leukemia or another cancer associated with BCMA-expressing cells relative to a negative control. In one aspect, the subject is a human.

The present invention also provides methods for preventing, treating and/or managing a disease associated with BCMA-expressing cells (e.g., a hematologic cancer or atypical cancer expessing BCMA), the methods comprising administering to a subject in need an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention that binds to the BCMA-expressing cell. In one aspect, the subject is a human. Non-limiting examples of disorders associated with BCMA-expressing cells include viral or fungal infections, and disorders related to mucosal immunity.

The present invention also provides methods for preventing, treating and/or managing a disease associated with BCMA-expressing cells, the methods comprising administering to a subject in need an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention that binds to the BCMA-expressing cell. In one aspect, the subject is a human.

The present invention provides methods for preventing relapse of cancer associated with BCMA-expressing cells, the methods comprising administering to a subject in need thereof an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)of the invention that binds to the BCMA-expressing cell. In one aspect, the methods comprise administering to the subject in need thereof an effective amount of an anti-BCMA CAR-expressing cell (e.g., BCMA CART cell or BCMA CAR-expressing NK cell)described herein that binds to the BCMA-expressing cell in combination with an effective amount of another therapy.

Methods using Biomarkers for Evaluating CAR-Effectiveness, Subject Suitability, or Sample Suitability

In another aspect, the invention features a method of evaluating or monitoring the effectiveness of a CAR-expressing cell therapy (e.g., a BCMA CAR therapy), in a subject (e.g., a subject having a cancer, e.g., a hematological cancer), or the suitability of a sample (e.g., an apheresis sample) for a CAR therapy (e.g., a BCMA CAR therapy). The method includes acquiring a value of effectiveness to the CAR therapy, subject suitability, or sample suitability, wherein said value is indicative of the effectiveness or suitability of the CAR-expressing cell therapy.

In some embodiments of any of the methods disclosed herein, the CAR-expressing cell therapy comprises a plurality (e.g., a population) of CAR-expressing immune effector cells, e.g., a plurality (e.g., a population) of T cells or NK cells, or a combination thereof. In one embodiment, the CAR-expressing cell therapy is a BCMACAR therapy.

In some embodiments of any of the methods disclosed herein, the subject is evaluated prior to receiving, during, or after receiving, the CAR-expressing cell therapy.

In some embodiments of any of the methods disclosed herein, a responder (e.g., a complete responder) has, or is identified as having, a greater level or activity of one, two, or more (all) of GZMK, PPF1BP2, or naïve T cells as compared to a non-responder.

In some embodiments of any of the methods disclosed herein, a non-responder has, or is identified as having, a greater level or activity of one, two, three, four, five, six, seven, or more (e.g., all) of IL22, IL-2RA, IL-21, IRF8, IL8, CCL17, CCL22, effector T cells, or regulatory T cells, as compared to a responder.

In an embodiment, a relapser is a patient having, or who is identified as having, an increased level of expression of one or more of (e.g., 2, 3, 4, or all of) the following genes, compared to non relapsers: MIR199A1, MIR1203, uc021ovp, ITM2C, and HLA-DQB1 and/or a decreased levels of expression of one or more of (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all of) the following genes, compared to non relapsers: PPIAL4D, TTTY10, TXLNG2P, MIR4650-1, KDM5D, USP9Y, PRKY, RPS4Y2, RPS4Y1, NCRNA00185, SULT1E1, and EIF1AY.

In some embodiments of any of the methods disclosed herein, a non-responder has, or is identified as having, a greater percentage of an immune cell exhaustion marker, *e.g.*, one, two or more immune checkpoint inhibitors (e.g., PD-1, PD-L1, TIM-3 and/or LAG-3). In one embodiment, a non-responder has, or is identified as having, a greater percentage of PD-1, PD-L1, or LAG-3 expressing immune effector cells (e.g., CD4+ T cells and/or CD8+ T cells) (e.g., CAR-expressing CD4+ cells and/or CD8+ T cells) compared to the percentage of PD-1 or LAG-3 expressing immune effector cells from a responder.

In one embodiment, a non-responder has, or is identified as having, a greater percentage of immune cells having an exhausted phenotype, *e.g.*, immune cells that co-express at least two exhaustion markers, *e.g.*, co-expresses PD-1, PD-L1 and/or TIM-3. In other embodiments, a non-responder has, or is identified as having, a greater percentage of immune cells having an exhausted phenotype, *e.g.*, immune cells that co-express at least two exhaustion markers, *e.g.*, co-expresses PD-1 and LAG-3.

In some embodiments of any of the methods disclosed herein, a non-responder has, or is identified as having, a greater percentage of PD-1/ PD-L1+/LAG-3+ cells in the CAR-expressing cell population (e.g., a BCMACAR+ cell population) compared to a responder (e.g., a complete responder) to the CAR-expressing cell therapy.

In some embodiments of any of the methods disclosed herein, a partial responder has, or is identified as having, a higher percentages of PD-1/ PD-L1+/LAG-3+ cells, than a responder, in the CAR-expressing cell population (e.g., a BCMACAR+ cell population).

In some embodiments of any of the methods disclosed herein, a non-responder has, or is identified as having, an exhausted phenotype of PD1/ PD-L1+ CAR+ and co-expression of LAG3 in the CAR-expressing cell population (e.g., a BCMACAR + cell population).

In some embodiments of any of the methods disclosed herein, a non-responder has, or is identified as having, a greater percentage of PD-1/ PD-L1+/TIM-3+ cells in the CAR-expressing cell population (e.g., a BCMACAR + cell population) compared to the responder (e.g., a complete responder).

In some embodiments of any of the methods disclosed herein, a partial responders has, or is identified as having, a higher percentage of PD-1/ PD-L1+/TIM-3+ cells, than responders, in the CAR-expressing cell population (e.g., a BCMACAR + cell population).

In some embodiments of any of the methods disclosed herein, the presence of CD8+ CD27+ CD45RO- T cells in an apheresis sample is a positive predictor of the subject response to a CAR-expressing cell therapy (e.g., a BCMACAR therapy).

In some embodiments of any of the methods disclosed herein, a high percentage of PD1+ CAR+ and LAG3+ or TIM3+ T cells in an apheresis sample is a poor prognostic predictor of the subject response to a CAR-expressing cell therapy (e.g., a BCMACAR therapy).

In some embodiments of any of the methods disclosed herein, the responder (e.g., the complete or partial responder) has one, two, three or more (or all) of the following profile:

(i) has a greater number of CD27+ immune effector cells compared to a reference value, e.g., a non-responder number of CD27+ immune effector cells;

(ii) (i) has a greater number of CD8+ T cells compared to a reference value, e.g., a non-responder number of CD8+ T cells;

(iii) has a lower number of immune cells expressing one or more checkpoint inhibitors, e.g., a checkpoint inhibitor chosen from PD-1, PD-L1, LAG-3, TIM-3, or KLRG-1, or a combination, compared to a reference value, e.g., a non-responder number of cells expressing one or more checkpoint inhibitors; or

(iv) has a greater number of one, two, three, four or more (all) of resting T_{EFF} cells, resting T_{REG} cells, naïve CD4 cells, unstimulated memory cells or early memory T cells, or a combination thereof, compared to a reference value, e.g., a non-responder number of resting T_{EFF} cells, resting T_{REG} cells, naïve CD4 cells, unstimulated memory cells or early memory T cells.

In some embodiments of any of the methods disclosed herein, the cytokine level or activity of (vi) is chosen from one, two, three, four, five, six, seven, eight, or more (or all) of cytokine CCL20/MIP3a, IL17A, IL6, GM-CSF, IFN-γ, IL10, IL13, IL2, IL21, IL4, IL5, IL9 or TNFα, or a combination thereof. The cytokine can be chosen from one, two, three, four or more (all) of IL-17a, CCL20, IL2, IL6, or TNFa. In one embodiment, an increased level or activity of a cytokine is chosen from one or both of IL-17a and CCL20, is indicative of increased responsiveness or decreased relapse.

In embodiments, the responder, a non-responder, a relapser or a non-relapser identified by the methods herein can be further evaluated according to clinical criteria. For example, a complete

responder has, or is identified as, a subject having a disease, e.g., a cancer, who exhibits a complete response, e.g., a complete remission, to a treatment. A complete response may be identified, e.g., using the NCCN Guidelines®, or Cheson et al, J Clin Oncol 17:1244 (1999) and Cheson et al., "Revised Response Criteria for Malignant Lymphoma", J Clin Oncol 25:579-586 (2007) (both of which are incorporated by reference herein in their entireties), as described herein. A partial responder has, or is identified as, a subject having a disease, e.g., a cancer, who exhibits a partial response, e.g., a partial remission, to a treatment. A partial response may be identified, e.g., using the NCCN Guidelines®, or Cheson criteria as described herein. A non-responder has, or is identified as, a subject having a disease, e.g., a cancer, who does not exhibit a response to a treatment, e.g., the patient has stable disease or progressive disease. A non-responder may be identified, e.g., using the NCCN Guidelines®, or Cheson criteria as described herein.

Alternatively, or in combination with the methods disclosed herein, responsive to said value, performing one, two, three four or more of:

administering e.g., to a responder or a non-relapser, a CAR-expressing cell therapy;

administered an altered dosing of a CAR-expressing cell therapy;

altering the schedule or time course of a CAR-expressing cell therapy;

administering, e.g., to a non-responder or a partial responder, an additional agent in combination with a CAR-expressing cell therapy, e.g., a checkpoint inhibitor, e.g., a checkpoint inhibitor described herein;

administering to a non-responder or partial responder a therapy that increases the number of younger T cells in the subject prior to treatment with a CAR-expressing cell therapy;

modifying a manufacturing process of a CAR-expressing cell therapy, e.g., enriching for younger T cells prior to introducing a nucleic acid encoding a CAR, or increasing the transduction efficiency, e.g., for a subject identified as a non-responder or a partial responder;

administering an alternative therapy, e.g., for a non-responder or partial responder or relapser; or

if the subject is, or is identified as, a non-responder or a relapser, decreasing the T_{REG} cell population and/or T_{REG} gene signature, *e.g.*, by one or more of CD25 depletion, administration of cyclophosphamide, anti-GITR antibody, or a combination thereof.

In certain embodiments, the subject is pre-treated with an anti-GITR antibody. In certain embodiment, the subject is treated with an anti-GITR antibody prior to infusion or re-infusion.

Combination Therapies

A CAR-expressing cell described herein may be used in combination with other known agents and therapies. Administered "in combination", as used herein, means that two (or more) different treatments are delivered to the subject during the course of the subject's affliction with the disorder, e.g., the two or more treatments are delivered after the subject has been diagnosed with the disorder and before the disorder has been cured or eliminated or treatment has ceased for other reasons. In some embodiments, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is overlap in terms of administration. This is sometimes referred to herein as "simultaneous" or "concurrent delivery". In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In some embodiments of either case, the treatment is more effective because of combined administration. For example, the second treatment is more effective, e.g., an equivalent effect is seen with less of the second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second treatment were administered in the absence of the first treatment, or the analogous situation is seen with the first treatment. In some embodiments, delivery is such that the reduction in a symptom, or other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

A CAR-expressing cell described herein and the at least one additional therapeutic agent can be administered simultaneously, in the same or in separate compositions, or sequentially. For sequential administration, the CAR-expressing cell described herein can be administered first, and the additional agent can be administered second, or the order of administration can be reversed.

The CAR therapy and/or other therapeutic agents, procedures or modalities can be administered during periods of active disorder, or during a period of remission or less active disease. The CAR therapy can be administered before the other treatment, concurrently with the treatment, post-treatment, or during remission of the disorder.

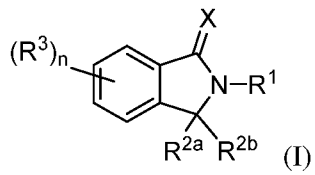
When administered in combination, the CAR therapy and the additional agent (e.g., second or third agent), or all, can be administered in an amount or dose that is higher, lower or the same than the amount or dosage of each agent used individually, e.g., as a monotherapy. In certain embodiments, the administered amount or dosage of the CAR therapy, the additional agent (e.g., second or third agent), or all, is lower (e.g., at least 20%, at least 30%, at least 40%, or at least 50%) than the amount or dosage of each agent used individually, e.g., as a monotherapy. In other embodiments, the amount or dosage of the CAR therapy, the additional agent (e.g., second or third agent), or all, that results in a desired effect (e.g.,

treatment of cancer) is lower (e.g., at least 20%, at least 30%, at least 40%, or at least 50% lower) than the amount or dosage of each agent used individually, e.g., as a monotherapy, required to achieve the same therapeutic effect.

Thalidomide class of compounds

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a member of the thalidomide class of compounds. In some embodiments, members of the thalidomide class of compounds include, but are not limited to, lenalidomide (CC-5013), pomalidomide (CC-4047 or ACTIMID), thalidomide, or salts or derivatives thereof. In some embodiments, the compound can be a mixture of one, two, three, or more members of the thalidomide class of compounds. Thalidomide analogs and immunomodulatory properties of thalidomide analogs are described in Bodera and Stankiewicz, Recent Pat Endocr Metab Immune Drug Discov. 2011 Sep;5(3):192-6, which is hereby incorporated by reference in its entirety. The structural complex of thalidomide analogs and the E3 ubiquitin is described in Gandhi et al., Br J Haematol. 2014 Mar;164(6):811-21, which is hereby incorporated by reference in its entirety. The modulation of the E3 ubiquitin ligase by thalidomide analogs is described in Fischer et al., Nature. 2014 Aug 7;512(7512):49-53, which is hereby incorporated by reference in its entirety.

In some embodiments, the compound comprises a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt, ester, hydrate, solvate, or tautomer thereof, wherein:

X is O or S;

R^1 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl, each of which is optionally substituted by one or more R^4;

each of R^{2a} and R^{2b} is independently hydrogen or C_1-C_6 alkyl; or R^{2a} and R^{2b} together with the carbon atom to which they are attached form a carbonyl group or a thiocarbonyl group;

each of R^3 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, $-C(O)R^A$, $-C(O)OR^B$, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, $-S(O)_xR^E$, $-S(O)_xN(R^C)(R^D)$, or $-N(R^C)S(O)_xR^E$, wherein each alkyl, alkenyl, alkynyl, and heteroalkyl is independently and optionally substituted with one or more R^6;

each R^4 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, oxo, $-C(O)R^A$, $-C(O)OR^B$, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, $-S(O)_xR^E$, -

$S(O)_xN(R^C)(R^D)$, -N $(R^C)S(O)_xR^E$, carbocyclyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, heteroalkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently and optionally substituted with one or more R^7;

each of R^A, R^B, R^C, R^D, and R^E is independently hydrogen or C_1-C_6 alkyl;

each R^6 is independently C_1-C_6 alkyl, oxo, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, -$N(R^C)C(O)R^A$, aryl, or heteroaryl, wherein each aryl and heteroaryl is independently and optionally substituted with one or more R^8;

each R^7 is independently halo, oxo, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, or -$N(R^C)C(O)R^A$;

each R^8 is independently C_1-C_6 alkyl, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, or -$N(R^C)C(O)R^A$;

n is 0, 1, 2, 3 or 4; and

x is 0, 1, or 2.

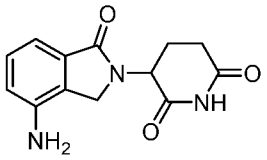
In some embodiments, X is O.

In some embodiments, R^1 is heterocyclyl. In some embodiments, R^1 is a 6-membered heterocyclyl or a 5-membered heterocyclyl. In some embodiments, R^1 is a nitrogen-containing heterocyclyl. In some embodiments, R^1 is piperidinyl (e.g., piperidine-2,6-dionyl).

In some embodiments, each of R^{2a} and R^{2b} is independently hydrogen. In some embodiments, R^{2a} and R^{2b} together with the carbon to which they are attached form a carbonyl group.

In some embodiments, R^3 is C_1-C_6 heteroalkyl, -$N(R^C)(R^D)$ or -$N(R^C)C(O)R^A$. In some embodiments, R^3 is C_1-C_6 heteroalkyl (e.g., $CH_2NHC(O)CH_2$-phenyl-t-butyl), -$N(R^C)(R^D)$ (e.g., NH_2), or -$N(R^C)C(O)R^A$ (e.g., $NHC(O)CH_3$).

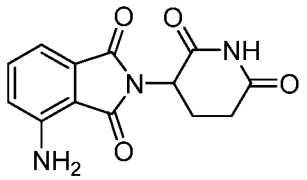
In an embodiment, X is O. In an embodiment, R^1 is heterocyclyl (e.g., piperidine-2,6-dionyl). In an embodiment, each of R^{2a} and R^{2b} is independently hydrogen. In an embodiment, n is 1. In an embodiment, R^3 is -$N(R^C)(R^D)$ (e.g., -NH_2). In an embodiment, the compound comprises lenalidomide, e.g., 3-(4-amino-1-oxoisoindolin-2-yl)piperidine-2,6-dione, or a pharmaceutically acceptable salt thereof. In an embodiment, the compound is lenalidomide, e.g., according to the following formula:



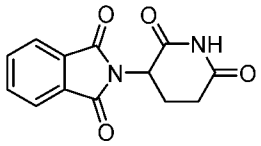
.

In an embodiment, X is O. In an embodiment, R^1 is heterocyclyl (e.g., piperidinyl-2,6-dionyl). In some embodiments, R^{2a} and R^{2b} together with the carbon to which they are attached form a carbonyl

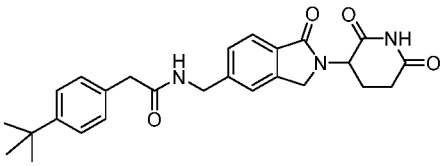
group. In an embodiment, n is 1. In an embodiment, R^3 is $-N(R^C)(R^D)$ (e.g., $-NH_2$). In an embodiment, the compound comprises pomalidomide, e.g., 4-amino-2-(2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione, or a pharmaceutically acceptable salt thereof. In an embodiment, the compound is pomalidomide, e.g., according to the following formula:



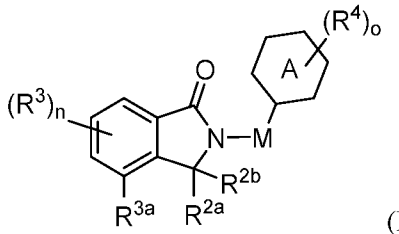
In an embodiment, X is O. In an embodiment, R^1 is heterocyclyl (e.g., piperidinyl-2,6-dionyl). In an embodiment, R^{2a} and R^{2b} together with the carbon to which they are attached form a carbonyl group. In an embodiment, n is 0. In an embodiment, the compound comprises thalidomide, e.g., 2-(2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione, or a pharmaceutically acceptable salt thereof. In an embodiment, the product is thalidomide, e.g., according to the following formula:



In an embodiment, X is O. In an embodiment, R^1 is heterocyclyl (e.g., piperidine-2,6-dionyl). In an embodiment, each of R^{2a} and R^{2b} is independently hydrogen. In an embodiment, n is 1. In an embodiment, R^3 is C_1-C_6 heteroalkyl (e.g., $CH_2NHC(O)CH_2$-phenyl-t-butyl) In an embodiment, the compound comprises 2-(4-(tert-butyl)phenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)acetamide, or a pharmaceutically acceptable salt thereof. In an embodiment, the compound has the structure as shown in the following formula:



In some embodiments, the compound is a compound of Formula (I-a):



(I-a)

or a pharmaceutically acceptable salt, ester, hydrate, or tautomer thereof, wherein:

Ring A is carbocyclyl, heterocyclyl, aryl, or heteroaryl, each of which optionally substituted with one or more R^4;

M is absent, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 heteroalkyl, wherein each alkyl, alkenyl, alkynyl, and heteroalkyl is optionally substituted with one or more R^4;

each of R^{2a} and R^{2b} is independently hydrogen or C_1-C_6 alkyl; or R^{2a} and R^{2b} together with the carbon atom to which they are attached to form a carbonyl group or thiocarbonyl group;

R^{3a} is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, -$C(O)R^A$, -$C(O)OR^B$, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, -$N(R^C)C(O)R^A$, -$S(O)_xR^E$, -$S(O)_xN(R^C)(R^D)$, or -$N(R^C)S(O)_xR^E$, wherein each alkyl, alkenyl, alkynyl, and heteroalkyl is optionally substituted with one or more R^6;

each of R^3 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, -$C(O)R^A$, -$C(O)OR^B$, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, -$N(R^C)C(O)R^A$, -$S(O)_xR^E$, -$S(O)_xN(R^C)(R^D)$, or -N (R^C)$S(O)_xR^E$, wherein each alkyl, alkenyl, alkynyl, and heteroalkyl is independently and optionally substituted with one or more R^6;

each R^4 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, oxo, -$C(O)R^A$, -$C(O)OR^B$, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, -$N(R^C)C(O)R^A$, $S(O)_xR^E$, -$S(O)_xN(R^C)(R^D)$, -N (R^C)$S(O)_xR^E$, carbocyclyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is independently and optionally substituted with one or more R^7;

each of R^A, R^B, R^C, R^D, and R^E is independently hydrogen or C_1-C_6 alkyl;

each R^6 is independently C_1-C_6 alkyl, oxo, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, -$N(R^C)C(O)R^A$, aryl, or heteroaryl, wherein each aryl or heteroaryl is independently and optionally substituted with one or more R^8;

each R^7 is independently halo, oxo, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, or -$N(R^C)C(O)R^A$;

each R^8 is independently C_1-C_6 alkyl, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, or -$N(R^C)C(O)R^A$;

n is 0, 1, 2, or 3;

o is 0, 1, 2, 3, 4, or 5; and

x is 0, 1, or 2.

In some embodiments, X is O.

In some embodiments, M is absent.

In some embodiments, Ring A is heterocyclyl. In some embodiments, Ring A is heterocyclyl, e.g., a 6-membered heterocyclyl or a 5-membered heterocyclyl. In some embodiments, Ring A is a

nitrogen-containing heterocyclyl. In some embodiments, Ring A is piperidinyl (e.g., piperidine-2,6-dionyl).

In some embodiments, M is absent and Ring A is heterocyclyl (e.g., piperidinyl, e.g., piperidine-2,6-dionyl).

In some embodiments, each of R^{2a} and R^{2b} is independently hydrogen. In some embodiments, R^{2a} and R^{2b} together with the carbon to which they are attached form a carbonyl group.

In some embodiments, R^{3a} is hydrogen, $-N(R^C)(R^D)$ or $-N(R^C)C(O)R^A$. In some embodiments, R^{3a} is hydrogen. In some embodiments, R^{3a} is $-N(R^C)(R^D)$ (e.g., $-NH_2$). In some embodiments, R^{3a} is $-N(R^C)C(O)R^A$ (e.g, $NHC(O)CH_3$).

In some embodiments, R^3 is C_1-C_6 heteroalkyl (e.g., $CH_2NHC(O)CH_2$-phenyl-t-butyl). In some embodiments, n is 0 or 1. In some embodiments, n is 0. In some embodiments, n is 1.

The compound may comprise one or more chiral centers or exist as one or more stereoisomers. In some embodiments, the compound comprises a single chiral center and is a mixture of stereoisomers, e.g., an R stereoisomer and an S stereoisomer. In some embodiments, the mixture comprises a ratio of R stereoisomers to S stereoisomers, for example, about a 1:1 ratio of R stereoisomers to S stereoisomers (i.e., a racemic mixture). In some embodiments, the mixture comprises a ratio of R stereoisomers to S stereoisomers of about 51:49, about 52: 48, about 53:47, about 54:46, about 55:45, about 60:40, about 65:35, about 70:30, about 75:25, about 80:20, about 85:15, about 90:10, about 95:5, or about 99:1. In some embodiments, the mixture comprises a ratio of S stereoisomers to R stereoisomers of about 51:49, about 52: 48, about 53:47, about 54:46, about 55:45, about 60:40, about 65:35, about 70:30, about 75:25, about 80:20, about 85:15, about 90:10, about 95:5, or about 99:1. In some embodiments, the compound is a single stereoisomer of Formula (I) or Formula (I-a), e.g., a single R stereoisomer or a single S stereoisomer.

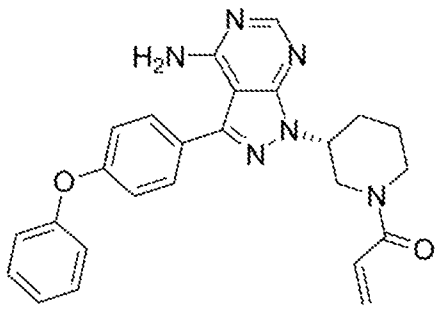
Kinase inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a kinase inhibitor. In one embodiment, the kinase inhibitor is a CDK4 inhibitor, e.g., a CDK4 inhibitor described herein, e.g., a CDK4/6 inhibitor, such as, e.g., 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-yl-pyridin-2-ylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one, hydrochloride (also referred to as palbociclib or PD0332991). In one embodiment, the kinase inhibitor is a BTK inhibitor, e.g., a BTK inhibitor described herein, such as, e.g., ibrutinib. In one embodiment, the kinase inhibitor is an mTOR inhibitor, e.g., an mTOR inhibitor described herein, such as, e.g., rapamycin, a rapamycin analog, OSI-027. The mTOR inhibitor can be, e.g., an mTORC1 inhibitor and/or an mTORC2 inhibitor, e.g., an

mTORC1 inhibitor and/or mTORC2 inhibitor described herein. In one embodiment, the kinase inhibitor is a MNK inhibitor, e.g., a MNK inhibitor described herein, such as, e.g., 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine. The MNK inhibitor can be, e.g., a MNK1a, MNK1b, MNK2a and/or MNK2b inhibitor. In one embodiment, the kinase inhibitor is a dual PI3K/mTOR inhibitor described herein, such as, e.g., PF-04695102. In one embodiment, the kinase inhibitor is a DGK inhibitor, e.g., a DGK inhibitor described herein, such as, e.g., DGKinh1 (D5919) or DGKinh2 (D5794).

In one embodiment, the kinase inhibitor is a BTK inhibitor selected from ibrutinib (PCI-32765); GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13. In a preferred embodiment, the BTK inhibitor does not reduce or inhibit the kinase activity of interleukin-2-inducible kinase (ITK), and is selected from GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13.

In one embodiment, the kinase inhibitor is a BTK inhibitor, e.g., ibrutinib (PCI-32765). In embodiments, a CAR-expressing cell described herein is administered to a subject in combination with a BTK inhibitor (e.g., ibrutinib). In embodiments, a CAR-expressing cell described herein is administered to a subject in combination with ibrutinib (also called PCI-32765). The structure of ibrutinib (1-[(3*R*)-3-[4-Amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-d]pyrimidin-1-yl]piperidin-1-yl]prop-2-en-1-one) is shown below.



In embodiments, the subject has CLL, mantle cell lymphoma (MCL), or small lymphocytic lymphoma (SLL). For example, the subject has a deletion in the short arm of chromosome 17 (del(17p), e.g., in a leukemic cell). In other examples, the subject does not have a del(17p). In embodiments, the subject has relapsed CLL or SLL, e.g., the subject has previously been administered a cancer therapy (e.g., previously been administered one, two, three, or four prior cancer therapies). In embodiments, the subject has refractory CLL or SLL. In other embodiments, the subject has follicular lymphoma, e.g., relapse or refractory follicular lymphoma. In some embodiments, ibrutinib is administered at a dosage of about 300-600 mg/day (e.g., about 300-350, 350-400, 400-450, 450-500, 500-550, or 550-600 mg/day, e.g., about 420 mg/day or about 560 mg/day), e.g., orally. In embodiments, the ibrutinib is

administered at a dose of about 250 mg, 300 mg, 350 mg, 400 mg, 420 mg, 440 mg, 460 mg, 480 mg, 500 mg, 520 mg, 540 mg, 560 mg, 580 mg, 600 mg (e.g., 250 mg, 420 mg or 560 mg) daily for a period of time, e.g., daily for 21 day cycle cycle, or daily for 28 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of ibrutinib are administered. In some embodiments, ibrutinib is administered in combination with rituximab. See, e.g., Burger et al. (2013) Ibrutinib In Combination With Rituximab (iR) Is Well Tolerated and Induces a High Rate Of Durable Remissions In Patients With High-Risk Chronic Lymphocytic Leukemia (CLL): New, Updated Results Of a Phase II Trial In 40 Patients, Abstract 675 presented at 55th ASH Annual Meeting and Exposition, New Orleans, LA 7-10 Dec. Without being bound by theory, it is thought that the addition of ibrutinib enhances the T cell proliferative response and may shift T cells from a T-helper-2 (Th2) to T-helper-1 (Th1) phenotype. Th1 and Th2 are phenotypes of helper T cells, with Th1 versus Th2 directing different immune response pathways. A Th1 phenotype is associated with proinflammatory responses, e.g., for killing cells, such as intracellular pathogens/viruses or cancerous cells, or perpetuating autoimmune responses. A Th2 phenotype is associated with eosinophil accumulation and anti-inflammatory responses.

EGFR Inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an inhibitor of Epidermal Growth Factor Receptor (EGFR).

In some embodiments, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757.

In some embodiments, the EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757, is a covalent, irreversible tyrosine kinase inhibitor. In certain embodiments, the EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757 inhibits activating EGFR mutations (L858R, ex19del). In other embodiments, the EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757 does not inhibit, or does not substantially inhibit, wild-type (wt) EGFR. Compound A40 has shown efficacy in EGFR mutant NSCLC patients. In some embodiments, the EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO

2013/184757 also inhibits one or more kinases in the TEC family of kinases. The Tec family kinases include, *e.g.,* ITK, BMX, TEC, RLK, and BTK, and are central in the propogation of T-cell receptor and chemokine receptor signaling (Schwartzberg *et al.* (2005) *Nat. Rev. Immunol.* p. 284-95). For example, Compound A40 can inhibit ITK with a biochemical IC50 of 1.3 nM. ITK is a critical enzyme for the survival of Th2 cells and its inhibition results in a shift in the balance between Th2 and Th1 cells.

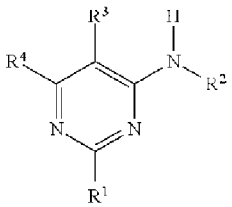
In some embodiments, the EGFR inhibitor is chosen from one of more of erlotinib, gefitinib, cetuximab, panitumumab, necitumumab, PF-00299804, nimotuzumab, or RO5083945.

Adenosine A2A Receptor Inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an adenosine A2a receptor (A2aR) antagonist (e.g., an inhibitor of A2aR pathway, e.g., an adenosine inhibitor, e.g., an inhibitor of A2aR or CD-73). In some embodiments, the A2aR antagonist is chosen from PBF509 (Palobiofarma/Novartis), CPI444/V81444 (Corvus/Genentech), AZD4635/HTL-1071 (AstraZeneca/Heptares), Vipadenant (Redox/Juno), GBV-2034 (Globavir), AB928 (Arcus Biosciences), Theophylline, Istradefylline (Kyowa Hakko Kogyo), Tozadenant/SYN-115 (Acorda), KW-6356 (Kyowa Hakko Kogyo), ST-4206 (Leadiant Biosciences), or Preladenant/SCH 420814 (Merck/Schering).

In some embodiments, the A2aR antagonist comprises PBF509 or a compound disclosed in U.S. Patent No. 8,796,284 or in International Application Publication No. WO 2017/025918, herein incorporated by reference in their entirety.

In some embodiments, the A2aR antagonist comprises a compound of formula (I):



wherein

R^1 represents a five-membered heteroaryl ring selected from the group consisting of a pyrazole, a thiazole, and a triazole ring optionally substituted by one or two halogen atoms or by one or two methyl groups;

R^2 represents a hydrogen atom;

R^3 represents bromine or chlorine atom;

R^4 represents independently:

a) a five-membered heteroaryl group optionally substituted by one or more halogen atoms or by one or more groups selected from the group consisting of alkyl, cycloalkyl, alkoxy, alkylthio, amino, mono- or dialkylamino

b) a group —N(R^5)(R^6) in which R^5 and R^6 represent independently:

a hydrogen atom;

an alkyl or cycloalkyl group of 3 to 6 carbon atoms, linear or branched, optionally substituted by one or more halogen atoms or by one or more groups selected from the group consisting of cycloalkyl (3-8 carbon atoms), hydroxy, alkoxy, amino, mono- and dialkylamino (1-8 carbon atoms);

or R^5 and R^6 form together with the nitrogen atom to that they are attached a saturated heterocyclic group of 4 to 6 members in which further heteroatom may be inserted, which is optionally substituted by one or more halogen atoms or by one or more alkyl groups (1-8 carbon atoms), hydroxy, lower alkoxy, amino, mono- or dialkylamino, or

c) a group —OR^7 or —SR^7, where R^7 represents independently:

an alkyl (1-8 carbon atoms) or cycloalkyl (3-8 carbon atoms) group, linear or branched, optionally substituted by one or more halogen atoms or by one or more groups selected from the group consisting of alkyl (1-8 carbon atoms), alkoxy (1-8 carbon atoms), amino, mono- or dialkylamino (1-8 carbon atoms); or

a Phenyl ring optionally substituted with one or more halogen atoms.

In certain embodiments, the A2aR antagonist comprises 5-bromo-2,6-di-(1*H*-pyrazol-1-yl)pyrimidin-4-amine.

In certain embodiments, the A2AR antagonist comprises CPI444/V81444. CPI-444 and other A2aR antagonists are disclosed in International Application Publication No. WO 2009/156737, herein incorporated by reference in its entirety. In certain embodiments, the A2aR antagonist is (*S*)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine. In certain embodiments, the A2aR antagonist is (*R*)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof. In certain embodiments, the A2aR antagonist is 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine.

In certain embodiments, the A2aR antagonist is AZD4635/HTL-1071. A2aR antagonists are disclosed in International Application Publication No. WO 2011/095625, herein incorporated by reference in its entirety. In certain embodiments, the A2aR antagonist is 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine.

In certain embodiments, the A2aR antagonist is ST-4206 (Leadiant Biosciences). In certain embodiments, the A2aR antagonist is an A2aR antagonist described in U.S. Patent No. 9,133,197, herein incorporated by reference in its entirety.

In certain embodiments, the A2AR antagonist is an A2aR antagonist described in U.S. Patent Nos. 8,114,845 and 9,029,393, U.S. Application Publication Nos. 2017/0015758 and 2016/0129108, herein incorporated by reference in their entirety.

In some embodiments, the A2aR antagonist is istradefylline (CAS Registry Number: 155270-99-8). Istradefylline is also known as KW-6002 or 8-[(E)-2-(3,4-dimethoxyphenyl)vinyl]-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione. Istradefylline is disclosed, *e.g.,* in LeWitt *et al.* (2008) *Annals of Neurology* 63 (3): 295–302).

In some embodiments, the A2aR antagonist is tozadenant (Biotie). Tozadenant is also known as SYN115 or 4-hydroxy-N-(4-methoxy-7-morpholin-4-yl-1,3-benzothiazol-2-yl)-4-methylpiperidine-1-carboxamide. Tozadenant blocks the effect of endogenous adenosine at the A2a receptors, resulting in the potentiation of the effect of dopamine at the D2 receptor and inhibition of the effect of glutamate at the mGluR5 receptor. In some embodiments, the A2aR antagonist is preladenant (CAS Registry Number: 377727-87-2). Preladenant is also known as SCH 420814 or 2-(2-Furanyl)-7-[2-[4-[4-(2-methoxyethoxy)phenyl]-1-piperazinyl]ethyl]7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-5-amine. Preladenant was developed as a drug that acted as a potent and selective antagonist at the adenosine A2A receptor.

In some embodiments, the A2aR antagonist is vipadenan. Vipadenan is also known as BIIB014, V2006, or 3-[(4-amino-3-methylphenyl)methyl]-7-(furan-2-yl)triazolo[4,5-d]pyrimidin-5-amine.

Other exemplary A2aR antagonists include, *e.g.,* ATL-444, MSX-3, SCH-58261, SCH-412,348, SCH-442,416, VER-6623, VER-6947, VER-7835, CGS-15943, or ZM-241,385.

IDO/TDO Inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO). In some embodiments, the IDO inhibitor is chosen from (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine (also known as epacadostat or INCB24360), indoximod (NLG8189), (1-methyl-D-tryptophan), α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol (also known as NLG919), indoximod, BMS-986205 (formerly F001287).

In some embodiments, the IDO/TDO inhibitor is indoximod (New Link Genetics). Indoximod, the D isomer of 1-methyl-tryptophan, is an orally administered small-molecule indoleamine 2,3-

dioxygenase (IDO) pathway inhibitor that disrupts the mechanisms by which tumors evade immune-mediated destruction.

In some embodiments, the IDO/TDO inhibitor is NLG919 (New Link Genetics). NLG919 is a potent IDO (indoleamine-(2,3)-dioxygenase) pathway inhibitor with Ki/EC50 of 7 nM/75 nM in cell-free assays.

In some embodiments, the IDO/TDO inhibitor is epacadostat (CAS Registry Number: 1204669-58-8). Epacadostat is also known as INCB24360 or INCB024360 (Incyte). Epacadostat is a potent and selective indoleamine 2,3-dioxygenase (IDO1) inhibitor with IC50 of 10 nM, highly selective over other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO).

In some embodiments, the IDO/TDO inhibitor is F001287 (Flexus/BMS). F001287 is a small molecule inhibitor of indoleamine 2,3-dioxygenase 1 (IDO1).

CD19 CAR

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a CD19 CAR-expressing cell therapy.

In one embodiment, the antigen binding domain of the CD19 CAR has the same or a similar binding specificity as the FMC63 scFv fragment described in Nicholson et al. Mol. Immun. 34 (16-17): 1157-1165 (1997). In one embodiment, the antigen binding domain of the CD19 CAR includes the scFv fragment described in Nicholson et al. *Mol. Immun.* 34 (16-17): 1157-1165 (1997).

In some embodiments, the CD19 CAR includes an antigen binding domain (*e.g.*, a humanized antigen binding domain) according to Table 3 of WO2014/153270, incorporated herein by reference. WO2014/153270 also describes methods of assaying the binding and efficacy of various CAR constructs.

In one aspect, the parental murine scFv sequence is the CAR19 construct provided in PCT publication WO2012/079000 (incorporated herein by reference). In one embodiment, the anti-CD19 binding domain is a scFv described in WO2012/079000.

In one embodiment, the CAR molecule comprises the fusion polypeptide sequence provided as SEQ ID NO: 12 in PCT publication WO2012/079000, which provides an scFv fragment of murine origin that specifically binds to human CD19.

In one embodiment, the CD19 CAR comprises an amino acid sequence provided as SEQ ID NO: 12 in PCT publication WO2012/079000. In embodiment, the amino acid sequence is

(MALPVTALLLPLALLLHAARP)diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliyhtsrlhsg vpsrfsgsgsgtdysltisnleqediatyfcqqgntlpytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvsgvslpdyg vswirqpprkglewlgviwgsettyynsalksrltiikdnsksqvflkmnslqtddtaiyycakhyyyggsyamdywgqgtsvtvsstttpaprp

ptpaptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeegg celrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdgl yqglstatkdtydalhmqalppr (SEQ ID NO: 2029), or a sequence substantially homologous thereto. The optional sequence of the signal peptide is shown in capital letters and parenthesis.

In one embodiment, the amino acid sequence is:

Diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliyhtsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqgn tlpytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvsgvslpdygvswirqpprkglewlgviwgsettyynsalksr ltiikdnsksqvflkmnslqtddtaiyycakhyyyggsyamdywgqgtsvtvssttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfa cdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeggcelrvkfsrsadapaykqgqnqlynelnlgrre eydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr (SEQ ID NO: 2030), or a sequence substantially homologous thereto.

In one embodiment, the CD19 CAR has the USAN designation TISAGENLECLEUCEL-T. In embodiments, CTL019 is made by a gene modification of T cells is mediated by stable insertion via transduction with a self-inactivating, replication deficient Lentiviral (LV) vector containing the CTL019 transgene under the control of the EF-1 alpha promoter. CTL019 can be a mixture of transgene positive and negative T cells that are delivered to the subject on the basis of percent transgene positive T cells.

In other embodiments, the CD19 CAR comprises an antigen binding domain (e.g., a humanized antigen binding domain) according to Table 3 of WO2014/153270, incorporated herein by reference.

Humanization of murine CD19 antibody is desired for the clinical setting, where the mouse-specific residues may induce a human-anti-mouse antigen (HAMA) response in patients who receive CART19 treatment, i.e., treatment with T cells transduced with the CAR19 construct. The production, characterization, and efficacy of humanized CD19 CAR sequences is described in International Application WO2014/153270 which is herein incorporated by reference in its entirety, including Examples 1-5 (p. 115-159).

In some embodiments, CD19 CAR constructs are described in PCT publication WO 2012/079000, incorporated herein by reference, and the amino acid sequence of the murine CD19 CAR and scFv constructs are shown in Table 8 below, or a sequence substantially identical to any of the aforesaid sequences (e.g., at least 85%, 90%, 95% or more identical to any of the sequences described herein).

Table 8. CD19 CAR Constructs

SEQ ID NO	**Region**
CTL019	
1300	CTL019 Full amino acid sequence
1301	CTL019 Full nucleotide sequence

1302	CTL019 scFv domain
mCAR1	
1303	mCAR1 scFv
1304	mCAR1 Full amino acid sequence
mCAR2	
1305	mCAR2 scFv
1306	mCAR2 amino acid sequence
1307	mCAR2 full amino acid sequence
mCAR3	
1308	mCAR3 scFv
1309	mCAR3 full amino acid sequence
SSJ25-C1	
1310	SSJ25-C1 VH sequence
1311	SSJ25-C1 VL
Humanized CAR1	
1312	CAR1 scFv domain
1313	CAR 1 – Full - aa
Humanized CAR2	
1314	CAR2 scFv domain - aa (Linker is underlined)
1315	CAR2 scFv domain - nt
1316	CAR 2 - Full - aa
1317	CAR 2 - Full - nt
1318	CAR2 - Soluble scFv - aa
Humanized CAR3	
1319	CAR3 scFv domain
1320	CAR 3 – Full – aa
Humanized CAR4	
1321	CAR4 scFv domain
1322	CAR 4 – Full - aa
Humanized CAR5	
1323	CAR5 scFv domain
1324	CAR 5 – Full - aa
Humanized CAR6	
1325	CAR6 scFv domain
1326	CAR6 –Full – aa
Humanized CAR7	
1327	CAR7 scFv domain
1328	CAR 7 Full - aa
Humanized CAR8	
1329	CAR8 scFv domain
1330	CAR 8 – Full - aa
Humanized CAR9	
1331	CAR9 scFv domain
1332	CAR 9 – Full - aa
Humanized CAR10	
1333	CAR10 scFv domain
1334	CAR 10 Full - aa
Humanized CAR11	
1335	CAR11 scFv domain
1336	CAR 11 Full - aa

Humanized CAR12	
1337	CAR12 scFv domain
1338	CAR 12 – Full - aa
Murine CART19	
1339	HCDR1 (Kabat)
1340	HCDR2 (Kabat)
1341	HCDR3 (Kabat)
1342	LCDR1 (Kabat)
1343	LCDR2 (Kabat)
1344	LCDR3 (Kabat)
Humanized CART19 a	
1345	HCDR1 (Kabat)
1346	HCDR2 (Kabat)
1347	HCDR3 (Kabat)
1348	LCDR1 (Kabat)
1349	LCDR2 (Kabat)
1350	LCDR3 (Kabat)
Humanized CART19 b	
1351	HCDR1 (Kabat)
1352	HCDR2 (Kabat)
1353	HCDR3 (Kabat)
1354	LCDR1 (Kabat)
1355	LCDR2 (Kabat)
1356	LCDR3 (Kabat)
Humanized CART19 c	
1357	HCDR1 (Kabat)
1358	HCDR2 (Kabat)
1359	HCDR3 (Kabat)
1360	LCDR1 (Kabat)
1361	LCDR2 (Kabat)
1362	LCDR3 (Kabat)

CD19 CAR constructs containing humanized anti-CD19 scFv domains are described in PCT publication WO 2014/153270, incorporated herein by reference.

The sequences of murine and humanized CDR sequences of the anti-CD19 scFv domains are shown in Table 9 for the heavy chain variable domains and in Table 10 for the light chain variable domains. The SEQ ID NOs refer to those found in Table 8.

Table 9. Heavy Chain Variable Domain CDR (Kabat) SEQ ID NO's of CD19 Antibodies

Candidate	HCDR1	HCDR2	HCDR3
murine_CART19	SEQ ID NO: 1339	SEQ ID NO: 1340	SEQ ID NO: 1341
humanized_CART19 a	SEQ ID NO: 1345	SEQ ID NO: 1346	SEQ ID NO: 1347
humanized_CART19 b	SEQ ID NO: 1351	SEQ ID NO: 1352	SEQ ID NO: 1353
humanized_CART19 c	SEQ ID NO: 1357	SEQ ID NO: 1358	SEQ ID NO: 1359

Table 10. Light Chain Variable Domain CDR (Kabat) SEQ ID NO's of CD19 Antibodies

Candidate	LCDR1	LCDR2	LCDR3
murine_CART19	SEQ ID NO: 1342	SEQ ID NO: 1343	SEQ ID NO: 1344
humanized_CART19 a	SEQ ID NO: 1348	SEQ ID NO: 1349	SEQ ID NO: 1350
humanized_CART19 b	SEQ ID NO: 1354	SEQ ID NO: 1355	SEQ ID NO: 1356
humanized_CART19 c	SEQ ID NO: 1360	SEQ ID NO: 1361	SEQ ID NO: 1362

Any known CD19 CAR, e.g., the CD19 antigen binding domain of any known CD19 CAR, in the art can be used in accordance with the present disclosure. For example, LG-740; CD19 CAR described in the US Pat. No. 8,399,645; US Pat. No. 7,446,190; Xu et al., Leuk Lymphoma. 2013 54(2):255-260(2012); Cruz et al., Blood 122(17):2965-2973 (2013); Brentjens et al., Blood, 118(18):4817-4828 (2011); Kochenderfer et al., Blood 116(20):4099-102 (2010); Kochenderfer et al., Blood 122 (25):4129-39(2013); and 16th Annu Meet Am Soc Gen Cell Ther (ASGCT) (May 15-18, Salt Lake City) 2013, Abst 10.

Exemplary CD19 CARs include CD19 CARs described herein, e.g., in one or more tables described herein, or an anti-CD19 CAR described in Xu et al. Blood 123.24(2014):3750-9; Kochenderfer et al. Blood 122.25(2013):4129-39, Cruz et al. Blood 122.17(2013):2965-73, NCT00586391, NCT01087294, NCT02456350, NCT00840853, NCT02659943, NCT02650999, NCT02640209, NCT01747486, NCT02546739, NCT02656147, NCT02772198, NCT00709033, NCT02081937, NCT00924326, NCT02735083, NCT02794246, NCT02746952, NCT01593696, NCT02134262, NCT01853631, NCT02443831, NCT02277522, NCT02348216, NCT02614066, NCT02030834, NCT02624258, NCT02625480, NCT02030847, NCT02644655, NCT02349698, NCT02813837, NCT02050347, NCT01683279, NCT02529813, NCT02537977, NCT02799550, NCT02672501, NCT02819583, NCT02028455, NCT01840566, NCT01318317, NCT01864889, NCT02706405, NCT01475058, NCT01430390, NCT02146924, NCT02051257, NCT02431988, NCT01815749, NCT02153580, NCT01865617, NCT02208362, NCT02685670, NCT02535364, NCT02631044, NCT02728882, NCT02735291, NCT01860937, NCT02822326, NCT02737085, NCT02465983, NCT02132624, NCT02782351, NCT01493453, NCT02652910, NCT02247609, NCT01029366, NCT01626495, NCT02721407, NCT01044069, NCT00422383, NCT01680991, NCT02794961, or NCT02456207, each of which is incorporated herein by reference in its entirety.

CD20 CAR

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a CD20 CAR-expressing cell therapy.

In one embodiment, the CD20 CAR comprises one or more of: LC CDR1, LC CDR2, LC

CDR3, HC CDR1, HC CDR2, HC CDR3, VH, VL, an scFv, or full-length sequence of a construct of **Tables 11, 12, 13**, e.g., CAR20-1, CAR20-2, CAR20-3, CAR20-4, CAR20-5, CAR20-6, CAR20-7, CAR20-8, CAR20-9, CAR20-10, CAR20-11, CAR20-12, CAR20-13, CAR20-14, CAR20-15, or CAR20-16, or a sequence substantially identical thereto (e.g., a sequence sharing 80%, 85%, 90%, or 95% identity thereto). Each full CD20 CAR amino acid sequence in Table 11 includes an optional signal peptide sequence of 21 amino acids corresponding to the amino acid sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 2031). Each full CAR nucleotide sequence in Table 11 includes an optional nucleotide signal peptide sequence corresponding to the first 63 nucleotides corresponding to the nucleotide sequence: ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTTCTGCTCCACGCCGCTCGGCC C (SEQ ID NO: 2032).

Table 11. CD20 CAR Constructs

SEQ ID NO:	**Ab region**
CD20-C3H2	
1363 (Kabat)	HCDR1
1364 (Kabat)	HCDR2
1365 (Kabat)	HCDR3
1366 (Chothia)	HCDR1
1367 (Chothia)	HCDR2
1368 (Chothia)	HCDR3
1369 (IMGT)	HCDR1
1370 (IMGT)	HCDR2
1371 (IMGT)	HCDR3
1372 (Combined Chothia and Kabat)	HCDR1
1373 (Combined Chothia and Kabat)	HCDR2
1374 (Combined Chothia and Kabat)	HCDR3
1375	VH
1376	DNA VH
1377 (Kabat)	LCDR1
1378 (Kabat)	LCDR2
1379 (Kabat)	LCDR3
1380 (Chothia)	LCDR1
1381 (Chothia)	LCDR2
1382 (Chothia)	LCDR3
1383 (IMGT)	LCDR1
1384 (IMGT)	LCDR2
1385 (IMGT)	LCDR3
1386 (Combined Chothia and Kabat)	LCDR1
1387 (Combined Chothia and Kabat)	LCDR2
1388 (Combined Chothia and Kabat)	LCDR3
1389	VL
1390	DNA VL
1391	Linker

1392	scFv (VH-linker-VL)
1393	DNA scFv (VH-linker-VL)
1394	Full CAR amino acid sequence
1395	Full CAR nucleic acid sequence
CD20-C5H1	
1396 (Kabat)	HCDR1
1397 (Kabat)	HCDR2
1398 (Kabat)	HCDR3
1399 (Chothia)	HCDR1
1400 (Chothia)	HCDR2
1401 (Chothia)	HCDR3
1402 (IMGT)	HCDR1
1403 (IMGT)	HCDR2
1404 (IMGT)	HCDR3
1405 (Combined Chothia and Kabat)	HCDR1
1406 (Combined Chothia and Kabat)	HCDR2
1407 (Combined Chothia and Kabat)	HCDR3
1408	VH
1409	DNA VH
1410 (Kabat)	LCDR1
1411 (Kabat)	LCDR2
1412 (Kabat)	LCDR3
1413 (Chothia)	LCDR1
1414 (Chothia)	LCDR2
1415 (Chothia)	LCDR3
1416 (IMGT)	LCDR1
1417 (IMGT)	LCDR2
1418 (IMGT)	LCDR3
1419 (Combined Chothia and Kabat)	LCDR1
1420 (Combined Chothia and Kabat)	LCDR2
1421 (Combined Chothia and Kabat)	LCDR3
1422	VL
1423	DNA VL
1424	Linker
1425	scFv (VH-linker-VL)
1426	DNA scFv (VH-linker-VL)
1427	Full CAR amino acid sequence
1428	Full CAR nucleic acid sequence
CD20-C2H1	
1429 (Kabat)	HCDR1
1430 (Kabat)	HCDR2
1431 (Kabat)	HCDR3
1432 (Chothia)	HCDR1
1433 (Chothia)	HCDR2
1434 (Chothia)	HCDR3
1435 (IMGT)	HCDR1
1436 (IMGT)	HCDR2
1437 (IMGT)	HCDR3
1438 (Combined Chothia and Kabat)	HCDR1
1439 (Combined Chothia and Kabat)	HCDR2

1440 (Combined Chothia and Kabat)	HCDR3
1441	VH
1442	DNA VH
1443 (Kabat)	LCDR1
1444 (Kabat)	LCDR2
1445 (Kabat)	LCDR3
1446 (Chothia)	LCDR1
1447 (Chothia)	LCDR2
1448 (Chothia)	LCDR3
1449 (IMGT)	LCDR1
1450 (IMGT)	LCDR2
1451 (IMGT)	LCDR3
1452 (Combined Chothia and Kabat)	LCDR1
1453 (Combined Chothia and Kabat)	LCDR2
1454 (Combined Chothia and Kabat)	LCDR3
1455	VL
1456	DNA VL
1457	Linker
1458	scFv (VH-linker-VL)
1459	DNA scFv (VH-linker-VL)
1460	Full CAR amino acid sequence
1461	Full CAR nucleic acid sequence
CD20-C2H2	
1462 (Kabat)	HCDR1
1463 (Kabat)	HCDR2
1464 (Kabat)	HCDR3
1465 (Chothia)	HCDR1
1466 (Chothia)	HCDR2
1467 (Chothia)	HCDR3
1468 (IMGT)	HCDR1
1469 (IMGT)	HCDR2
1470 (IMGT)	HCDR3
1471 (Combined Chothia and Kabat)	HCDR1
1472 (Combined Chothia and Kabat)	HCDR2
1473 (Combined Chothia and Kabat)	HCDR3
1474	VH
1475	DNA VH
1476 (Kabat)	LCDR1
1477 (Kabat)	LCDR2
1478 (Kabat)	LCDR3
1479 (Chothia)	LCDR1
1480 (Chothia)	LCDR2
1481 (Chothia)	LCDR3
1482 (IMGT)	LCDR1
1483 (IMGT)	LCDR2
1484 (IMGT)	LCDR3
1485 (Combined Chothia and Kabat)	LCDR1
1486 (Combined Chothia and Kabat)	LCDR2
1487 (Combined Chothia and Kabat)	LCDR3
1488	VL

1489	DNA VL
1490	Linker
1491	scFv (VH-linker-VL)
1492	DNA scFv (VH-linker-VL)
1493	Full CAR amino acid sequence
1494	Full CAR nucleic acid sequence
CD20-C2H3	
1495 (Kabat)	HCDR1
1496 (Kabat)	HCDR2
1497 (Kabat)	HCDR3
1498 (Chothia)	HCDR1
1499 (Chothia)	HCDR2
1500 (Chothia)	HCDR3
1501 (IMGT)	HCDR1
1502 (IMGT)	HCDR2
1503 (IMGT)	HCDR3
1504 (Combined Chothia and Kabat)	HCDR1
1505 (Combined Chothia and Kabat)	HCDR2
1506 (Combined Chothia and Kabat)	HCDR3
1507	VH
1508	DNA VH
1509 (Kabat)	LCDR1
1510 (Kabat)	LCDR2
1511 (Kabat)	LCDR3
1512 (Chothia)	LCDR1
1513 (Chothia)	LCDR2
1514 (Chothia)	LCDR3
1515 (IMGT)	LCDR1
1516 (IMGT)	LCDR2
1517 (IMGT)	LCDR3
1518 (Combined Chothia and Kabat)	LCDR1
1519 (Combined Chothia and Kabat)	LCDR2
1520 (Combined Chothia and Kabat)	LCDR3
1521	VL
1522	DNA VL
1523	Linker
1524	scFv (VH-linker-VL)
1525	DNA scFv (VH-linker-VL)
1526	Full CAR amino acid sequence
1527	Full CAR nucleic acid sequence
CD20-C2H4	
1528 (Kabat)	HCDR1
1529 (Kabat)	HCDR2
1530 (Kabat)	HCDR3
1531 (Chothia)	HCDR1
1532 (Chothia)	HCDR2
1533 (Chothia)	HCDR3
1534 (IMGT)	HCDR1
1535 (IMGT)	HCDR2

1536 (IMGT)	HCDR3
1537 (Combined Chothia and Kabat)	HCDR1
1538 (Combined Chothia and Kabat)	HCDR2
1539 (Combined Chothia and Kabat)	HCDR3
1540	VH
1541	DNA VH
1542 (Kabat)	LCDR1
1543 (Kabat)	LCDR2
1544 (Kabat)	LCDR3
1545 (Chothia)	LCDR1
1546 (Chothia)	LCDR2
1547 (Chothia)	LCDR3
1548 (IMGT)	LCDR1
1549 (IMGT)	LCDR2
1550 (IMGT)	LCDR3
1551 (Combined Chothia and Kabat)	LCDR1
1552 (Combined Chothia and Kabat)	LCDR2
1553 (Combined Chothia and Kabat)	LCDR3
1554	VL
1555	DNA VL
1556	Linker
1557	scFv (VH-linker-VL)
1558	DNA scFv (VH-linker-VL)
1559	Full CAR amino acid sequence
1560	Full CAR nucleic acid sequence
CD20-C3H1	
1561 (Kabat)	HCDR1
1562 (Kabat)	HCDR2
1563 (Kabat)	HCDR3
1564 (Chothia)	HCDR1
1565 (Chothia)	HCDR2
1566 (Chothia)	HCDR3
1567 (IMGT)	HCDR1
1568 (IMGT)	HCDR2
1569 (IMGT)	HCDR3
1570 (Combined Chothia and Kabat)	HCDR1
1571 (Combined Chothia and Kabat)	HCDR2
1572 (Combined Chothia and Kabat)	HCDR3
1573	VH
1574	DNA VH
1575 (Kabat)	LCDR1
1576 (Kabat)	LCDR2
1577 (Kabat)	LCDR3
1578 (Chothia)	LCDR1
1579 (Chothia)	LCDR2
1580 (Chothia)	LCDR3
1581 (IMGT)	LCDR1
1582 (IMGT)	LCDR2
1583 (IMGT)	LCDR3
1584 (Combined Chothia and Kabat)	LCDR1

1585 (Combined Chothia and Kabat)	LCDR2
1586 (Combined Chothia and Kabat)	LCDR3
1587	VL
1588	DNA VL
1589	Linker
1590	scFv (VH-linker-VL)
1591	DNA scFv (VH-linker-VL)
1592	Full CAR amino acid sequence
1593	Full CAR nucleic acid sequence
CD20-C3H3	
1594 (Kabat)	HCDR1
1595 (Kabat)	HCDR2
1596 (Kabat)	HCDR3
1597 (Chothia)	HCDR1
1598 (Chothia)	HCDR2
1599 (Chothia)	HCDR3
1600 (IMGT)	HCDR1
1601 (IMGT)	HCDR2
1602 (IMGT)	HCDR3
1603	VH
1604	DNA VH
1605 (Kabat)	LCDR1
1606 (Kabat)	LCDR2
1607 (Kabat)	LCDR3
1608 (Chothia)	LCDR1
1609 (Chothia)	LCDR2
1610 (Chothia)	LCDR3
1611 (IMGT)	LCDR1
1612 (IMGT)	LCDR2
1613 (IMGT)	LCDR3
1614 (Combined Chothia and Kabat)	LCDR1
1615 (Combined Chothia and Kabat)	LCDR2
1616 (Combined Chothia and Kabat)	LCDR3
1617	VL
1618	DNA VL
1619	Linker
1620	scFv (VH-linker-VL)
1621	DNA scFv (VH-linker-VL)
1622	Full CAR amino acid sequence
1623	Full CAR nucleic acid sequence
CD20-C3H4	
1624 (Kabat)	HCDR1
1625 (Kabat)	HCDR2
1626 (Kabat)	HCDR3
1627 (Chothia)	HCDR1
1628 (Chothia)	HCDR2
1629 (Chothia)	HCDR3
1630 (IMGT)	HCDR1
1631 (IMGT)	HCDR2
1632 (IMGT)	HCDR3

1633 (Combined Chothia and Kabat)	HCDR1
1634 (Combined Chothia and Kabat)	HCDR2
1635 (Combined Chothia and Kabat)	HCDR3
1636	VH
1637	DNA VH
1638 (Kabat)	LCDR1
1639 (Kabat)	LCDR2
1640 (Kabat)	LCDR3
1641 (Chothia)	LCDR1
1642 (Chothia)	LCDR2
1643 (Chothia)	LCDR3
1644 (IMGT)	LCDR1
1645 (IMGT)	LCDR2
1646 (IMGT)	LCDR3
1647 (Combined Chothia and Kabat)	LCDR1
1648 (Combined Chothia and Kabat)	LCDR2
1649 (Combined Chothia and Kabat)	LCDR3
1650	VL
1651	DNA VL
1652	Linker
1653	scFv (VH-linker-VL)
1654	DNA scFv (VH-linker-VL)
1655	Full CAR amino acid sequence
1656	Full CAR nucleic acid sequence
CD20-C5H2	
1657 (Kabat)	HCDR1
1658 (Kabat)	HCDR2
1659 (Kabat)	HCDR3
1660 (Chothia)	HCDR1
1661 (Chothia)	HCDR2
1662 (Chothia)	HCDR3
1663 (IMGT)	HCDR1
1664 (IMGT)	HCDR2
1665 (IMGT)	HCDR3
1666 (Combined Chothia and Kabat)	HCDR1
1667 (Combined Chothia and Kabat)	HCDR2
1668 (Combined Chothia and Kabat)	HCDR3
1669	VH
1670	DNA VH
1671 (Kabat)	LCDR1
1672 (Kabat)	LCDR2
1673 (Kabat)	LCDR3
1674 (Chothia)	LCDR1
1675 (Chothia)	LCDR2
1676 (Chothia)	LCDR3
1677 (IMGT)	LCDR1
1678 (IMGT)	LCDR2
1679 (IMGT)	LCDR3
1680 (Combined Chothia and Kabat)	LCDR1
1681 (Combined Chothia and Kabat)	LCDR2

1682 (Combined Chothia and Kabat)	LCDR3
1683	VL
1684	DNA VL
1685	Linker
1686	scFv (VH-linker-VL)
1687	DNA scFv (VH-linker-VL)
1688	Full CAR amino acid sequence
1689	Full CAR nucleic acid sequence
CD20-C5H3	
1690 (Kabat)	HCDR1
1691 (Kabat)	HCDR2
1692 (Kabat)	HCDR3
1693 (Chothia)	HCDR1
1694 (Chothia)	HCDR2
1695 (Chothia)	HCDR3
1696 (IMGT)	HCDR1
1697 (IMGT)	HCDR2
1698 (IMGT)	HCDR3
1699 (Combined Chothia and Kabat)	HCDR1
1700 (Combined Chothia and Kabat)	HCDR2
1701 (Combined Chothia and Kabat)	HCDR3
1702	VH
1703	DNA VH
1704 (Kabat)	LCDR1
1705 (Kabat)	LCDR2
1706 (Kabat)	LCDR3
1707 (Chothia)	LCDR1
1708 (Chothia)	LCDR2
1709 (Chothia)	LCDR3
1710 (IMGT)	LCDR1
1711 (IMGT)	LCDR2
1712 (IMGT)	LCDR3
1713 (Combined Chothia and Kabat)	LCDR1
1714 (Combined Chothia and Kabat)	LCDR2
1715 (Combined Chothia and Kabat)	LCDR3
1716	VL
1717	DNA VL
1718	Linker
1719	scFv (VH-linker-VL)
1720	DNA scFv (VH-linker-VL)
1721	Full CAR amino acid sequence
1722	Full CAR nucleic acid sequence
CD20-C5H4	
1723 (Kabat)	HCDR1
1724 (Kabat)	HCDR2
1725 (Kabat)	HCDR3
1726 (Chothia)	HCDR1
1727 (Chothia)	HCDR2
1728 (Chothia)	HCDR3
1729 (IMGT)	HCDR1

1730 (IMGT)	HCDR2
1731 (IMGT)	HCDR3
1732 (Combined Chothia and Kabat)	HCDR1
1733 (Combined Chothia and Kabat)	HCDR2
1734 (Combined Chothia and Kabat)	HCDR3
1735	VH
1736	DNA VH
1737 (Kabat)	LCDR1
1738 (Kabat)	LCDR2
1739 (Kabat)	LCDR3
1740 (Chothia)	LCDR1
1741 (Chothia)	LCDR2
1742 (Chothia)	LCDR3
1743 (IMGT)	LCDR1
1744 (IMGT)	LCDR2
1745 (IMGT)	LCDR3
1746 (Combined Chothia and Kabat)	LCDR1
1747 (Combined Chothia and Kabat)	LCDR2
1748 (Combined Chothia and Kabat)	LCDR3
1749	VL
1750	DNA VL
1751	Linker
1752	scFv (VH-linker-VL)
1753	DNA scFv (VH-linker-VL)
1754	Full CAR amino acid sequence
1755	Full CAR nucleic acid sequence
CD20-C8H1	
1756 (Kabat)	HCDR1
1757 (Kabat)	HCDR2
1758 (Kabat)	HCDR3
1759 (Chothia)	HCDR1
1760 (Chothia)	HCDR2
1761 (Chothia)	HCDR3
1762 (IMGT)	HCDR1
1763 (IMGT)	HCDR2
1764 (IMGT)	HCDR3
1765 (Combined Chothia and Kabat)	HCDR1
1766 (Combined Chothia and Kabat)	HCDR2
1767 (Combined Chothia and Kabat)	HCDR3
1768	VH
1769	DNA VH
1770 (Kabat)	LCDR1
1771 (Kabat)	LCDR2
1772 (Kabat)	LCDR3
1773 (Chothia)	LCDR1
1774 (Chothia)	LCDR2
1775 (Chothia)	LCDR3
1776 (IMGT)	LCDR1
1777 (IMGT)	LCDR2
1778 (IMGT)	LCDR3

1779 (Combined Chothia and Kabat)	LCDR1
1780 (Combined Chothia and Kabat)	LCDR2
1781 (Combined Chothia and Kabat)	LCDR3
1782	VL
1783	DNA VL
1784	Linker
1785	scFv (VH-linker-VL)
1786	DNA scFv (VH-linker-VL)
1787	Full CAR amino acid sequence
1788	Full CAR nucleic acid sequence
CD20-C8H2	
1789 (Kabat)	HCDR1
1790 (Kabat)	HCDR2
1791 (Kabat)	HCDR3
1792 (Chothia)	HCDR1
1793 (Chothia)	HCDR2
1794 (Chothia)	HCDR3
1795 (IMGT)	HCDR1
1796 (IMGT)	HCDR2
1797 (IMGT)	HCDR3
1798 (Combined Chothia and Kabat)	HCDR1
1799 (Combined Chothia and Kabat)	HCDR2
1800 (Combined Chothia and Kabat)	HCDR3
1801	VH
1802	DNA VH
1803 (Kabat)	LCDR1
1804 (Kabat)	LCDR2
1805 (Kabat)	LCDR3
1806 (Chothia)	LCDR1
1807 (Chothia)	LCDR2
1808 (Chothia)	LCDR3
1809 (IMGT)	LCDR1
1810 (IMGT)	LCDR2
1811 (IMGT)	LCDR3
1812 (Combined Chothia and Kabat)	LCDR1
1813 (Combined Chothia and Kabat)	LCDR2
1814 (Combined Chothia and Kabat)	LCDR3
1815	VL
1816	DNA VL
1817	Linker
1818	scFv (VH-linker-VL)
1819	DNA scFv (VH-linker-VL)
1820	Full CAR amino acid sequence
1821	Full CAR nucleic acid sequence
CD20-C8H3	
1822 (Kabat)	HCDR1
1823 (Kabat)	HCDR2
1824 (Kabat)	HCDR3
1825 (Chothia)	HCDR1

1826 (Chothia)	HCDR2
1827 (Chothia)	HCDR3
1828 (IMGT)	HCDR1
1829 (IMGT)	HCDR2
1830 (IMGT)	HCDR3
1831 (Combined Chothia and Kabat)	HCDR1
1832 (Combined Chothia and Kabat)	HCDR2
1833 (Combined Chothia and Kabat)	HCDR3
1834	VH
1835	DNA VH
1836 (Kabat)	LCDR1
1837 (Kabat)	LCDR2
1838 (Kabat)	LCDR3
1839 (Chothia)	LCDR1
1840 (Chothia)	LCDR2
1841 (Chothia)	LCDR3
1842 (IMGT)	LCDR1
1843 (IMGT)	LCDR2
1844 (IMGT)	LCDR3
1845 (Combined Chothia and Kabat)	LCDR1
1846 (Combined Chothia and Kabat)	LCDR2
1847 (Combined Chothia and Kabat)	LCDR3
1848	VL
1849	DNA VL
1850	Linker
1851	scFv (VH-linker-VL)
1852	DNA scFv (VH-linker-VL)
1853	Full CAR amino acid sequence
1854	Full CAR nucleic acid sequence
CD20-C8H4	
1855 (Kabat)	HCDR1
1856 (Kabat)	HCDR2
1857 (Kabat)	HCDR3
1858 (Chothia)	HCDR1
1859 (Chothia)	HCDR2
1860 (Chothia)	HCDR3
1861 (IMGT)	HCDR1
1862 (IMGT)	HCDR2
1863 (IMGT)	HCDR3
1864 (Combined Chothia and Kabat)	HCDR1
1865 (Combined Chothia and Kabat)	HCDR2
1866 (Combined Chothia and Kabat)	HCDR3
1867	VH
1868	DNA VH
1869 (Kabat)	LCDR1
1870 (Kabat)	LCDR2
1871 (Kabat)	LCDR3
1872 (Chothia)	LCDR1
1873 (Chothia)	LCDR2
1874 (Chothia)	LCDR3

1875 (IMGT)	LCDR1
1876 (IMGT)	LCDR2
1877 (IMGT)	LCDR3
1878 (Combined Chothia and Kabat)	LCDR1
1879 (Combined Chothia and Kabat)	LCDR2
1880 (Combined Chothia and Kabat)	LCDR3
1881	VL
1882	DNA VL
1883	Linker
1884	scFv (VH-linker-VL)
1885	DNA scFv (VH-linker-VL)
1886	Full CAR amino acid sequence
1887	Full CAR nucleic acid sequence
CD20-C2	
1888	VH
1889	DNA VH
1890	VL
1891	DNA VL
CD20-C3	
1892	VH
1893	DNA VH
1894	VL
1895	DNA VL
CD20-C5	
1896	VH
1897	DNA VH
1898	VL
1899	DNA VL
CD20-C6	
1900	VH
1901	DNA VH
1902	VL
1903	DNA VL
CD20-C7	
1904	VH
1905	DNA VH
1906	VL
1907	DNA VL
CD20-C8	
1908	VH
1909	DNA VH
1910	VL
1911	DNA VL
CD20-3m	
1912	VH
1913	DNA VH
1914	VL
1915	DNA VL
1916	Linker
1917	scFv (VH-linker-VL)

CD20-3J	
1918	VH
1919	DNA VH
1920	VL
1921	DNA VL
1922	Linker
1923	scFv (VH-linker-VL)
CD20-3H5k1	
1924	VH
1925	DNA VH
1926	VL
1927	DNA VL
1928	Linker
1929	scFv (VH-linker-VL)
CD20-3H5k3	
1930	VH
1931	DNA VH
1932	VL
1933	DNA VL
1934	Linker
1935	scFv (VH-linker-VL)
CD20-Ofa	
1936 (Kabat)	HCDR1
1937 (Kabat)	HCDR2
1938 (Kabat)	HCDR3
1939 (Chothia)	HCDR1
1940 (Chothia)	HCDR2
1941 (Chothia)	HCDR3
1942 (IMGT)	HCDR1
1943 (IMGT)	HCDR2
1944 (IMGT)	HCDR3
1945	VH
1946	DNA VH
1947 (Kabat)	LCDR1
1948 (Kabat)	LCDR2
1949 (Kabat)	LCDR3
1950 (Chothia)	LCDR1
1951 (Chothia)	LCDR2
1952 (Chothia)	LCDR3
1953 (IMGT)	LCDR1
1954 (IMGT)	LCDR2
1955 (IMGT)	LCDR3
1956	VL
1957	DNA VL
1958	Linker
1959	scFv (VH-linker-VL)
1960	DNA scFv (VH-linker-VL)
CD20-3	
1961	VH
1962	VL

1963	Linker
1964	scFv (VH-linker-VL)
CD20-8aBBz	
1965	VH
1966	DNA VH
1967	VL
1968	DNA VL
1969	Linker
1970	scFv (VH-linker-VL)
1971	DNA scFv (VH-linker-VL)

5

An overview of the sequences identifications of CDR (Kabat) sequences of the CD20 scFv domains of Table 11 are shown in Table 12 for the heavy chain variable domains and in Table 13 for the light chain variable domains. The SEQ ID NOs refer to those found in Table 11.

Table 12. Heavy Chain Variable Domain CDR (Kabat) SEQ ID NO's of CD20 CAR molecules

Candidate	**HCDR1**	**HCDR2**	**HCDR3**
CD20-C3H2	1363	1364	1365
CD20-C5H1	1396	1397	1398
CD20-C2H1	1429	1430	1431
CD20-C2H2	1462	1463	1464
CD20-C2H3	1495	1496	1497
CD20-C2H4	1528	1529	1530
CD20-C3H1	1561	1562	1563
CD20-C3H3	1594	1595	1596
CD20-C3H4	1624	1625	1626
CD20-C5H2	1657	1658	1659
CD20-C5H3	1690	1691	1692
CD20-C5H4	1723	1724	1725
CD20-C8H1	1756	1757	1758
CD20-C8H2	1789	1790	1791
CD20-C8H3	1822	1823	1824
CD20-C8H4	1855	1856	1857

10

Table 13. Light Chain Variable Domain CDR (Kabat) SEQ ID NO's of CD20 Antibody Molecules

Candidate	**LCDR1**	**LCDR2**	**LCDR3**
CD20-C3H2	1377	1378	1379
CD20-C5H1	1410	1411	1412
CD20-C2H1	1443	1444	1445
CD20-C2H2	1476	1477	1478
CD20-C2H3	1509	1510	1511
CD20-C2H4	1542	1543	1544
CD20-C3H1	1575	1576	1577

CD20-C3H3	1605	1606	1607
CD20-C3H4	1638	1639	1640
CD20-C5H2	1671	1672	1673
CD20-C5H3	1704	1705	1706
CD20-C5H4	1737	1738	1739
CD20-C8H1	1770	1771	1772
CD20-C8H2	1803	1804	1805
CD20-C8H3	1836	1837	1838
CD20-C8H4	1869	1870	1871

Additional CD20 inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a CD20 inhibitor.

In one embodiment, the CD20 inhibitor is an anti-CD20 antibody or fragment thereof. In an embodiment, the antibody is a monospecific antibody and in another embodiment the antibody is a bispecific antibody. In an embodiment, the CD20 inhibitor is a chimeric mouse/human monoclonal antibody, e.g., rituximab. In an embodiment, the CD20 inhibitor is a human monoclonal antibody such as ofatumumab. In an embodiment, the CD20 inhibitor is a humanized antibody such as ocrelizumab, veltuzumab, obinutuzumab, ocaratuzumab, or PRO131921 (Genentech). In an embodiment, the CD20 inhibitor is a fusion protein comprising a portion of an anti-CD20 antibody, such as TRU-015 (Trubion Pharmaceuticals).

CD22 CAR

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a CD22 CAR-expressing cell therapy (e.g., cells expressing a CAR that binds to human CD22).

In some embodiments, the CD22 CAR-expressing cell therapy includes an antigen binding domain according to WO2016/164731, incorporated herein by reference.

The sequences of CD22 CAR are provided below. In some embodiments, the CD22 CAR is CD22-65. In some embodiments, the CD22 CAR is CD22-65s. In some embodiments, the CD22 CAR is CD22-65ss.

Human CD22 CAR CD22-65 scFv sequence

EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWYDDY
ASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT
VSSGGGGSGGGGSGGGGSQSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGK

APKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLT VL (SEQ ID NO: 1972)

Human CD22 CAR CD22-65s scFc sequence (linker shown by italics and underline) EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWYDDY ASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSS*GGGGS*QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSN RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL (SEQ ID NO: 2036)

Human CD22 CAR CD22-65ss scFc sequence EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWYDDY ASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSSQSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGV SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL (SEQ ID NO: 1973)

Human CD22 CAR heavy chain variable region EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWYDDY ASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSS (SEQ ID NO: 1974)

Human CD22 CAR light chain variable region QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNR FSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL (SEQ ID NO: 1975)

Table 14. Heavy Chain Variable Domain CDRs of CD22 CAR (CD22-65)

Candidate	HCDR1	SEQ ID NO:	HCDR2	SEQ ID NO:	HCDR3	SEQ ID NO:
CD22-65 Combined	GDSML SNSDT WN	1976	RTYHRSTWYDDYA SSVRG	1978	VRLQDGNSWSD AFDV	1980
CD22-65 Kabat	SNSDT WN	1977	RTYHRSTWYDDYA SSVRG	1979	VRLQDGNSWSD AFDV	1981

Table 15. Light Chain Variable Domain CDRs of CD22 CAR (CD22-65). The LC CDR sequences in this table have the same sequence under the Kabat or combined definitions.

Candidate	LCDR1	SEQ ID NO:	LCDR2	SEQ ID NO:	LCDR3	SEQ ID NO:
CD22-65 Combined	TGTSSDVGGYNYVS	1982	DVSNRPS	1983	SSYTSSSTLYV	1984

In some embodiments, the antigen binding domain comprises a HC CDR1, a HC CDR2, and a HC CDR3 of any heavy chain binding domain amino acid sequences listed in **Table 14**. In embodiments, the antigen binding domain further comprises a LC CDR1, a LC CDR2, and a LC CDR3. In embodiments, the antigen binding domain comprises a LC CDR1, a LC CDR2, and a LC CDR3 amino acid sequences listed in **Table 15.**

In some embodiments, the antigen binding domain comprises one, two or all of LC CDR1, LC CDR2, and LC CDR3 of any light chain binding domain amino acid sequences listed in **Table 15**, and one, two or all of HC CDR1, HC CDR2, and HC CDR3 of any heavy chain binding domain amino acid sequences listed in **Table 14**.

In some embodiments, the CDRs are defined according to the Kabat numbering scheme, the Chothia numbering scheme, or a combination thereof.

The order in which the VL and VH domains appear in the scFv can be varied (i.e., VL-VH, or VH-VL orientation), and where any of one, two, three or four copies of the "G4S" (SEQ ID NO: 1032) subunit, in which each subunit comprises the sequence GGGGS (SEQ ID NO: 1032) (e.g., $(G4S)_3$ (SEQ ID NO: 1040) or $(G4S)_4$ (SEQ ID NO: 1039)), can connect the variable domains to create the entirety of the scFv domain. Alternatively, the CAR construct can include, for example, a linker including the sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1985). Alternatively, the CAR construct can include, for example, a linker including the sequence LAEAAAK (SEQ ID NO: 2033). In an embodiment, the CAR construct does not include a linker between the VL and VH domains.

These clones all contained a Q/K residue change in the signal domain of the co-stimulatory domain derived from CD3zeta chain.

Additional CD22 inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a CD20 inhibitor. In some embodiments, the CD20 inhibitor is a small molecule or an anti-CD20 antibody molecule.

In an embodiment, the antibody is a monospecific antibody, optionally conjugated to a second agent such as a chemotherapeutic agent. For instance, in an embodiment the antibody is an anti-CD22 monoclonal antibody-MMAE conjugate (e.g., DCDT2980S). In an embodiment, the antibody is an scFv of an anti-CD22 antibody, e.g., an scFv of antibody RFB4. This scFv can be fused to all of or a fragment of Pseudomonas exotoxin-A (e.g., BL22). In an embodiment, the antibody is a humanized anti-CD22 monoclonal antibody (e.g., epratuzumab). In an embodiment, the antibody or fragment

thereof comprises the Fv portion of an anti-CD22 antibody, which is optionally covalently fused to all or a fragment or (e.g., a 38 KDa fragment of) Pseudomonas exotoxin-A (e.g., moxetumomab pasudotox). In an embodiment, the anti-CD22 antibody is an anti-CD19/CD22 bispecific antibody, optionally conjugated to a toxin. For instance, in one embodiment, the anti-CD22 antibody comprises an anti-CD19/CD22 bispecific portion, (e.g., two scFv ligands, recognizing human CD19 and CD22) optionally linked to all of or a portion of diphtheria toxin (DT), e.g., first 389 amino acids of diphtheria toxin (DT), DT 390, e.g., a ligand-directed toxin such as DT2219ARL). In another embodiment, the bispecific portion (e.g., anti-CD19/anti-CD22) is linked to a toxin such as deglycosylated ricin A chain (e.g., Combotox).

In some embodiments, the CD22 inhibitor is a multispecific antibody molecule, e.g., a bispecific antibody molecule, e.g., a bispecific antibody molecule that binds to CD20 and CD3. Exemplary bispecific antibody molecules that bind to CD20 and CD3 are disclosed in WO2016086189 and WO2016182751, herein incorporated by reference in their entirety. In some embodiments, the bispecific antibody molecule that binds to CD20 and CD3 is XENP13676 as disclosed in Figure 74, SEQ ID NOs: 323, 324, and 325 of WO2016086189.

Multispecific CAR

In some embodiments, the CAR molecule disclosed herein is a multispecific, e.g., bispecific, CAR molecule comprising one, two, or more binding specificities, e.g., a first binding specificity for a first antigen, e.g., a B-cell epitope, and a second binding specificity for the same or a different antigen, e.g., B cell epitope.

In one embodiment, the first and second binding specificity is an antibody molecule, e.g., an antigen binding domain (e.g., a scFv). Within each antibody molecule (e.g., scFv) of a bispecific CAR molecule, the VH can be upstream or downstream of the VL. In some embodiments, the upstream antibody or antibody fragment (e.g., scFv) is arranged with its VH (VH_1) upstream of its VL (VL_1) and the downstream antibody or antibody fragment (e.g., scFv) is arranged with its VL (VL_2) upstream of its VH (VH_2), such that the overall bispecific CAR molecule has the arrangement VH_1-VL_1-VL_2-VH_2, from an N- to C-terminal orientation.

In some embodiments, the upstream antibody or antibody fragment or antigen binding domain (e.g., scFv) is arranged with its VL (VL_1) upstream of its VH (VH_1) and the downstream antibody or antibody fragment (e.g., scFv) is arranged with its VH (VH_2) upstream of its VL (VL_2), such that the overall bispecific CAR molecule has the arrangement VL_1-VH_1-VH_2-VL_2, from an N- to C-terminal orientation.

In some embodiments, the upstream antibody or antibody fragment (e.g., scFv) is arranged with its VL (VL_1) upstream of its VH (VH_1) and the downstream antibody or antibody fragment or antigen binding domain (e.g., scFv) is arranged with its VL (VL_2) upstream of its VH (VH_2), such that the overall bispecific CAR molecule has the arrangement VL_1-VH_1-VL_2-VH_2, from an N- to C-terminal orientation.

In some embodiments, the upstream antibody or antibody fragment or antigen binding domain (e.g., scFv) is arranged with its VH (VH_1) upstream of its VL (VL_1) and the downstream antibody or antibody fragment (e.g., scFv) is arranged with its VH (VH_2) upstream of its VL (VL_2), such that the overall bispecific CAR molecule has the arrangement VH_1-VL_1-VH_2-VL_2, from an N- to C-terminal orientation.

In any of the aforesaid configurations, optionally, a linker is disposed between the two antibodies or antibody fragments or antigen binding domains (e.g., scFvs), e.g., between VL_1 and VL_2 if the construct is arranged as VH_1-VL_1-VL_2-VH_2; between VH_1 and VH_2 if the construct is arranged as VL_1-VH_1-VH_2-VL_2; between VH_1 and VL_2 if the construct is arranged as VL_1-VH_1-VL_2-VH_2; or between VL_1 and VH_2 if the construct is arranged as VH_1-VL_1-VH_2-VL_2. In general, the linker between the two antibody fragments or antigen binding domains, e.g.,scFvs, should be long enough to avoid mispairing between the domains of the two scFvs. The linker may be a linker as described herein. In some embodiments, the linker is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the linker comprises, e.g., consists of, the amino acid sequence: LAEAAAK (SEQ ID NO: 2033).

In any of the aforesaid configurations, optionally, a linker is disposed between the VL and VH of the first antigen binding domains, e.g., scFv. Optionally, a linker is disposed between the VL and VH of the second antigen binding domains, e.g., scFv. In constructs that have multiple linkers, any two or more of the linkers can be the same or different. Accordingly, in some embodiments, a bispecific CAR comprises VLs, VHs, and optionally one or more linkers in an arrangement as described herein.

In some embodiments, each antibody molecule, e.g., each antigen binding domain (e.g., each scFv) comprises a linker between the VH and the VL regions. In some embodiments, the linker between the VH and the VL regions is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In other embodiments, the linker is

$(Gly_4\text{-}Ser)_n$, wherein n= 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the VH and VL regions are connected without a linker.

In certain embodiments, the CAR molecule is a bispecific CAR molecule having a first binding specificity for a first B-cell epitope and a second binding specificity for the same or a different B-cell antigen. For instance, in some embodiments the bispecific CAR molecule has a first binding specificity for BCMA and a second binding specificity for one or more of BCMA, CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a. In some embodiments the bispecific CAR molecule has a first binding specificity for BCMA and a second binding specificity for CD19. In some embodiments the bispecific CAR molecule has a first binding specificity for BCMA and a second binding specificity for CD20. In some embodiments the bispecific CAR molecule has a first binding specificity for BCMA and a second binding specificity for CD22.

In one embodiment, the CAR molecule is a bispecific CAR molecule having a binding specificity, e.g., a first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22. In one embodiment, the binding specificity is configured with its VL (VL_1) upstream of its VH (VH_1) and the downstream antibody or antibody fragment or antigen binding domains (e.g., scFv) is arranged with its VL (VL_2) upstream of its VH (VH_2), such that the overall bispecific CAR molecule has the arrangement $VL_1\text{-}VH_1\text{-}VL_2\text{-}VH_2$, from an N- to C-terminal orientation. In some embodiments, the first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 (e.g., first and/or second scFv to BCMA, CD19, CD20, and/or CD22) comprises a linker between the VH and the VL regions. In some embodiments, the linker between the VH and the VL regions is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the VH and VL regions are connected without a linker.

In another embodiment, the binding specificity, e.g., a first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 is configured with its VL (VL_1) upstream of its VH (VH_1) and the downstream antibody or antibody fragment or antigen binding domains (e.g., scFv) is arranged with its VH (VH_2) upstream of its VL (VL_2), such that the overall bispecific CAR molecule has the arrangement $VL_1\text{-}VH_1\text{-}VH_2\text{-}VL_2$, from an N- to C-terminal orientation. In some embodiments, the first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 (e.g., first and/or second scFv to BCMA, CD19, CD20, and/or CD22) comprises a linker between the VH and the VL regions. In some embodiments, the linker between the VH and the VL regions is a $(Gly_4\text{-}Ser)_n$ linker

(SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the VH and VL regions are connected without a linker.

In another embodiment, the binding specificity, e.g., a first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 is configured with its VH (VH_1) upstream of its VL (VL_1) and the downstream antibody or antibody fragment or antigen binding domain (e.g., scFv) is arranged with its VL (VL_2) upstream of its VH (VH_2), such that the overall bispecific CAR molecule has the arrangement VH_1-VL_1-VL_2-VH_2, from an N- to C-terminal orientation. In some embodiments, the first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 (e.g., first and/or second scFv to BCMA, CD19, CD20, and/or CD22) comprises a linker between the VH and the VL regions. In some embodiments, the linker between the VH and the VL regions is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the VH and VL regions are connected without a linker.

In another embodiment, the binding specificity, e.g., a first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 is configured with its VH (VH_1) upstream of its VL (VL_1) and the downstream antibody or antibody fragment or antigen binding domain (e.g., scFv) is arranged with its VH (VH_2) upstream of its VL (VL_2), such that the overall bispecific CAR molecule has the arrangement VH_1-VL_1-VH_2-VL_2, from an N- to C-terminal orientation. In some embodiments, the first and/or second binding specificity, to BCMA, CD19, CD20, and/or CD22 (e.g., first and/or second scFv to BCMA, CD19, CD20, and/or CD22) comprises a linker between the VH and the VL regions. In some embodiments, the linker between the VH and the VL regions is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the VH and VL regions are connected without a linker.

In some embodiments, the bispecific CAR molecule comprises a first binding specificity to BCMA, e.g., any of the binding specificities to BCMA described herein, and a second binding specificity to CD19, e.g., any of the binding specificities to CD19 as described herein. In some

embodiments, the bispecific CAR molecule comprises a first binding specificity to BCMA, e.g., any of the binding specificities to BCMA described herein, and a second binding specificity to CD20, e.g., any of the binding specificities to CD20 as described herein. In some embodiments, the bispecific CAR molecule comprises a first binding specificity to BCMA, e.g., any of the binding specificities to BCMA described herein, and a second binding specificity to CD22, e.g., any of the binding specificities to CD22 as described herein. In one embodiment, the first and second binding specificity are in a contiguous polypeptide chain, e.g., a single chain. In some embodiments, the first and second binding specificities, optionally, comprise a linker as described herein. In some embodiments, the linker is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the linker comprises, e.g., consists of, the amino acid sequence: LAEAAAK (SEQ ID NO: 2033).

In some embodiments, the CAR molecule disclosed herein comprises a bispecific CAR comprising a fist and second binding specificities, e.g., as described herein (e.g., two antibody molecules, e.g., two scFvs as described herein). In some embodiments, the bispecific CAR comprises two antibody molecules, wherein the first binding specificity, e.g., the first antibody molecule (e.g., the first antigen binding domain, e.g., the first scFv) is closer to the transmembrane domain, also referred to herein as the proximal antibody molecule (e.g., proximal antigen binding domain) and the second binding specificity, e.g., the second antibody molecule (e.g., second antigen binding domain, e.g., the second scFv) is further away from the membrane, also referred to herein as the distal antibody molecule (e.g., the distal antigen binding domain). Thus, from N-to-C-terminus, the CAR molecule comprises a distal binding specificity, e.g., a distal antibody molecule (e.g., a distal antigen binding domain, e.g., a distal scFV or scFv2), optionally, a linker, followed by a proximal binding specificity, e.g., a proximal antibody molecule (e.g., a proximal antigen binding domain, e.g., a proximal scFv or scFv1), optionally via a linker, to a transmembrane domain and an intracellular domain, e.g., as described herein. In some embodiments, the CAR molecule comprises a proximal or distal binding specificity for BCMA, e.g., a BCMA binding specificity as described herein. In one embodiment, the CAR molecule comprises a proximal binding specificity for BCMA, e.g., a BCMA binding specificity as described herein, and a distal binding specificity for CD19, e.g., a CD19 binding specificity as described herein. In one embodiment, the CAR molecule comprises a proximal binding specificity for BCMA, e.g., a BCMA binding specificity as described herein, and a distal binding specificity for CD20, e.g., a CD20 binding specificity as described herein. In one embodiment, the CAR molecule comprises a proximal binding

specificity for BCMA, e.g., a BCMA binding specificity as described herein, and a distal binding specificity for CD22, e.g., a CD22 binding specificity as described herein. In one embodiment, the CAR molecule comprises a distal binding specificity for BCMA, e.g., a BCMA binding specificity as described herein, and a proximal binding specificity for CD19, e.g., a CD19 binding specificity as described herein. In one embodiment, the CAR molecule comprises a distal binding specificity for BCMA, e.g., a BCMA binding specificity as described herein, and a proximal binding specificity for CD20, e.g., a CD20 binding specificity as described herein. In one embodiment, the CAR molecule comprises a distal binding specificity for BCMA, e.g., a BCMA binding specificity as described herein, and a proximal binding specificity for CD22, e.g., a CD22 binding specificity as described herein.

In one embodiment, the CAR molecule comprises a distal to the membrane binding specificity to BCMA, e.g., a VL1-VH1 binding specificity to BCMA, and a proximal to the membrane binding specificity to CD19, CD20, or CD22, e.g., a VL2-VH2 or VH2-VL1 binding specificity to CD19. In one embodiment, the first and second binding specificity are in a contiguous polypeptide chain, e.g., a single chain. In some embodiments, the first and second binding specificities, optionally, comprise a linker as described herein. In some embodiments, the linker is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the linker comprises, e.g., consists of, the amino acid sequence: LAEAAAK (SEQ ID NO: 2033).

In one embodiment, the CAR molecule comprises a proximal to the membrane binding specificity to BCMA, e.g., a VL1-VH1 binding specificity to BCMA, and a distal to the membrane binding specificity to CD19, CD20, or CD22, e.g., a VL2-VH2 or VH2-VL1 binding specificity to CD19, CD20, or CD22. In one embodiment, the first and second binding specificity are in a contiguous polypeptide chain, e.g., a single chain. In some embodiments, the first and second binding specificities, optionally, comprise a linker as described herein. In some embodiments, the linker is a $(Gly_4\text{-}Ser)_n$ linker (SEQ ID NO: 2034), wherein n is 1, 2, 3, 4, 5, or 6. In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 1 (SEQ ID NO: 1032), e.g., the linker has the amino acid sequence Gly_4-Ser (SEQ ID NO: 1032). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n = 3 (SEQ ID NO: 1040). In some embodiments, the linker is $(Gly_4\text{-}Ser)_n$, wherein n= 4 (SEQ ID NO: 1039). In some embodiments, the linker comprises, e.g., consists of, the amino acid sequence: LAEAAAK (SEQ ID NO: 2033).

FCRL2 or FCRL5 inhibitor

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a FCRL2 or FCRL5 inhibitor. In some embodiments, the FCRL2 or FCRL5 inhibitor is an anti-FCRL2 antibody molecule, e.g., a bispecific antibody molecule, e.g., a bispecific antibody that binds to FCRL2 and CD3. In some embodiments, the FCRL2 or FCRL5 inhibitor is an anti-FCRL5 antibody molecule, e.g., a bispecific antibody molecule, e.g., a bispecific antibody that binds to FCRL5 and CD3. In some embodiments, the FCRL2 or FCRL5 inhibitor is a FCRL2 CAR-expressing cell therapy. In some embodiments, the FCRL2 or FCRL5 inhibitor is a FCRL5 CAR-expressing cell therapy.

Exemplary anti-FCRL5 antibody molecules are disclosed in US20150098900, US20160368985, WO2017096120 (e.g., antibodies ET200-001, ET200-002, ET200-003, ET200-006, ET200-007, ET200-008, ET200-009, ET200-010, ET200-011, ET200-012, ET200-013, ET200-014, ET200-015, ET200-016, ET200-017, ET200-018, ET200-019, ET200-020, ET200-021, ET200-022, ET200-023, ET200-024, ET200-025, ET200-026, ET200-027, ET200-028, ET200-029, ET200-030, ET200-031, ET200-032, ET200-033, ET200-034, ET200-035, ET200-037, ET200-038, ET200-039, ET200-040, ET200-041, ET200-042, ET200-043, ET200-044, ET200-045, ET200-069, ET200-078, ET200-079, ET200-081, ET200-097, ET200-098, ET200-099, ET200-100, ET200-101, ET200-102, ET200-103, ET200-104, ET200-105, ET200-106, ET200-107, ET200-108, ET200-109, ET200-110, ET200-111, ET200-112, ET200-113, ET200-114, ET200-115, ET200-116, ET200-117, ET200-118, ET200-119, ET200-120, ET200-121, ET200-122, ET200-123, ET200-125, ET200-005 and ET200-124 disclosed in WO2017096120), herein incorporated by reference in their entirety.

Exemplary FCRL5 CAR molecules are disclosed in WO2016090337, herein incorporated by reference in its entirety.

IL-15 and/or IL-15Ra

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with IL-15. In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an IL15/IL-15Ra complex. In some embodiments, the IL-15/IL-15Ra complex is chosen from NIZ985 (Novartis), ATL-803 (Altor) or CYP0150 (Cytune).

Exemplary IL-15/IL-15Ra complexes

In one embodiment, the IL-15/IL-15Ra complex comprises human IL-15 complexed with a soluble form of human IL-15Ra. The complex may comprise IL-15 covalently or noncovalently bound

to a soluble form of IL-15Ra. In a particular embodiment, the human IL-15 is noncovalently bonded to a soluble form of IL-15Ra. In a particular embodiment, the human IL-15 of the composition comprises an amino acid sequence of SEQ ID NO: 1001 in Table 16 and the soluble form of human IL-15Ra comprises an amino acid sequence of SEQ ID NO:1002 in Table 16, as described in WO 2014/066527, incorporated by reference in its entirety. The molecules described herein can be made by vectors, host cells, and methods described in WO 2007/084342, incorporated by reference in its entirety.

Table 16. Amino acid and nucleotide sequences of exemplary IL-15/IL-15Ra complexes

NIZ985		
SEQ ID NO: 1001	Human IL-15	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAM KCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTE SGCKECEELEEKNIKEFLQSFVHIVQMFINTS
SEQ ID NO: 1002	Human Soluble IL-15Ra	ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSS LTECVLNKATNVAHWTTPSLKCIRDPALVHQRPAPPSTVT TAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGSQL MPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQP PGVYPQG

Other exemplary IL-15/IL-15Ra complexes

In one embodiment, the IL-15/IL-15Ra complex is ALT-803, an IL-15/IL-15Ra Fc fusion protein (IL-15N72D:IL-15RaSu/Fc soluble complex). ALT-803 is disclosed in WO 2008/143794, incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra Fc fusion protein comprises the sequences as disclosed in Table 17.

In one embodiment, the IL-15/IL-15Ra complex comprises IL-15 fused to the sushi domain of IL-15Ra (CYP0150, Cytune). The sushi domain of IL-15Ra refers to a domain beginning at the first cysteine residue after the signal peptide of IL-15Ra, and ending at the fourth cysteine residue after said signal peptide. The complex of IL-15 fused to the sushi domain of IL-15Ra is disclosed in WO 2007/04606 and WO 2012/175222, incorporated by reference in their entirety. In one embodiment, the IL-15/IL-15Ra sushi domain fusion comprises the sequences as disclosed in Table 17.

Table 17. Amino acid sequences of other exemplary IL-15/IL-15Ra complexes

ALT-803 (Altor)		
SEQ ID NO: 1003	IL-15N72D	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMK CFLLELQVISLESGDASIHDTVENLIILANDSLSSNGNVTESG CKECEELEEKNIKEFLQSFVHIVQMFINTS
SEQ ID NO: 1004	IL-15RaSu/ Fc	ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSL TECVLNKATNVAHWTTPSLKCIREPKSCDKTHTCPPCPAPE LLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW

		LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK
IL-15 / IL-15Ra sushi domain fusion (Cytune)		
SEQ ID NO:1005	Human IL-15	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMK CFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESG CKECEELEXKNIKEFLQSFVHIVQMFINTS Where X is E or K
SEQ ID NO:1006	Human IL-15Ra sushi and hinge domains	ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSL TECVLNKATNVAHWTTPSLKCIRDPALVHQRPAPP

PD-1 inhibitor

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a PD-1 inhibitor. In some embodiments, the PD-1 inhibitor is chosen from PDR001 (Novartis), Nivolumab (Bristol-Myers Squibb), Pembrolizumab (Merck & Co), Pidilizumab (CureTech), MEDI0680 (Medimmune), REGN2810 (Regeneron), TSR-042 (Tesaro), PF-06801591 (Pfizer), BGB-A317 (Beigene), BGB-108 (Beigene), INCSHR1210 (Incyte), or AMP-224 (Amplimmune).

Exemplary PD-1 Inhibitors

In one embodiment, the PD-1 inhibitor is an anti-PD-1 antibody molecule. In one embodiment, the PD-1 inhibitor is an anti-PD-1 antibody molecule as described in US 2015/0210769, published on July 30, 2015, entitled "Antibody Molecules to PD-1 and Uses Thereof," incorporated by reference in its entirety.

In one embodiment, the anti-PD-1 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 18 (*e.g.*, from the heavy and light chain variable region sequences of BAP049-Clone-E or BAP049-Clone-B disclosed in Table 18), or encoded by a nucleotide sequence shown in Table 18. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 18). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 18). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 18). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GYTFTTYWMH (SEQ ID NO: 541). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 18, or encoded by a nucleotide sequence shown in Table 18.

In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 501, a VHCDR2 amino acid sequence of SEQ ID NO: 502, and a VHCDR3 amino acid sequence of SEQ ID NO: 503; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 510, a VLCDR2 amino acid sequence of SEQ ID NO: 511, and a VLCDR3 amino acid sequence of SEQ ID NO: 512, each disclosed in Table 18.

In one embodiment, the antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 524, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 525, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 526; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 529, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 530, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 531, each disclosed in Table 18.

In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 506. In one embodiment, the anti-PD-1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 520, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 520. In one embodiment, the anti-PD-1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 516, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 516. In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506 and a VL comprising the amino acid sequence of SEQ ID NO: 520. In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506 and a VL comprising the amino acid sequence of SEQ ID NO: 516.

In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 507, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 507. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 521 or 517, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 521 or 517. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 507 and a VL encoded by the nucleotide sequence of SEQ ID NO: 521 or 517.

In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 508. In one embodiment, the anti-PD-1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 522, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 522. In one embodiment,

the anti-PD-1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 518, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 518. In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508 and a light chain comprising the amino acid sequence of SEQ ID NO: 522. In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508 and a light chain comprising the amino acid sequence of SEQ ID NO: 518.

In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 509, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 509. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 523 or 519, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 523 or 519. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 509 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 523 or 519.

The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0210769, incorporated by reference in its entirety.

Table 18. Amino acid and nucleotide sequences of exemplary anti-PD-1 antibody molecules

BAP049-Clone-B HC	
SEQ ID NO: 501 (Kabat)	HCDR1
SEQ ID NO: 502 (Kabat)	HCDR2
SEQ ID NO: 503 (Kabat)	HCDR3
SEQ ID NO: 504 (Chothia)	HCDR1
SEQ ID NO: 505 (Chothia)	HCDR2
SEQ ID NO: 503 (Chothia)	HCDR3
SEQ ID NO: 506	VH
SEQ ID NO: 507	DNA VH
SEQ ID NO: 508	Heavy chain
SEQ ID NO: 509	DNA heavy chain
BAP049-Clone-B LC	
SEQ ID NO: 510 (Kabat)	LCDR1
SEQ ID NO: 511 (Kabat)	LCDR2
SEQ ID NO: 512 (Kabat)	LCDR3
SEQ ID NO: 513 (Chothia)	LCDR1
SEQ ID NO: 514 (Chothia)	LCDR2
SEQ ID NO: 515 (Chothia)	LCDR3
SEQ ID NO: 516	VL
SEQ ID NO: 517	DNA VL
SEQ ID NO: 518	Light chain
SEQ ID NO: 519	DNA light chain
BAP049-Clone-E HC	

SEQ ID NO: 501 (Kabat)	HCDR1
SEQ ID NO: 502 (Kabat)	HCDR2
SEQ ID NO: 503 (Kabat)	HCDR3
SEQ ID NO: 504 (Chothia)	HCDR1
SEQ ID NO: 505 (Chothia)	HCDR2
SEQ ID NO: 503 (Chothia)	HCDR3
SEQ ID NO: 506	VH
SEQ ID NO: 507	DNA VH
SEQ ID NO: 508	Heavy chain
SEQ ID NO: 509	DNA heavy chain
BAP049-Clone-E LC	
SEQ ID NO: 510 (Kabat)	LCDR1
SEQ ID NO: 511 (Kabat)	LCDR2
SEQ ID NO: 512 (Kabat)	LCDR3
SEQ ID NO: 513 (Chothia)	LCDR1
SEQ ID NO: 514 (Chothia)	LCDR2
SEQ ID NO: 515 (Chothia)	LCDR3
SEQ ID NO: 520	VL
SEQ ID NO: 521	DNA VL
SEQ ID NO: 522	Light chain
SEQ ID NO: 523	DNA light chain
BAP049-Clone-B HC	
SEQ ID NO: 524 (Kabat)	HCDR1
SEQ ID NO: 525 (Kabat)	HCDR2
SEQ ID NO: 526 (Kabat)	HCDR3
SEQ ID NO: 527 (Chothia)	HCDR1
SEQ ID NO: 528 (Chothia)	HCDR2
SEQ ID NO: 526 (Chothia)	HCDR3
BAP049-Clone-B LC	
SEQ ID NO: 529 (Kabat)	LCDR1
SEQ ID NO: 530 (Kabat)	LCDR2
SEQ ID NO: 531 (Kabat)	LCDR3
SEQ ID NO: 532 (Chothia)	LCDR1
SEQ ID NO: 533 (Chothia)	LCDR2
SEQ ID NO: 534 (Chothia)	LCDR3
BAP049-Clone-E HC	
SEQ ID NO: 524 (Kabat)	HCDR1
SEQ ID NO: 525 (Kabat)	HCDR2
SEQ ID NO: 526 (Kabat)	HCDR3
SEQ ID NO: 527 (Chothia)	HCDR1
SEQ ID NO: 528 (Chothia)	HCDR2
SEQ ID NO: 526 (Chothia)	HCDR3
BAP049-Clone-E LC	
SEQ ID NO: 529 (Kabat)	LCDR1
SEQ ID NO: 530 (Kabat)	LCDR2
SEQ ID NO: 531 (Kabat)	LCDR3
SEQ ID NO: 532 (Chothia)	LCDR1
SEQ ID NO: 533 (Chothia)	LCDR2
SEQ ID NO: 534 (Chothia)	LCDR3

Other Exemplary PD-1 Inhibitors

In one embodiment, the anti-PD-1 antibody molecule is Nivolumab (Bristol-Myers Squibb), also known as MDX-1106, MDX-1106-04, ONO-4538, BMS-936558, or OPDIVO®. Nivolumab (clone 5C4) and other anti-PD-1 antibodies are disclosed in US 8,008,449 and WO 2006/121168, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Nivolumab, *e.g.*, as disclosed in Table 19.

In one embodiment, the anti-PD-1 antibody molecule is Pembrolizumab (Merck & Co), also known as Lambrolizumab, MK-3475, MK03475, SCH-900475, or KEYTRUDA®. Pembrolizumab and other anti-PD-1 antibodies are disclosed in Hamid, O. *et al.* (2013) *New England Journal of Medicine* 369 (2): 134–44, US 8,354,509, and WO 2009/114335, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Pembrolizumab, *e.g.*, as disclosed in Table 19.

In one embodiment, the anti-PD-1 antibody molecule is Pidilizumab (CureTech), also known as CT-011. Pidilizumab and other anti-PD-1 antibodies are disclosed in Rosenblatt, J. *et al.* (2011) *J Immunotherapy* 34(5): 409-18, US 7,695,715, US 7,332,582, and US 8,686,119, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Pidilizumab, *e.g.*, as disclosed in Table 19.

In one embodiment, the anti-PD-1 antibody molecule is MEDI0680 (Medimmune), also known as AMP-514. MEDI0680 and other anti-PD-1 antibodies are disclosed in US 9,205,148 and WO 2012/145493, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MEDI0680.

In one embodiment, the anti-PD-1 antibody molecule is REGN2810 (Regeneron). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of REGN2810.

In one embodiment, the anti-PD-1 antibody molecule is PF-06801591 (Pfizer). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or

collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of PF-06801591.

In one embodiment, the anti-PD-1 antibody molecule is BGB-A317 or BGB-108 (Beigene). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BGB-A317 or BGB-108.

In one embodiment, the anti-PD-1 antibody molecule is INCSHR1210 (Incyte), also known as INCSHR01210 or SHR-1210. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INCSHR1210.

In one embodiment, the anti-PD-1 antibody molecule is TSR-042 (Tesaro), also known as ANB011. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-042.

Further known anti-PD-1 antibodies include those described, *e.g.*, in WO 2015/112800, WO 2016/092419, WO 2015/085847, WO 2014/179664, WO 2014/194302, WO 2014/209804, WO 2015/200119, US 8,735,553, US 7,488,802, US 8,927,697, US 8,993,731, and US 9,102,727, incorporated by reference in their entirety.

In one embodiment, the anti-PD-1 antibody is an antibody that competes for binding with, and/or binds to the same epitope on PD-1 as, one of the anti-PD-1 antibodies described herein.

In one embodiment, the PD-1 inhibitor is a peptide that inhibits the PD-1 signaling pathway, *e.g.*, as described in US 8,907,053, incorporated by reference in its entirety. In one embodiment, the PD-1 inhibitor is an immunoadhesin (*e.g.*, an immunoadhesin comprising an extracellular or PD-1 binding portion of PD-L1 or PD-L2 fused to a constant region (*e.g.*, an Fc region of an immunoglobulin sequence). In one embodiment, the PD-1 inhibitor is AMP-224 (B7-DCIg (Amplimmune), *e.g.*, disclosed in WO 2010/027827 and WO 2011/066342, incorporated by reference in their entirety).

Table 19. Amino acid sequences of other exemplary anti-PD-1 antibody molecules

Nivolumab	
SEQ ID NO: 535	Heavy chain
SEQ ID NO: 536	Light chain
Pembrolizumab	
SEQ ID NO: 537	Heavy chain
SEQ ID NO: 538	Light chain
Pidilizumab	

SEQ ID NO: 539	Heavy chain
SEQ ID NO: 540	Light chain

PD-L1 Inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a PD-L1 inhibitor. In some embodiments, the PD-L1 inhibitor is chosen from FAZ053 (Novartis), Atezolizumab (Genentech/Roche), Avelumab (Merck Serono and Pfizer), Durvalumab (MedImmune/AstraZeneca), or BMS-936559 (Bristol-Myers Squibb).

Exemplary PD-L1 Inhibitors

In one embodiment, the PD-L1 inhibitor is an anti-PD-L1 antibody molecule. In one embodiment, the PD-L1 inhibitor is an anti-PD-L1 antibody molecule as disclosed in US 2016/0108123, published on April 21, 2016, entitled "Antibody Molecules to PD-L1 and Uses Thereof," incorporated by reference in its entirety.

In one embodiment, the anti-PD-L1 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 20 (*e.g.*, from the heavy and light chain variable region sequences of BAP058-Clone O or BAP058-Clone N disclosed in Table 20), or encoded by a nucleotide sequence shown in Table 20. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 20). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 20). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 20). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GYTFTSYWMY (SEQ ID NO: 647). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.,* conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 20, or encoded by a nucleotide sequence shown in Table 20.

In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 601, a VHCDR2 amino acid sequence of SEQ ID NO: 602, and a VHCDR3 amino acid sequence of SEQ ID NO: 603; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 609, a VLCDR2 amino acid sequence of SEQ ID NO: 610, and a VLCDR3 amino acid sequence of SEQ ID NO: 611, each disclosed in Table 20.

In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 628, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 629, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 630; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 633, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 634, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 635, each disclosed in Table 20.

In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 606, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 606. In one embodiment, the anti-PD-L1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 616, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 616. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 620, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 620. In one embodiment, the anti-PD-L1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 624, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 624. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 606 and a VL comprising the amino acid sequence of SEQ ID NO: 616. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 620 and a VL comprising the amino acid sequence of SEQ ID NO: 624.

In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 607, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 607. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 617, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 617. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 621, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 621. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 625, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 625. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 607 and a VL encoded by the nucleotide sequence of SEQ ID NO: 617. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 621 and a VL encoded by the nucleotide sequence of SEQ ID NO: 625.

In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 608, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 608. In one embodiment, the anti-PD-L1 antibody molecule

comprises a light chain comprising the amino acid sequence of SEQ ID NO: 618, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 618. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 622, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 622. In one embodiment, the anti-PD-L1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 626, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 626. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 608 and a light chain comprising the amino acid sequence of SEQ ID NO: 618. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 622 and a light chain comprising the amino acid sequence of SEQ ID NO: 626.

In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 615, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 615. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 619, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 619. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 623, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 623. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 627, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 627. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 615 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 619. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 623 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 627.

The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2016/0108123, incorporated by reference in its entirety.

Table 20. Amino acid and nucleotide sequences of exemplary anti-PD-L1 antibody molecules

BAP058-Clone O HC	
SEQ ID NO: 601 (Kabat)	HCDR1
SEQ ID NO: 602 (Kabat)	HCDR2
SEQ ID NO: 603 (Kabat)	HCDR3
SEQ ID NO: 604 (Chothia)	HCDR1
SEQ ID NO: 605 (Chothia)	HCDR2
SEQ ID NO: 603 (Chothia)	HCDR3
SEQ ID NO: 606	VH
SEQ ID NO: 607	DNA VH

SEQ ID NO: 608	Heavy chain
SEQ ID NO: 615	DNA heavy chain
BAP058-Clone O LC	
SEQ ID NO: 609 (Kabat)	LCDR1
SEQ ID NO: 610 (Kabat)	LCDR2
SEQ ID NO: 611(Kabat)	LCDR3
SEQ ID NO: 612 (Chothia)	LCDR1
SEQ ID NO: 613 (Chothia)	LCDR2
SEQ ID NO: 614 (Chothia)	LCDR3
SEQ ID NO: 616	VL
SEQ ID NO: 617	DNA VL
SEQ ID NO: 618	Light chain
SEQ ID NO: 619	DNA light chain
BAP058-Clone N HC	
SEQ ID NO: 601 (Kabat)	HCDR1
SEQ ID NO: 602 (Kabat)	HCDR2
SEQ ID NO: 603 (Kabat)	HCDR3
SEQ ID NO: 604 (Chothia)	HCDR1
SEQ ID NO: 605 (Chothia)	HCDR2
SEQ ID NO: 603 (Chothia)	HCDR3
SEQ ID NO: 620	VH
SEQ ID NO: 621	DNA VH
SEQ ID NO: 622	Heavy chain
SEQ ID NO: 623	DNA heavy chain
BAP058-Clone N LC	
SEQ ID NO: 609 (Kabat)	LCDR1
SEQ ID NO: 610 (Kabat)	LCDR2
SEQ ID NO: 611(Kabat)	LCDR3
SEQ ID NO: 612 (Chothia)	LCDR1
SEQ ID NO: 613 (Chothia)	LCDR2
SEQ ID NO: 614 (Chothia)	LCDR3
SEQ ID NO: 624	VL
SEQ ID NO: 625	DNA VL
SEQ ID NO: 626	Light chain
SEQ ID NO: 627	DNA light chain
BAP058-Clone O HC	
SEQ ID NO: 628 (Kabat)	HCDR1
SEQ ID NO: 629 (Kabat)	HCDR2
SEQ ID NO: 630 (Kabat)	HCDR3
SEQ ID NO: 631 (Chothia)	HCDR1
SEQ ID NO: 632 (Chothia)	HCDR2
SEQ ID NO: 630 (Chothia)	HCDR3
BAP058-Clone O LC	
SEQ ID NO: 633 (Kabat)	LCDR1
SEQ ID NO: 634 (Kabat)	LCDR2
SEQ ID NO: 635 (Kabat)	LCDR3
SEQ ID NO: 636 (Chothia)	LCDR1
SEQ ID NO: 637 (Chothia)	LCDR2
SEQ ID NO: 638 (Chothia)	LCDR3
BAP058-Clone N HC	

SEQ ID NO: 628 (Kabat)	HCDR1
SEQ ID NO: 629 (Kabat)	HCDR2
SEQ ID NO: 630 (Kabat)	HCDR3
SEQ ID NO: 631 (Chothia)	HCDR1
SEQ ID NO: 632 (Chothia)	HCDR2
SEQ ID NO: 630 (Chothia)	HCDR3
BAP058-Clone N LC	
SEQ ID NO: 633 (Kabat)	LCDR1
SEQ ID NO: 634 (Kabat)	LCDR2
SEQ ID NO: 635 (Kabat)	LCDR3
SEQ ID NO: 636 (Chothia)	LCDR1
SEQ ID NO: 637 (Chothia)	LCDR2
SEQ ID NO: 638 (Chothia)	LCDR3

Other Exemplary PD-L1 Inhibitors

In one embodiment, the anti-PD-L1 antibody molecule is Atezolizumab (Genentech/Roche), also known as MPDL3280A, RG7446, RO5541267, YW243.55.S70, or TECENTRIQ™. Atezolizumab and other anti-PD-L1 antibodies are disclosed in US 8,217,149, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Atezolizuma, *e.g.*, as disclosed in Table 21.

In one embodiment, the anti-PD-L1 antibody molecule is Avelumab (Merck Serono and Pfizer), also known as MSB0010718C. Avelumab and other anti-PD-L1 antibodies are disclosed in WO 2013/079174, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Avelumab, *e.g.*, as disclosed in Table 21.

In one embodiment, the anti-PD-L1 antibody molecule is Durvalumab (MedImmune/AstraZeneca), also known as MEDI4736. Durvalumab and other anti-PD-L1 antibodies are disclosed in US 8,779,108, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Durvalumab, *e.g.*, as disclosed in Table 21.

In one embodiment, the anti-PD-L1 antibody molecule is BMS-936559 (Bristol-Myers Squibb), also known as MDX-1105 or 12A4. BMS-936559 and other anti-PD-L1 antibodies are disclosed in US 7,943,743 and WO 2015/081158, incorporated by reference in their entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the

CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-936559, *e.g.*, as disclosed in Table 21.

Further known anti-PD-L1 antibodies include those described, *e.g.*, in WO 2015/181342, WO 2014/100079, WO 2016/000619, WO 2014/022758, WO 2014/055897, WO 2015/061668, WO 2013/079174, WO 2012/145493, WO 2015/112805, WO 2015/109124, WO 2015/195163, US 8,168,179, US 8,552,154, US 8,460,927, and US 9,175,082, incorporated by reference in their entirety.

In one embodiment, the anti-PD-L1 antibody is an antibody that competes for binding with, and/or binds to the same epitope on PD-L1 as, one of the anti-PD-L1 antibodies described herein.

Table 21. Amino acid sequences of other exemplary anti-PD-L1 antibody molecules

Atezolizumab	
SEQ ID NO: 639	Heavy chain
SEQ ID NO: 640	Light chain
Avelumab	
SEQ ID NO: 641	Heavy chain
SEQ ID NO: 642	Light chain
Durvalumab	
SEQ ID NO: 643	Heavy chain
SEQ ID NO: 644	Light chain
BMS-936559	
SEQ ID NO: 645	VH
SEQ ID NO: 646	VL

LAG-3 Inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a LAG-3 inhibitor. In some embodiments, the LAG-3 inhibitor is chosen from LAG525 (Novartis), BMS-986016 (Bristol-Myers Squibb), or TSR-033 (Tesaro).

Exemplary LAG-3 Inhibitors

In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule. In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule as disclosed in US 2015/0259420, published on September 17, 2015, entitled "Antibody Molecules to LAG-3 and Uses Thereof," incorporated by reference in its entirety.

In one embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 22 (*e.g.*, from the heavy and light chain variable region sequences of BAP050-Clone I or BAP050-Clone J disclosed in

Table 22), or encoded by a nucleotide sequence shown in Table 22. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 22). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 22). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 22). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GFTLTNYGMN (SEQ ID NO: 766). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 22, or encoded by a nucleotide sequence shown in Table 22.

In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 701, a VHCDR2 amino acid sequence of SEQ ID NO: 702, and a VHCDR3 amino acid sequence of SEQ ID NO: 703; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 710, a VLCDR2 amino acid sequence of SEQ ID NO: 711, and a VLCDR3 amino acid sequence of SEQ ID NO: 712, each disclosed in Table 22.

In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 736 or 737, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 738 or 739, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 740 or 741; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 746 or 747, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 748 or 749, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 750 or 751, each disclosed in Table 22. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 758 or 737, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 759 or 739, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 760 or 741; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 746 or 747, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 748 or 749, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 750 or 751, each disclosed in Table 22.

In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 706, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 706. In one embodiment, the anti-LAG-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 718, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 718. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 724, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 724. In one embodiment, the anti-LAG-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO:

730, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 730. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 706 and a VL comprising the amino acid sequence of SEQ ID NO: 718. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 724 and a VL comprising the amino acid sequence of SEQ ID NO: 730.

In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 707 or 708, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 707 or 708. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 719 or 720, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 719 or 720. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 725 or 726, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 725 or 726. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 731 or 732, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 731 or 732. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 707 or 708 and a VL encoded by the nucleotide sequence of SEQ ID NO: 719 or 720. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 725 or 726 and a VL encoded by the nucleotide sequence of SEQ ID NO: 731 or 732.

In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 709, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 709. In one embodiment, the anti-LAG-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 721, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 721. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 727, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 727. In one embodiment, the anti-LAG-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 733, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 733. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 709 and a light chain comprising the amino acid sequence of SEQ ID NO: 721. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 727 and a light chain comprising the amino acid sequence of SEQ ID NO: 733.

In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 716 or 717, or a nucleotide sequence at least 85%, 90%, 95%, or 99%

identical or higher to SEQ ID NO: 716 or 717. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 722 or 723, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 722 or 723. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 728 or 729, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 728 or 729. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 734 or 735, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 734 or 735. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 716 or 717 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 722 or 723. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 728 or 729 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 734 or 735.

The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0259420, incorporated by reference in its entirety.

Table 22. Amino acid and nucleotide sequences of exemplary anti-LAG-3 antibody molecules

BAP050-Clone I HC	
SEQ ID NO: 701 (Kabat)	HCDR1
SEQ ID NO: 702 (Kabat)	HCDR2
SEQ ID NO: 703 (Kabat)	HCDR3
SEQ ID NO: 704 (Chothia)	HCDR1
SEQ ID NO: 705 (Chothia)	HCDR2
SEQ ID NO: 703 (Chothia)	HCDR3
SEQ ID NO:706	VH
SEQ ID NO: 707	DNA VH
SEQ ID NO: 708	DNA VH
SEQ ID NO: 709	Heavy chain
SEQ ID NO: 716	DNA heavy chain
SEQ ID NO: 717	DNA heavy chain
BAP050-Clone I LC	
SEQ ID NO: 710 (Kabat)	LCDR1
SEQ ID NO: 711 (Kabat)	LCDR2
SEQ ID NO: 712 (Kabat)	LCDR3
SEQ ID NO: 713 (Chothia)	LCDR1
SEQ ID NO: 714 (Chothia)	LCDR2
SEQ ID NO: 715 (Chothia)	LCDR3
SEQ ID NO: 718	VL
SEQ ID NO: 719	DNA VL
SEQ ID NO: 720	DNA VL
SEQ ID NO: 721	Light chain
SEQ ID NO: 722	DNA light chain

SEQ ID NO: 723	DNA light chain
BAP050-Clone J HC	
SEQ ID NO: 701 (Kabat)	HCDR1
SEQ ID NO: 702 (Kabat)	HCDR2
SEQ ID NO: 703 (Kabat)	HCDR3
SEQ ID NO: 704 (Chothia)	HCDR1
SEQ ID NO: 705 (Chothia)	HCDR2
SEQ ID NO: 703 (Chothia)	HCDR3
SEQ ID NO: 724	VH
SEQ ID NO: 725	DNA VH
SEQ ID NO: 726	DNA VH
SEQ ID NO: 727	Heavy chain
SEQ ID NO: 728	DNA heavy chain
SEQ ID NO: 729	DNA heavy chain
BAP050-Clone J LC	
SEQ ID NO: 710 (Kabat)	LCDR1
SEQ ID NO: 711 (Kabat)	LCDR2
SEQ ID NO: 712 (Kabat)	LCDR3
SEQ ID NO: 713 (Chothia)	LCDR1
SEQ ID NO: 714 (Chothia)	LCDR2
SEQ ID NO: 715 (Chothia)	LCDR3
SEQ ID NO: 730	VL
SEQ ID NO: 731	DNA VL
SEQ ID NO: 732	DNA VL
SEQ ID NO: 733	Light chain
SEQ ID NO: 734	DNA light chain
SEQ ID NO: 735	DNA light chain
BAP050-Clone I HC	
SEQ ID NO: 736 (Kabat)	HCDR1
SEQ ID NO: 737 (Kabat)	HCDR1
SEQ ID NO: 738 (Kabat)	HCDR2
SEQ ID NO: 739 (Kabat)	HCDR2
SEQ ID NO: 740 (Kabat)	HCDR3
SEQ ID NO: 741 (Kabat)	HCDR3
SEQ ID NO: 742 (Chothia)	HCDR1
SEQ ID NO: 743 (Chothia)	HCDR1
SEQ ID NO: 744 (Chothia)	HCDR2
SEQ ID NO: 745 (Chothia)	HCDR2
SEQ ID NO: 740 (Chothia)	HCDR3
SEQ ID NO: 741 (Chothia)	HCDR3
BAP050-Clone I LC	
SEQ ID NO: 746 (Kabat)	LCDR1
SEQ ID NO: 747 (Kabat)	LCDR1
SEQ ID NO: 748 (Kabat)	LCDR2
SEQ ID NO: 749 (Kabat)	LCDR2
SEQ ID NO: 750 (Kabat)	LCDR3
SEQ ID NO: 751 (Kabat)	LCDR3
SEQ ID NO: 752 (Chothia)	LCDR1
SEQ ID NO: 753 (Chothia)	LCDR1

SEQ ID NO: 754 (Chothia)	LCDR2
SEQ ID NO: 755 (Chothia)	LCDR2
SEQ ID NO: 756 (Chothia)	LCDR3
SEQ ID NO: 757 (Chothia)	LCDR3
BAP050-Clone J HC	
SEQ ID NO: 758 (Kabat)	HCDR1
SEQ ID NO: 737 (Kabat)	HCDR1
SEQ ID NO: 759 (Kabat)	HCDR2
SEQ ID NO: 739 (Kabat)	HCDR2
SEQ ID NO: 760 (Kabat)	HCDR3
SEQ ID NO: 741 (Kabat)	HCDR3
SEQ ID NO: 761 (Chothia)	HCDR1
SEQ ID NO: 743 (Chothia)	HCDR1
SEQ ID NO: 744 (Chothia)	HCDR2
SEQ ID NO: 745 (Chothia)	HCDR2
SEQ ID NO: 760 (Chothia)	HCDR3
SEQ ID NO: 741 (Chothia)	HCDR3
BAP050-Clone J LC	
SEQ ID NO: 746 (Kabat)	LCDR1
SEQ ID NO: 747 (Kabat)	LCDR1
SEQ ID NO: 748 (Kabat)	LCDR2
SEQ ID NO: 749 (Kabat)	LCDR2
SEQ ID NO: 750 (Kabat)	LCDR3
SEQ ID NO: 751 (Kabat)	LCDR3
SEQ ID NO: 752 (Chothia)	LCDR1
SEQ ID NO: 753 (Chothia)	LCDR1
SEQ ID NO: 754 (Chothia)	LCDR2
SEQ ID NO: 755 (Chothia)	LCDR2
SEQ ID NO: 756 (Chothia)	LCDR3
SEQ ID NO: 757 (Chothia)	LCDR3

Other Exemplary LAG-3 Inhibitors

In one embodiment, the anti-LAG-3 antibody molecule is BMS-986016 (Bristol-Myers Squibb), also known as BMS986016. BMS-986016 and other anti-LAG-3 antibodies are disclosed in WO 2015/116539 and US 9,505,839, incorporated by reference in their entirety. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-986016, *e.g.*, as disclosed in Table 23.

In one embodiment, the anti-LAG-3 antibody molecule is TSR-033 (Tesaro). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-033.

In one embodiment, the anti-LAG-3 antibody molecule is IMP731 or GSK2831781 (GSK and Prima BioMed). IMP731 and other anti-LAG-3 antibodies are disclosed in WO 2008/132601 and US 9,244,059, incorporated by reference in their entirety. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of IMP731, *e.g.*, as disclosed in Table 23. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of GSK2831781.

In one embodiment, the anti-LAG-3 antibody molecule is IMP761 (Prima BioMed). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of IMP761.

Further known anti-LAG-3 antibodies include those described, *e.g.*, in WO 2008/132601, WO 2010/019570, WO 2014/140180, WO 2015/116539, WO 2015/200119, WO 2016/028672, US 9,244,059, US 9,505,839, incorporated by reference in their entirety.

In one embodiment, the anti-LAG-3 antibody is an antibody that competes for binding with, and/or binds to the same epitope on LAG-3 as, one of the anti-LAG-3 antibodies described herein.

In one embodiment, the anti-LAG-3 inhibitor is a soluble LAG-3 protein, *e.g.*, IMP321 (Prima BioMed), *e.g.*, as disclosed in WO 2009/044273, incorporated by reference in its entirety.

Table 23. Amino acid sequences of other exemplary anti-LAG-3 antibody molecules

BMS-986016	
SEQ ID NO: 762	Heavy chain
SEQ ID NO: 763	Light chain
IMP731	
SEQ ID NO: 764	Heavy chain
SEQ ID NO: 765	Light chain

TIM-3 Inhibitors

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a TIM-3 inhibitor. In some embodiments, the TIM-3 inhibitor is MGB453 (Novartis) or TSR-022 (Tesaro).

Exemplary TIM-3 Inhibitors

In one embodiment, the TIM-3 inhibitor is an anti-TIM-3 antibody molecule. In one embodiment, the TIM-3 inhibitor is an anti-TIM-3 antibody molecule as disclosed in US 2015/0218274, published on August 6, 2015, entitled "Antibody Molecules to TIM-3 and Uses Thereof," incorporated by reference in its entirety.

In one embodiment, the anti-TIM-3 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 24 (*e.g.*, from the heavy and light chain variable region sequences of ABTIM3-hum11 or ABTIM3-hum03 disclosed in Table 24), or encoded by a nucleotide sequence shown in Table 24. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 24). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 24). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.,* conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 24, or encoded by a nucleotide sequence shown in Table 24.

In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 801, a VHCDR2 amino acid sequence of SEQ ID NO: 802, and a VHCDR3 amino acid sequence of SEQ ID NO: 803; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 810, a VLCDR2 amino acid sequence of SEQ ID NO: 811, and a VLCDR3 amino acid sequence of SEQ ID NO: 812, each disclosed in Table 24. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 801, a VHCDR2 amino acid sequence of SEQ ID NO: 820, and a VHCDR3 amino acid sequence of SEQ ID NO: 803; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 810, a VLCDR2 amino acid sequence of SEQ ID NO: 811, and a VLCDR3 amino acid sequence of SEQ ID NO: 812, each disclosed in Table 24.

In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 806, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 806. In one embodiment, the anti-TIM-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 816, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 816. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 822, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 822. In one embodiment, the anti-TIM-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 826, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 826.

In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 806 and a VL comprising the amino acid sequence of SEQ ID NO: 816. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 822 and a VL comprising the amino acid sequence of SEQ ID NO: 826.

In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 807, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 807. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 817, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 817. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 823, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 823. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 827, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 827. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 807 and a VL encoded by the nucleotide sequence of SEQ ID NO: 817. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 823 and a VL encoded by the nucleotide sequence of SEQ ID NO: 827.

In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 808, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 808. In one embodiment, the anti-TIM-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 818, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 818. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 824, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 824. In one embodiment, the anti-TIM-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 828, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 828. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 808 and a light chain comprising the amino acid sequence of SEQ ID NO: 818. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 824 and a light chain comprising the amino acid sequence of SEQ ID NO: 828.

In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 809, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 809. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 819, or a nucleotide sequence at least 85%, 90%, 95%, or

99% identical or higher to SEQ ID NO: 819. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 825, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 825. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 829, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 829. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 809 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 819. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 825 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 829.

The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0218274, incorporated by reference in its entirety.

Table 24. Amino acid and nucleotide sequences of exemplary anti-TIM-3 antibody molecules

ABTIM3-hum11	
SEQ ID NO: 801 (Kabat)	HCDR1
SEQ ID NO: 802 (Kabat)	HCDR2
SEQ ID NO: 803 (Kabat)	HCDR3
SEQ ID NO: 804 (Chothia)	HCDR1
SEQ ID NO: 805 (Chothia)	HCDR2
SEQ ID NO: 803 (Chothia)	HCDR3
SEQ ID NO: 806	VH
SEQ ID NO: 807	DNA VH
SEQ ID NO: 808	Heavy chain
SEQ ID NO: 809	DNA heavy chain
SEQ ID NO: 810 (Kabat)	LCDR1
SEQ ID NO: 811 (Kabat)	LCDR2
SEQ ID NO: 812 (Kabat)	LCDR3
SEQ ID NO: 813 (Chothia)	LCDR1
SEQ ID NO: 814 (Chothia)	LCDR2
SEQ ID NO: 815 (Chothia)	LCDR3
SEQ ID NO: 816	VL
SEQ ID NO: 817	DNA VL
SEQ ID NO: 818	Light chain
SEQ ID NO: 819	DNA light chain
ABTIM3-hum03	
SEQ ID NO: 801 (Kabat)	HCDR1
SEQ ID NO: 820 (Kabat)	HCDR2
SEQ ID NO: 803 (Kabat)	HCDR3
SEQ ID NO: 804 (Chothia)	HCDR1
SEQ ID NO: 821 (Chothia)	HCDR2
SEQ ID NO: 803 (Chothia)	HCDR3
SEQ ID NO: 822	VH
SEQ ID NO: 823	DNA VH

SEQ ID NO: 824	Heavy chain
SEQ ID NO: 825	DNA heavy chain
SEQ ID NO: 810 (Kabat)	LCDR1
SEQ ID NO: 811 (Kabat)	LCDR2
SEQ ID NO: 812 (Kabat)	LCDR3
SEQ ID NO: 813 (Chothia)	LCDR1
SEQ ID NO: 814 (Chothia)	LCDR2
SEQ ID NO: 815 (Chothia)	LCDR3
SEQ ID NO: 826	VL
SEQ ID NO: 827	DNA VL
SEQ ID NO: 828	Light chain
SEQ ID NO: 829	DNA light chain

Other Exemplary TIM-3 Inhibitors

In one embodiment, the anti-TIM-3 antibody molecule is TSR-022 (AnaptysBio/Tesaro). In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-022. In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of APE5137 or APE5121, *e.g.*, as disclosed in Table 25. APE5137, APE5121, and other anti-TIM-3 antibodies are disclosed in WO 2016/161270, incorporated by reference in its entirety.

In one embodiment, the anti-TIM-3 antibody molecule is the antibody clone F38-2E2. In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of F38-2E2.

Further known anti-TIM-3 antibodies include those described, *e.g.*, in WO 2016/111947, WO 2016/071448, WO 2016/144803, US 8,552,156, US 8,841,418, and US 9,163,087, incorporated by reference in their entirety.

In one embodiment, the anti-TIM-3 antibody is an antibody that competes for binding with, and/or binds to the same epitope on TIM-3 as, one of the anti-TIM-3 antibodies described herein.

Table 25. Amino acid sequences of other exemplary anti-TIM-3 antibody molecules

APE5137	
SEQ ID NO: 830	VH
SEQ ID NO: 831	VL
APE5121	
SEQ ID NO: 832	VH
SEQ ID NO: 833	VL

TGF-β Inhibitors

In certain embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a transforming growth factor beta (also known as TGF-β, TGFβ, TGFb, or TGF-beta, used interchangeably herein) inhibitor.

TGF-β belongs to a large family of structurally-related cytokines including, *e.g.,* bone morphogenetic proteins (BMPs), growth and differentiation factors, activins and inhibins. In some embodiments, the TGF-β inhibitors described herein can bind and/or inhibit one or more isoforms of TGF-β (*e.g.,* one, two, or all of TGF-β1, TGF-β2, or TGF-β3).

In some embodiments, the TGF-β inhibitor comprises XOMA 089, or a compound disclosed in International Application Publication No. WO 2012/167143, which is incorporated by reference in its entirety.

XOMA 089 is also known as XPA.42.089. XOMA 089 is a fully human monoclonal antibody that specifically binds and neutralizes TGF-beta 1 and 2 ligands.

The heavy chain variable region of XOMA 089 has the amino acid sequence of: QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTANYAQK FQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGLWEVRALPSVYWGQGTLVTVSS (SEQ ID NO: 1986) (disclosed as SEQ ID NO: 6 in WO 2012/167143). The light chain variable region of XOMA 089 has the amino acid sequence of: SYELTQPPSVSVAPGQTARITCGANDIGSKSVHWYQQKAGQAPVLVVSEDIIRPSGIPERISGSNS GNTATLTISRVEAGDEADYYCQVWDRDSDQYVFGTGTKVTVLG (SEQ ID NO: 1987) (disclosed as SEQ ID NO: 8 in WO 2012/167143).

XOMA 089 binds with high affinity to the human TGF-β isoforms. Generally, XOMA 089 binds with high affinity to TGF-β1 and TGF-β2, and to a lesser extent to TGF-β3. In Biacore assays, the K_D of XOMA 089 on human TGF-β is 14.6 pM for TGF-β1, 67.3 pM for TGF-β2, and 948 pM for TGF-β3. Given the high affinity binding to all three TGF-β isoforms, in certain embodiments, XOMA 089 is expected to bind to TGF-β1, 2 and 3 at a dose of XOMA 089 as described herein. XOMA 089 cross-reacts with rodent and cynomolgus monkey TGF-β and shows functional activity *in vitro* and *in vivo*, making rodent and cynomolgus monkey relevant species for toxicology studies.

In some embodiments, the TGF-β inhibitor comprises fresolimumab (CAS Registry Number: 948564-73-6). Fresolimumab is also known as GC1008. Fresolimumab is a human monoclonal antibody that binds to and inhibits TGF-beta isoforms 1, 2 and 3.

The heavy chain of fresolimumab has the amino acid sequence of: QVQLVQSGAEVKKPGSSVKVSCKASGYTFSSNVISWVRQAPGQGLEWMGGVIPIVDIANYAQR

FKGRVTITADESTSTTYMELSSLRSEDTAVYYCASTLGLVLDAMDYWGQGTLVTVSSASTKGP
SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
PSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLS
LGK (SEQ ID NO: 1988).

The light chain of fresolimumab has the amino acid sequence of:
ETVLTQSPGTLSLSPGERATLSCRASQSLGSSYLAWYQQKPGQAPRLLIYGASSRAPGIPDRFSG
SGSGTDFTLTISRLEPEDFAVYYCQQYADSPITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTA
SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVY
ACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 1989).

Fresolimumab is disclosed, *e.g.,* in International Application Publication No. WO 2006/086469, and U.S. Patent Nos. 8,383,780 and 8,591,901, which are incorporated by reference in their entirety.

Anti-CD73 Antibody Molecules

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an anti-CD73 antibody molecule. In one embodiment, an anti-CD73 antibody molecule is a full antibody molecule or an antigen-binding fragment thereof. In some embodiments, the anti-CD73 antibody molecule is chosen from any of the antibody molecules listed in Table 26. In other embodiments, the anti-CD73 antibody molecule comprises a heavy chain variable domain sequence, a light chain variable domain sequence, or both, as disclosed in Table 26. In certain embodiments, the anti-CD73 antibody molecule binds to a CD73 protein and reduces, *e.g.*, inhibits or antagonizes, an activity of CD73, *e.g.*, human CD73.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/075099, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is MEDI 9447, *e.g.*, as disclosed in WO2016/075099. Alternative names for MEDI 9447 include clone 10.3 or 73combo3. MEDI 9447 is an IgG1 antibody that inhibits, *e.g.*, antagonizes, an activity of CD73. MEDI 9447 and other anti-CD73 antibody molecules are also disclosed in WO2016/075176 and US2016/0129108, the entire contents of which are herein incorporated by reference in their entirety.

In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of MEDI 9477. The amino acid sequence of the heavy chain variable domain of MEDI 9477 is disclosed as SEQ ID NO: 1990 (see Table 26). The amino acid

sequence of the light chain variable domain of MEDI 9477 is disclosed as SEQ ID NO: 1991 (see Table 26).

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/081748, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is 11F11, *e.g.*, as disclosed in WO2016/081748. 11F11 is an IgG2 antibody that inhibits, *e.g.*, antagonizes, an activity of CD73. Antibodies derived from 11F11, *e.g.*, CD73.4, and CD73.10; clones of 11F11, *e.g.*, 11F11-1 and 11F11-2; and other anti-CD73 antibody molecules are disclosed in WO2016/081748 and US 9,605,080, the entire contents of which are herein incorporated by reference in their entirety.

In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of 11F11-1 or 11F11-2. The amino acid sequence of the heavy chain variable domain of 11F11-1 is disclosed as SEQ ID NO: 1998 (see Table 26). The amino acid sequence of the light chain variable domain of 11F11-1 is disclosed as SEQ ID NO: 1999 (see Table 26). The amino acid sequence of the heavy chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 1994 (see Table 26). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 1995 (see Table 26). In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain, a light chain, or both, of 11F11-1 or 11F11-2. The heavy and light chain amino acid sequences of 11F11-1 are disclosed as SEQ ID NO: 1996 and SEQ ID NO:1997, respectively (see Table 26). The heavy and light chain amino acid sequences of 11F11-2 are disclosed as SEQ ID NO: 1992 and SEQ ID NO:1993, respectively (see Table 26).

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in *e.g.*, US 9,605,080, herein incorporated by reference in its entirety.

In one embodiment, the anti-CD73 antibody molecule is CD73.4, *e.g.*, as disclosed in US 9,605,080. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of CD73.4. The amino acid sequence of the heavy chain variable domain of CD73.4 is disclosed as SEQ ID NO: 2000 (see Table 26). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 2001 (see Table 26).

In one embodiment, the anti-CD73 antibody molecule is CD73.10, *e.g.*, as disclosed in US 9,605,080. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of CD73.10. The amino acid sequence of the heavy chain variable domain of CD73.10 is disclosed as SEQ ID NO: 2002 (see Table 26). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 2003 (see Table 26).

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2009/0203538, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is 067-213, *e.g.*, as disclosed in WO2009/0203538.

In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of 067-213. The amino acid sequence of the heavy chain variable domain of 067-213 is disclosed as SEQ ID NO: 2004 (see Table 26). The amino acid sequence of the light chain variable domain of 067-213 is disclosed as SEQ ID NO: 2005 (see Table 26).

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US 9,090,697, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is TY/23, *e.g.*, as disclosed in US 9,090,697. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of TY/23.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/055609, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2016/055609.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/146818, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2016/146818.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2004/079013, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2004/079013.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2012/125850, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2012/125850.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2015/004400, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2015/004400.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2007/146968, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73

antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2007146968.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US2007/0042392, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in US2007/0042392.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US2009/0138977, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in US2009/0138977.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in Flocke et al., Eur J Cell Biol. 1992 Jun;58(1):62-70, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in Flocke et al., Eur J Cell Biol. 1992 Jun;58(1):62-70.

In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in Stagg et al., PNAS. 2010 Jan 107(4): 1547-1552, herein incorporated by reference in its entirety. In some embodiments, the anti-CD73 antibody molecule is TY/23 or TY11.8, as disclosed in Stagg et al. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in Stagg et al.

Table 26: Sequences of exemplary anti-CD73 antibody molecules

WO201/6075099 **MEDI 9447**	
SEQ ID NO: 1990	VH
SEQ ID NO: 1991	VL
WO2016/081748 **11F11-2**	
SEQ ID NO: 1992	HC
SEQ ID NO: 1993	LC
SEQ ID NO: 1994	VH
SEQ ID NO: 1995	VL kappa
WO2016/081748 **11F11-1**	
SEQ ID NO: 1996	HC
SEQ ID NO: 1997	LC
SEQ ID NO: 1998	VH
SEQ ID NO: 1999	VL kappa
US9605080	

CD73.4	
SEQ ID NO: 2000	VH
SEQ ID NO: 2001	VL kappa
US9605080 **CD73.10**	
SEQ ID NO: 2002	VH
SEQ ID NO: 2003	VL kappa
US9388249 **067-213**	
SEQ ID NO: 2004	VH
SEQ ID NO: 2005	VL

The anti-CD73 antibody molecules used in the combination therapies disclosed herein can include any of the VH/VL sequences disclosed in Table 26, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical thereto). Exemplary sequences for CD73 antibodies include:

(i) the VH and VL amino acid sequences for MEDI 9447, SEQ ID NOs: 1990-1991, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 1990-1991);

(ii) the HC and LC amino acid sequences for 11F11-2, SEQ ID NOs: 1992-1993, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 1992-1993);

(iii) the VH and VL amino acid sequences for 11F11-2, SEQ ID NOs: 1994-1995, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 1994-1995);

(iv) the HC and LC amino acid sequences for 11F11-1, SEQ ID NOs: 1996 and 1997, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 1996 and 1997);

(v) the VH and VL amino acid sequences for 11F11-1, SEQ ID NOs: 1998-1999, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 1998-1999);

(vi) the VH and VL amino acid sequences for CD73.4, SEQ ID NOs: 2000-2001, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 2000-2001);

(vii) the VH and VL amino acid sequences for CD73.10, SEQ ID NOs: 2002-2003, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 2002-2003); or

(viii) the VH and VL amino acid sequences for 067-213, SEQ ID NOs: 2004-2005, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 2004-2005).

IL-17 Inhibitor

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an interleukine-17 (IL-17) inhibitor.

In some embodiments, the IL-17 inhibitor is secukinumab (CAS Registry Numbers: 875356-43-7 (heavy chain) and 875356-44-8 (light chain)). Secukinumab is also known as AIN457 and COSENTYX®. Secukinumab is a recombinant human monoclonal IgG1/κ antibody that binds specifically to IL-17A. It is expressed in a recombinant Chinese Hamster Ovary (CHO) cell line.

Secukinumab is described, *e.g.,* in WO 2006/013107, US 7,807,155, US 8,119,131, US 8,617,552, and EP 1776142. The heavy chain variable region of secukinumab has the amino acid sequence of: EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMNWVRQAPGKGLEWVAAINQDGSEKYYV GSVKGRFTISRDNAKNSLYLQMNSLRVEDTAVYYCVRDYYDILTDYYIHYWYFDLWGRGTLV TVSS (SEQ ID NO: 2006) (disclosed as SEQ ID NO: 8 in WO 2006/013107). The light chain variable region of secukinumab has the amino acid sequence of: EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYGSSPCTFGQGTRLEIKR (SEQ ID NO: 2007) (disclosed as SEQ ID NO: 10 in WO 2006/013107). The heavy chain CDR1 of secukinumab has the amino acid sequence of NYWMN (SEQ ID NO: 2008) (disclosed as SEQ ID NO: 1 in WO 2006/013107). The heavy chain CDR2 of secukinumab has the amino acid sequence of AINQDGSEKYYVGSVKG (SEQ ID NO: 2009) (disclosed as SEQ ID NO: 2 in WO 2006/013107). The heavy chain CDR3 of secukinumab has the amino acid sequence of DYYDILTDYYIHYWYFDL (SEQ ID NO: 2010) (disclosed as SEQ ID NO: 3 in WO 2006/013107). The light chain CDR1 of secukinumab has the amino acid sequence of RASQSVSSSYLA (SEQ ID NO: 2011) (disclosed as SEQ ID NO: 4 in WO 2006/013107). The light chain CDR2 of secukinumab has the amino acid sequence of GASSRAT (SEQ ID NO: 2012) (disclosed as SEQ ID NO: 5 in WO 2006/013107). The light chain CDR3 of secukinumab has the amino acid sequence of GASSRAT (SEQ ID NO: 2013) (disclosed as SEQ ID NO: 6 in WO 2006/013107).

In some embodiments, the IL-17 inhibitor is CJM112. CJM112 is also known as XAB4. CJM112 is a fully human monoclonal antibody (*e.g.,* of the IgG1/κ isotype) that targets IL-17A.

CJM112 is disclosed, *e.g.,* in WO 2014/122613. The heavy chain of CJM112 has the amino acid sequence of:
EVQLVESGGDLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYYV
DSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDRGSLYYWGQGTLVTVSSASTKGPS
VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
PSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLSPGK (SEQ ID NO: 2014) (disclosed as SEQ ID NO: 14 in WO 2014/122613). The light chain of CJM112 has the amino acid sequence of:
AIQLTQSPSSLSASVGDRVTITCRPSQGINWELAWYQQKPGKAPKLLIYDASSLEQGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQFNSYPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTAS
VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYA
CEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 2015) (disclosed as SEQ ID NO: 44 in WO 2014/122613).

CJM112 can bind to human, cynomolgus, mouse and rat IL-17A and neutralize the bioactivity of these cytokines *in vitro* and *in vivo.* IL-17A, a member of the IL-17 family, is a major proinflammatory cytokine that has been indicated to play important roles in many immune mediated conditions, such as psoriasis and cancers (Witowski *et al.* (2004) *Cell Mol. Life Sci.* p. 567-79; Miossec and Kolls (2012) *Nat. Rev. Drug Discov.* p. 763-76).

In some embodiments, the IL-17 inhibitor is ixekizumab (CAS Registry Number: 1143503-69-8). Ixekizumab is also known as LY2439821. Ixekizumab is a humanized IgG4 monoclonal antibody that targets IL-17A.

Ixekizumab is described, *e.g.,* in WO 2007/070750, US 7,838,638, and US 8,110,191. The heavy chain variable region of ixekizumab has the amino acid sequence of:
QVQLVQSGAEVKKPGSSVKVSCKASGYSFTDYHIHWVRQAPGQGLEWMGVINPMYGTTDYN
QRFKGRVTITADESTSTAYMELSSLRSEDTAVYYCARYDYFTGTGVYWGQGTLVTVSS (SEQ ID NO: 2016) (disclosed as SEQ ID NO: 118 in WO 2007/070750). The light chain variable region of ixekizumab has the amino acid sequence of:
DIVMTQTPLSLSVTPGQPASISCRSSRSLVHSRGNTYLHWYLQKPGQSPQLLIYKVSNRFIGVPD
RFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHLPFTFGQGTKLEIK (SEQ ID NO: 2017) (disclosed as SEQ ID NO: 241 in WO 2007/070750).

In some embodiments, the IL-17 inhibitor is brodalumab (CAS Registry Number: 1174395-19-7). Brodalumab is also known as AMG 827 or AM-14. Brodalumab binds to the interleukin-17 receptor A (IL-17RA) and prevents IL-17 from activating the receptor.

Brodalumab is disclosed, *e.g.,* in WO 2008/054603, US 7,767,206, US 7,786,284, US 7,833,527, US 7,939,070, US 8,435,518, US 8,545,842, US 8,790,648, and US 9,073,999. The heavy chain CDR1 of brodalumab has the amino acid sequence of RYGIS (SEQ ID NO: 2018) (as disclosed as SEQ ID NO: 146 in WO 2008/054603). The heavy chain CDR2 of brodalumab has the amino acid sequence of WISTYSGNTNYAQKLQG (SEQ ID NO: 2019) (as disclosed as SEQ ID NO: 147 in WO 2008/054603). The heavy chain CDR3 of brodalumab has the amino acid sequence of RQLYFDY (SEQ ID NO: 2020) (as disclosed as SEQ ID NO: 148 in WO 2008/054603). The light chain CDR1 of brodalumab has the amino acid sequence of RASQSVSSNLA (SEQ ID NO: 2021) (as disclosed as SEQ ID NO: 224 in WO 2008/054603). The heavy chain CDR2 of brodalumab has the amino acid sequence of DASTRAT (SEQ ID NO: 2022) (as disclosed as SEQ ID NO: 225 in WO 2008/054603). The heavy chain CDR3 of brodalumab has the amino acid sequence of QQYDNWPLT (SEQ ID NO: 2023) (as disclosed as SEQ ID NO: 226 in WO 2008/054603).

IL-1β Inhibitor

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with an interleukine-1 beta (IL-1β) inhibitor.

The Interleukin-1 (IL-1) family of cytokines is a group of secreted pleotropic cytokines with a central role in inflammation and immune response. Increases in IL-1 are observed in multiple clinical settings including cancer (Apte *et al.* (2006) *Cancer Metastasis Rev.* p. 387-408; Dinarello (2010) *Eur. J. Immunol.* p. 599-606). The IL-1 family comprises, inter alia, IL-1 beta (IL-1β), and IL-1alpha (IL-1a). IL-1β is elevated in lung, breast and colorectal cancer (Voronov *et al.* (2014) *Front Physiol.* p. 114) and is associated with poor prognosis (Apte *et al.* (2000) *Adv. Exp. Med. Biol.* p. 277-88). Without wishing to be bound by theory, it is believed that in some embodiments, secreted IL-1β, derived from the tumor microenvironment and by malignant cells, promotes tumor cell proliferation, increases invasiveness and dampens anti-tumor immune response, in part by recruiting inhibitory neutrophils (Apte *et al.* (2006) *Cancer Metastasis Rev.* p. 387-408; Miller *et al.* (2007) J. Immunol. p. 6933-42). Experimental data indicate that inhibition of IL-1β results in a decrease in tumor burden and metastasis (Voronov *et al.* (2003) *Proc. Natl. Acad. Sci. U.S.A.* p. 2645-50).

In some embodiments, the IL-1β inhibitor is chosen from Anakinra or Rilonacept.

In some embodiments, the IL-1β inhibitor is Anakinra (Amgen), also known as Kineret. Anakinra is an IL-1Ra antagonist that competes with IL-1β for binding to the cell surface receptor.

In some embodiments, the IL-1β inhibitor is Rilonacept (Regeneron), also known as Arcalyst. Rilonacept is a fusion protein consisting of the ligand-binding domains of the extracellular portions of the human interleukin-1 receptor component (IL-1R1) and IL-1 receptor accessory protein (IL-1RAcP) linked to the fragment-crystallizable portion (Fc region) of human IgG1. Rilonacept is an IL-1β inhibitor which, *e.g.,* binds and neturalizes IL-1.

CD32B inhibitor

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with CD32B inhibitor.

In some embodiments, the CD32B inhibitor is an anti-CD32B antibody molecule. Exemplary anti-CD32B antibody molecules are disclosed in US8187593, US8778339, US8802089, US20060073142, US20170198040, US20130251706, and WO2009083009, herein incorporated by reference in their entirety. In some embodiments, the anti-CD32B antibody molecule is an antibody molecule disclosed in US20170198040.

Chemotherapeutic agents

In some embodiments, the BCMA CAR-expressing cell therapy is administered in combination with a chemotherapeutic agent. Exemplary chemotherapeutic agents include an anthracycline (e.g., doxorubicin (e.g., liposomal doxorubicin)), a vinca alkaloid (e.g., vinblastine, vincristine, vindesine, vinorelbine), an alkylating agent (e.g., cyclophosphamide, decarbazine, melphalan, ifosfamide, temozolomide), an immune cell antibody (e.g., alemtuzamab, gemtuzumab, rituximab, tositumomab), an antimetabolite (including, e.g., folic acid antagonists, pyrimidine analogs, purine analogs and adenosine deaminase inhibitors (e.g., fludarabine)), an mTOR inhibitor, a TNFR glucocorticoid induced TNFR related protein (GITR) agonist, a proteasome inhibitor (e.g., aclacinomycin A, gliotoxin or bortezomib), an immunomodulator such as thalidomide or a thalidomide derivative (e.g., lenalidomide).

General Chemotherapeutic agents considered for use in combination therapies include anastrozole (Arimidex®), bicalutamide (Casodex®), bleomycin sulfate (Blenoxane®), busulfan (Myleran®), busulfan injection (Busulfex®), capecitabine (Xeloda®), N4-pentoxycarbonyl-5-deoxy-5-fluorocytidine, carboplatin (Paraplatin®), carmustine (BiCNU®), chlorambucil (Leukeran®), cisplatin (Platinol®), cladribine (Leustatin®), cyclophosphamide (Cytoxan® or Neosar®), cytarabine, cytosine arabinoside (Cytosar-U®), cytarabine liposome injection (DepoCyt®), dacarbazine (DTIC-Dome®), dactinomycin (Actinomycin D, Cosmegan), daunorubicin hydrochloride (Cerubidine®), daunorubicin citrate liposome injection (DaunoXome®), dexamethasone, docetaxel (Taxotere®), doxorubicin hydrochloride (Adriamycin®, Rubex®), etoposide (Vepesid®), fludarabine phosphate (Fludara®), 5-

fluorouracil (Adrucil®, Efudex®), flutamide (Eulexin®), tezacitibine, Gemcitabine (difluorodeoxycitidine), hydroxyurea (Hydrea®), Idarubicin (Idamycin®), ifosfamide (IFEX®), irinotecan (Camptosar®), L-asparaginase (ELSPAR®), leucovorin calcium, melphalan (Alkeran®), 6-mercaptopurine (Purinethol®), methotrexate (Folex®), mitoxantrone (Novantrone®), mylotarg, paclitaxel (Taxol®), phoenix (Yttrium90/MX-DTPA), pentostatin, polifeprosan 20 with carmustine implant (Gliadel®), tamoxifen citrate (Nolvadex®), teniposide (Vumon®), 6-thioguanine, thiotepa, tirapazamine (Tirazone®), topotecan hydrochloride for injection (Hycamptin®), vinblastine (Velban®), vincristine (Oncovin®), and vinorelbine (Navelbine®).

Exemplary alkylating agents include, without limitation, nitrogen mustards, ethylenimine derivatives, alkyl sulfonates, nitrosoureas and triazenes): uracil mustard (Aminouracil Mustard®, Chlorethaminacil®, Demethyldopan®, Desmethyldopan®, Haemanthamine®, Nordopan®, Uracil nitrogen mustard®, Uracillost®, Uracilmostaza®, Uramustin®, Uramustine®), chlormethine (Mustargen®), cyclophosphamide (Cytoxan®, Neosar®, Clafen®, Endoxan®, Procytox®, Revimmune™), ifosfamide (Mitoxana®), melphalan (Alkeran®), Chlorambucil (Leukeran®), pipobroman (Amedel®, Vercyte®), triethylenemelamine (Hemel®, Hexalen®, Hexastat®), triethylenethiophosphoramine, Temozolomide (Temodar®), thiotepa (Thioplex®), busulfan (Busilvex®, Myleran®), carmustine (BiCNU®), lomustine (CeeNU®), streptozocin (Zanosar®), and Dacarbazine (DTIC-Dome®). Additional exemplary alkylating agents include, without limitation, Oxaliplatin (Eloxatin®); Temozolomide (Temodar® and Temodal®); Dactinomycin (also known as actinomycin-D, Cosmegen®); Melphalan (also known as L-PAM, L-sarcolysin, and phenylalanine mustard, Alkeran®); Altretamine (also known as hexamethylmelamine (HMM), Hexalen®); Carmustine (BiCNU®); Bendamustine (Treanda®); Busulfan (Busulfex® and Myleran®); Carboplatin (Paraplatin®); Lomustine (also known as CCNU, CeeNU®); Cisplatin (also known as CDDP, Platinol® and Platinol®-AQ); Chlorambucil (Leukeran®); Cyclophosphamide (Cytoxan® and Neosar®); Dacarbazine (also known as DTIC, DIC and imidazole carboxamide, DTIC-Dome®); Altretamine (also known as hexamethylmelamine (HMM), Hexalen®); Ifosfamide (Ifex®); Prednumustine; Procarbazine (Matulane®); Mechlorethamine (also known as nitrogen mustard, mustine and mechloroethamine hydrochloride, Mustargen®); Streptozocin (Zanosar®); Thiotepa (also known as thiophosphoamide, TESPA and TSPA, Thioplex®); Cyclophosphamide (Endoxan®, Cytoxan®, Neosar®, Procytox®, Revimmune®); and Bendamustine HCl (Treanda®).

Exemplary mTOR inhibitors include, e.g., temsirolimus; ridaforolimus (formally known as deferolimus, (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*, 23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.$0^{4,9}$] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl

dimethylphosphinate, also known as AP23573 and MK8669, and described in PCT Publication No. WO 03/064383); everolimus (Afinitor® or RAD001); rapamycin (AY22989, Sirolimus®); simapimod (CAS 164301-51-3); emsirolimus, (5-{2,4-Bis[(3*S*)-3-methylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-Amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF04691502, CAS 1013101-36-4); and N^2-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4*H*-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L-α-aspartylL-serine- (SEQ ID NO: 2035), inner salt (SF1126, CAS 936487-67-1), and XL765.

Exemplary immunomodulators include, e.g., afutuzumab (available from Roche®); pegfilgrastim (Neulasta®); lenalidomide (CC-5013, Revlimid®); thalidomide (Thalomid®), actimid (CC4047); and IRX-2 (mixture of human cytokines including interleukin 1, interleukin 2, and interferon γ, CAS 951209-71-5, available from IRX Therapeutics).

Exemplary anthracyclines include, e.g., doxorubicin (Adriamycin® and Rubex®); bleomycin (lenoxane®); daunorubicin (dauorubicin hydrochloride, daunomycin, and rubidomycin hydrochloride, Cerubidine®); daunorubicin liposomal (daunorubicin citrate liposome, DaunoXome®); mitoxantrone (DHAD, Novantrone®); epirubicin (Ellence™); idarubicin (Idamycin®, Idamycin PFS®); mitomycin C (Mutamycin®); geldanamycin; herbimycin; ravidomycin; and desacetylravidomycin.

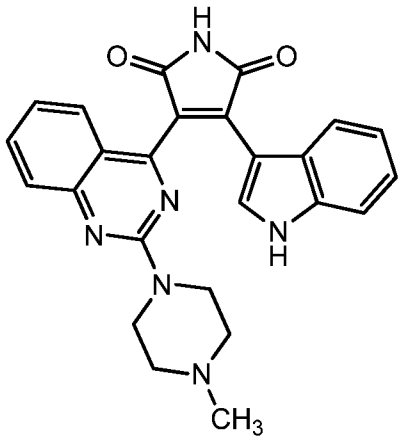
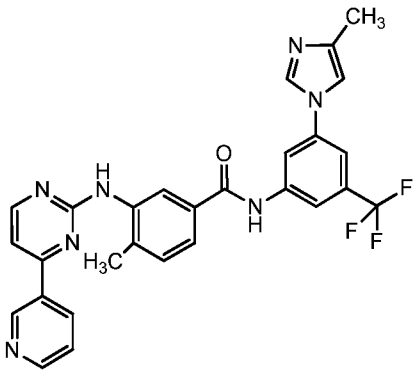
Exemplary vinca alkaloids include, e.g., vinorelbine tartrate (Navelbine®), Vincristine (Oncovin®), and Vindesine (Eldisine®)); vinblastine (also known as vinblastine sulfate, vincaleukoblastine and VLB, Alkaban-AQ® and Velban®); and vinorelbine (Navelbine®).

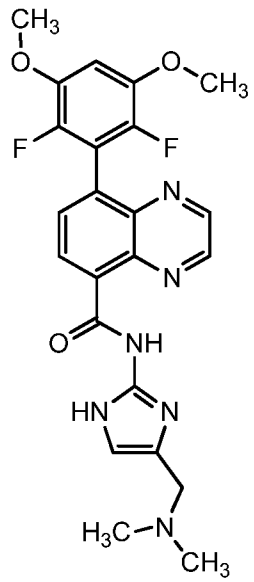
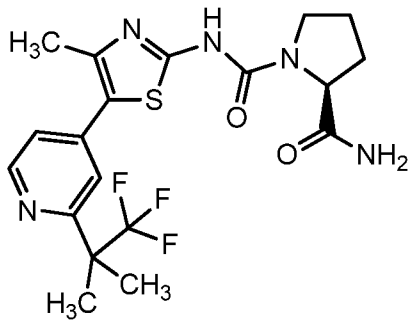
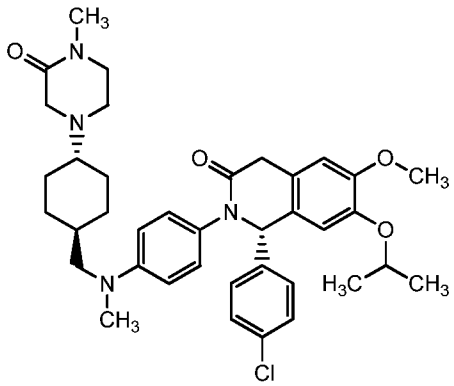
Exemplary proteosome inhibitors include bortezomib (Velcade®); carfilzomib (PX-171-007, (*S*)-4-Methyl-*N*-((*S*)-1-(((*S*)-4-methyl-1-((*R*)-2-methyloxiran-2-yl)-1-oxopentan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)-2-((*S*)-2-(2-morpholinoacetamido)-4-phenylbutanamido)-pentanamide); marizomib (NPI-0052); ixazomib citrate (MLN-9708); delanzomib (CEP-18770); and *O*-Methyl-*N*-[(2-methyl-5-thiazolyl)carbonyl]-L-seryl-*O*-methyl-*N*-[(1*S*)-2-[(2*R*)-2-methyl-2-oxiranyl]-2-oxo-1-(phenylmethyl)ethyl]- L-serinamide (ONX-0912).

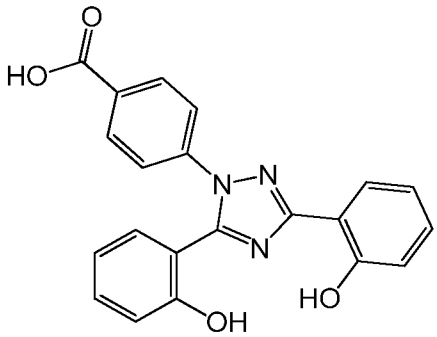
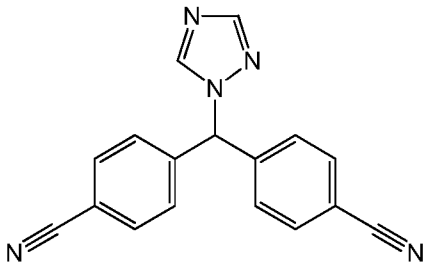
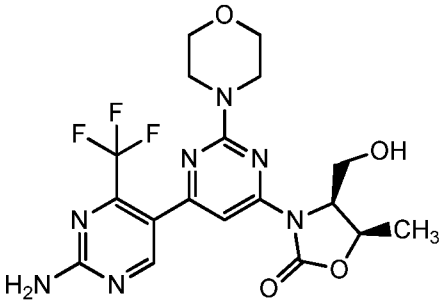
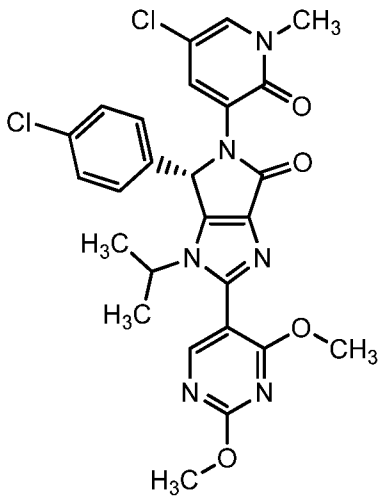
Additional agents for combination

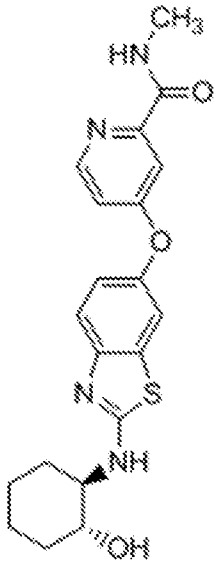
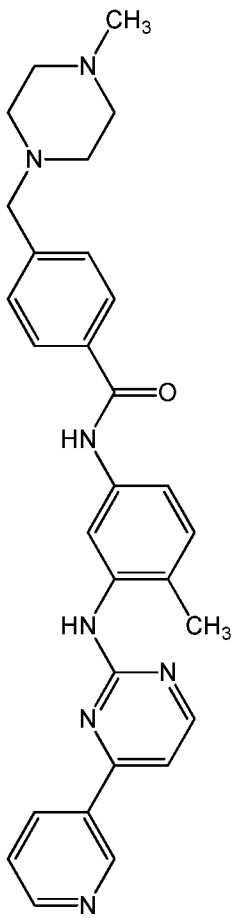
Table 27. Selected therapeutic agents that can be administered in combination with the BCMA CAR-expressing cell therapy, e.g., as a single agent or in combination with other agents described herein.

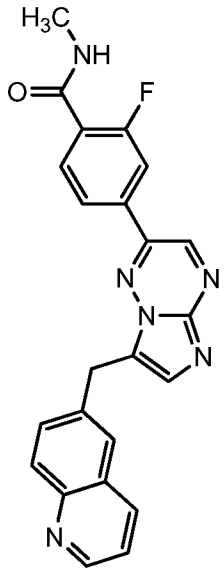
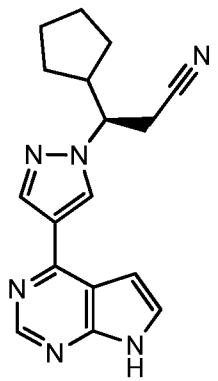
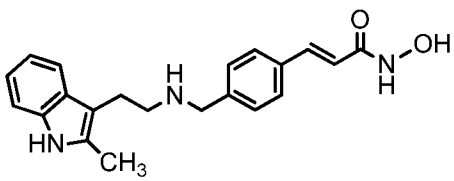
Each publication listed in this Table is herein incorporated by reference in its entirety, including all structural formulae therein.

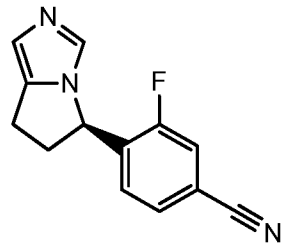
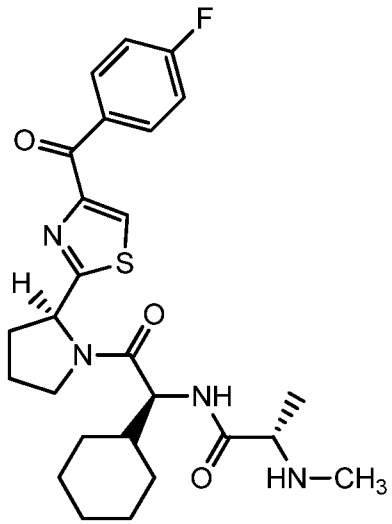
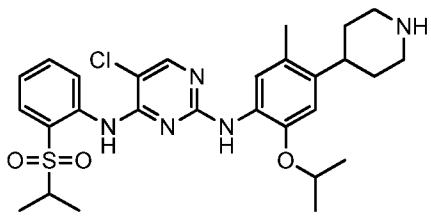
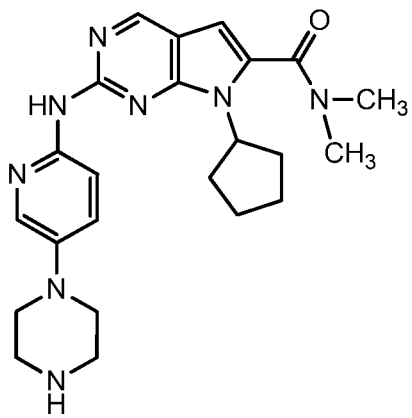
Compound Designation	Generic Name Tradename	Compound Structure	Patents / Patent Application Publications
A1	Sotrastaurin		EP 1682103 US 2007/142401 WO 2005/039549
A2	Nilotinib HCl monohydrate TASIGNA ®	 HCl • H_20	WO 2004/005281 US 7,169,791

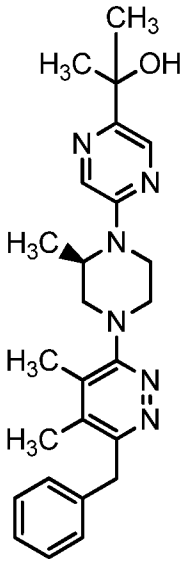
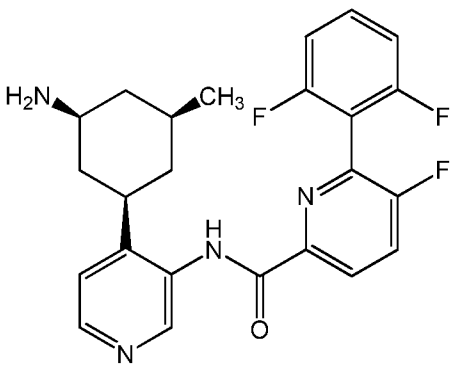
A7			WO 2009/141386 US 2010/0105667
A8			WO 2010/029082
A10			WO 2011/076786

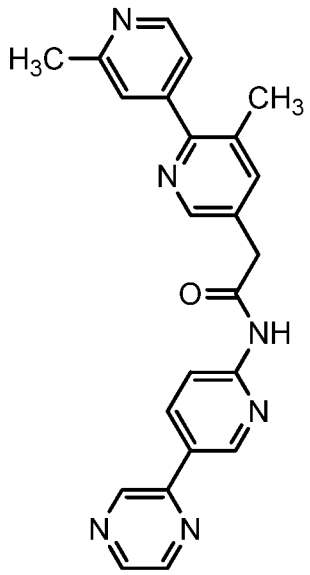
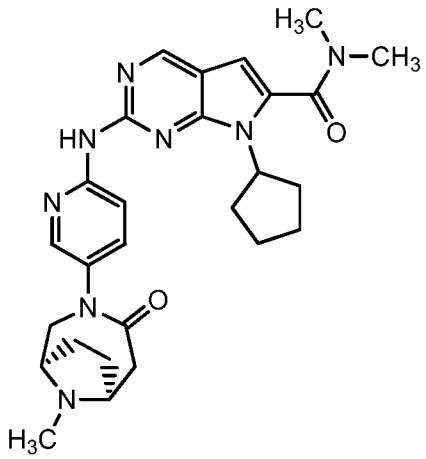
A11	Deferasirox EXJADE®		WO 1997/049395
A12	Letrozole FEMARA®		US 4,978,672
A13			WO 2013/124826 US 2013/0225574
A14			WO 2013/111105

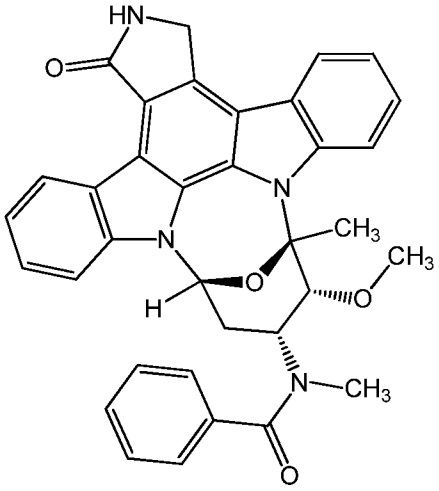
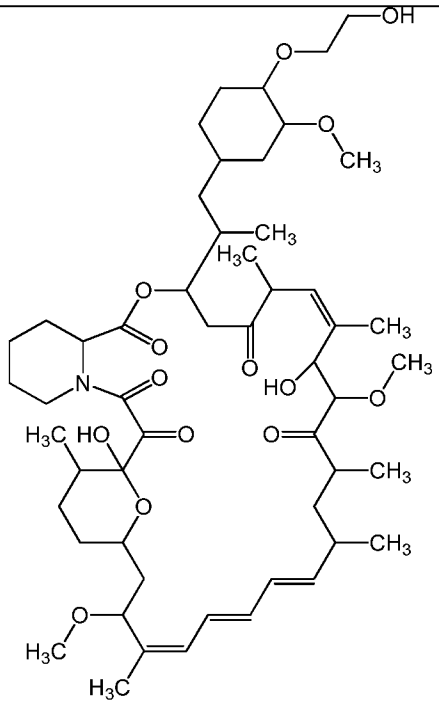
A15			WO 2007/121484
A16	Imatinib mesylate GLEEVEC ®	 Mesylate	WO 1999/003854

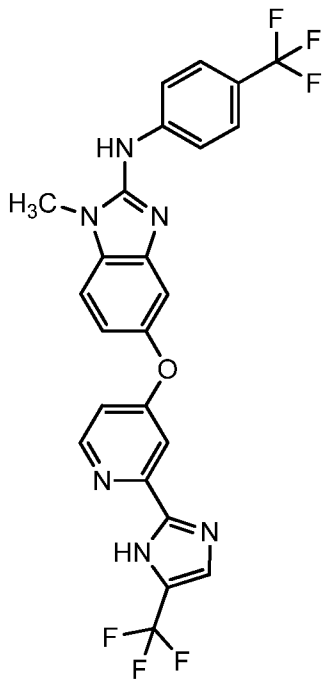
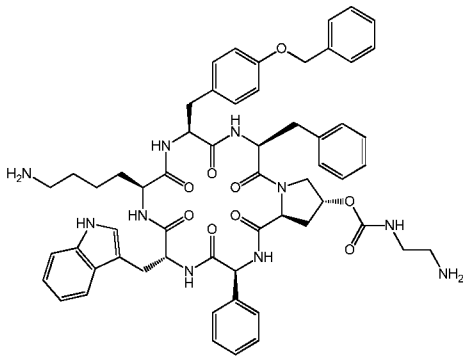
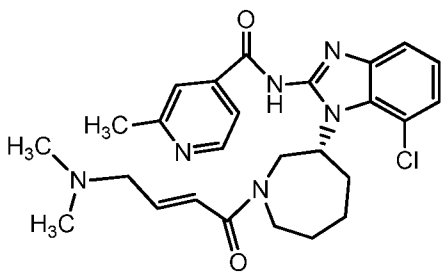
A17		 Dihydrochloric salt	EP 2099447 US 7,767,675 US 8,420,645
A18	Ruxolitinib Phosphate JAKAFI®	 H_3PO_4	WO 2007/070514 EP 2474545 US 7,598,257 WO 2014/018632
A19	Panobinostat		WO 2014/072493 WO 2002/022577 EP 1870399

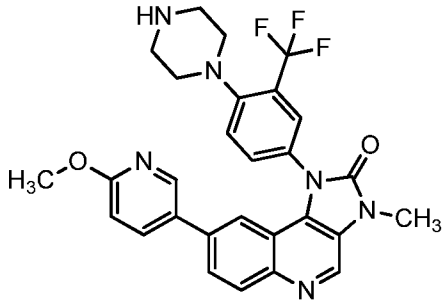
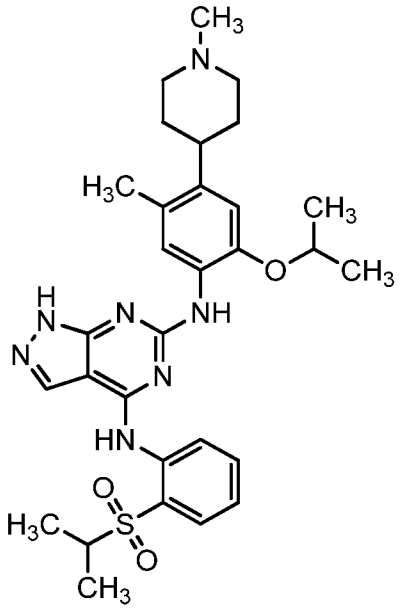
A20	Osilodrostat		WO 2007/024945
A21			WO 2008/016893 EP 2051990 US 8,546,336
A23	ceritinib ZYKADIA™		WO 2008/073687 US 8,039,479
A24			US 8,415,355 US 8,685,980

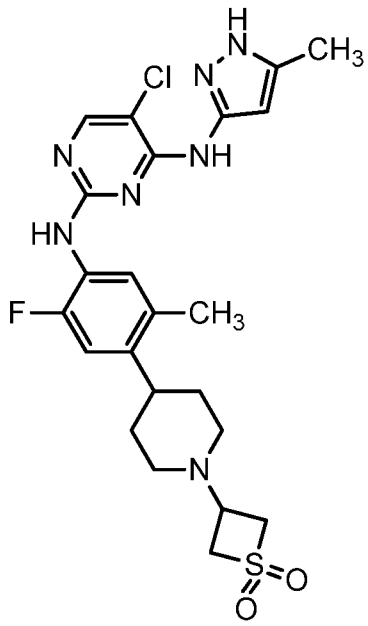
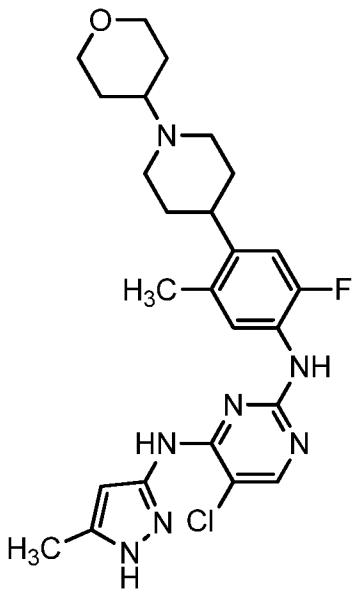
A25			WO 2010/007120
A26		Human monoclonal antibody to PRLR	US 7,867,493
A27			WO 2010/026124 EP 2344474 US 2010/0056576 WO2008/106692

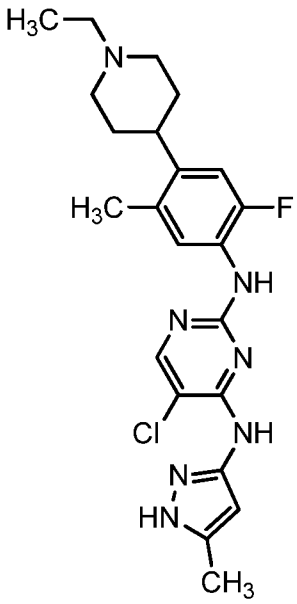
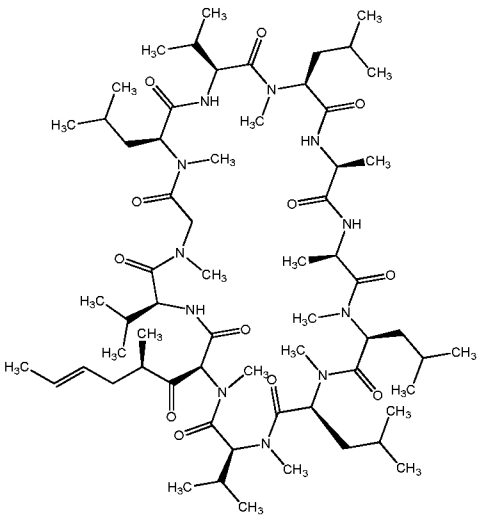
A28			WO 2010/101849
A30			WO 2011/101409
A31		Human monoclonal antibody to HER3	WO 2012/022814 EP 2606070 US 8,735,551
A32		Antibody Drug Conjugate (ADC)	WO 2014/160160 Ab: 12425 (*see* Table 1, paragraph [00191]) Linker: SMCC (*see* paragraph [00117] Payload: DM1 (*see* paragraph [00111] *See* also Claim 29
A33		Monoclonal antibody or Fab to M-CSF	WO 2004/045532

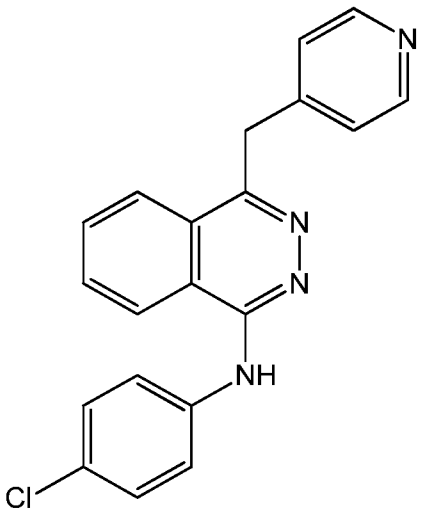
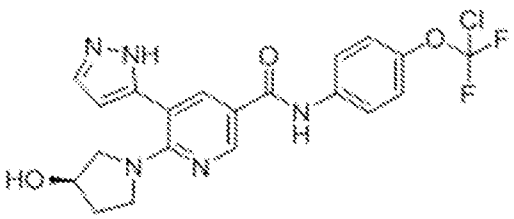
A35	Midostaurin		WO 2003/037347 EP 1441737 US 2012/252785
A36	Everolimus AFINITOR ®		WO 2014/085318

A37			WO 2007/030377 US 7,482,367
A38	Pasireotide diaspartate SIGNIFOR ®		WO2002/010192 US 7,473,761
A40			WO 2013/184757

A41			WO 2006/122806
A42			WO 2008/073687 US 8,372,858

A43			WO 2010/002655 US 8,519,129
A44			WO 2010/002655 US 8,519,129

A45			WO 2010/002655
A46	Valspodar AMDRAY™		EP 296122

A47	Vatalanib succinate	 succinate	WO 98/35958
A48		IDH inhibitor	WO2014/141104
A49		BCR-ABL inhibitor 	WO2013/171639 WO2013/171640 WO2013/171641 WO2013/171642
A50		cRAF inhibitor	WO2014/151616
A51		ERK1/2 ATP competitive inhibitor	WO2015/066188

Biopolymer delivery methods

In some embodiments, one or more CAR-expressing cells as disclosed herein can be administered or delivered to the subject via a biopolymer scaffold, e.g., a biopolymer implant. Biopolymer scaffolds can support or enhance the delivery, expansion, and/or dispersion of the CAR-expressing cells described herein. A biopolymer scaffold comprises a biocompatible (e.g., does not substantially induce an inflammatory or immune response) and/or a biodegradable polymer that can be naturally occurring or synthetic.

Examples of suitable biopolymers include, but are not limited to, agar, agarose, alginate, alginate/calcium phosphate cement (CPC), beta-galactosidase (β-GAL), (1 ,2,3,4,6-pentaacetyl a-D-galactose), cellulose, chitin, chitosan, collagen, elastin, gelatin, hyaluronic acid collagen, hydroxyapatite, poly(3-hydroxybutyrate-co-3-hydroxy-hexanoate) (PHBHHx), poly(lactide), poly(caprolactone) (PCL), poly(lactide-co-glycolide) (PLG), polyethylene oxide (PEO), poly(lactic-co-glycolic acid) (PLGA), polypropylene oxide (PPO), polyvinyl alcohol) (PVA), silk, soy protein, and soy

protein isolate, alone or in combination with any other polymer composition, in any concentration and in any ratio. The biopolymer can be augmented or modified with adhesion- or migration-promoting molecules, e.g., collagen-mimetic peptides that bind to the collagen receptor of lymphocytes, and/or stimulatory molecules to enhance the delivery, expansion, or function, e.g., anti-cancer activity, of the cells to be delivered. The biopolymer scaffold can be an injectable, e.g., a gel or a semi-solid, or a solid composition.

In some embodiments, CAR-expressing cells described herein are seeded onto the biopolymer scaffold prior to delivery to the subject. In embodiments, the biopolymer scaffold further comprises one or more additional therapeutic agents described herein (e.g., another CAR-expressing cell, an antibody, or a small molecule) or agents that enhance the activity of a CAR-expressing cell, e.g., incorporated or conjugated to the biopolymers of the scaffold. In embodiments, the biopolymer scaffold is injected, e.g., intratumorally, or surgically implanted at the tumor or within a proximity of the tumor sufficient to mediate an anti-tumor effect. Additional examples of biopolymer compositions and methods for their delivery are described in Stephan et al., *Nature Biotechnology*, 2015, 33:97-101; and WO2014/110591.

Pharmaceutical compositions and treatments

Pharmaceutical compositions of the present invention may comprise a CAR-expressing cell, e.g., a plurality of CAR-expressing cells, as described herein, in combination with one or more pharmaceutically or physiologically acceptable carriers, diluents or excipients. Such compositions may comprise buffers such as neutral buffered saline, phosphate buffered saline and the like; carbohydrates such as glucose, mannose, sucrose or dextrans, mannitol; proteins; polypeptides or amino acids such as glycine; antioxidants; chelating agents such as EDTA or glutathione; adjuvants (e.g., aluminum hydroxide); and preservatives. Compositions of the present invention are in one aspect formulated for intravenous administration.

Pharmaceutical compositions of the present invention may be administered in a manner appropriate to the disease to be treated (or prevented). The quantity and frequency of administration will be determined by such factors as the condition of the patient, and the type and severity of the patient's disease, although appropriate dosages may be determined by clinical trials.

In one embodiment, the pharmaceutical composition is substantially free of, e.g., there are no detectable levels of a contaminant, e.g., selected from the group consisting of endotoxin, mycoplasma, replication competent lentivirus (RCL), p24, VSV-G nucleic acid, HIV gag, residual anti-CD3/anti-CD28 coated beads, mouse antibodies, pooled human serum, bovine serum albumin, bovine serum, culture media components, vector packaging cell or plasmid components, a bacterium and a fungus. In

one embodiment, the bacterium is at least one selected from the group consisting of Alcaligenes faecalis, Candida albicans, Escherichia coli, Haemophilus influenza, Neisseria meningitides, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumonia, and Streptococcus pyogenes group A.

When "an immunologically effective amount," "an anti-tumor effective amount," "a tumor-inhibiting effective amount," or "therapeutic amount" is indicated, the precise amount of the compositions of the present invention to be administered can be determined by a physician with consideration of individual differences in age, weight, tumor size, extent of infection or metastasis, and condition of the patient (subject). It can generally be stated that a pharmaceutical composition comprising the T cells described herein may be administered at a dosage of 10^4 to 10^9 cells/kg body weight, in some instances 10^5 to 10^6 cells/kg body weight, including all integer values within those ranges. T cell compositions may also be administered multiple times at these dosages. The cells can be administered by using infusion techniques that are commonly known in immunotherapy (see, e.g., Rosenberg et al., New Eng. J. of Med. 319:1676, 1988)..

In certain aspects, it may be desired to administer activated T cells to a subject and then subsequently redraw blood (or have an apheresis performed), activate T cells therefrom according to the present invention, and reinfuse the patient with these activated and expanded T cells. This process can be carried out multiple times every few weeks. In certain aspects, T cells can be activated from blood draws of from 10cc to 400cc. In certain aspects, T cells are activated from blood draws of 20cc, 30cc, 40cc, 50cc, 60cc, 70cc, 80cc, 90cc, or 100cc.

The administration of the subject compositions may be carried out in any convenient manner, including by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation. The compositions described herein may be administered to a patient trans arterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, or intraperitoneally. In one aspect, the T cell compositions of the present invention are administered to a patient by intradermal or subcutaneous injection. In one aspect, the CAR-expressing cell (e.g., T cell or NK cell) compositions of the present invention are administered by i.v. injection. The compositions of CAR-expressing cells (e.g., T cells or NK cells) may be injected directly into a tumor, lymph node, or site of infection.

In a particular exemplary aspect, subjects may undergo leukapheresis, wherein leukocytes are collected, enriched, or depleted ex vivo to select and/or isolate the cells of interest, e.g., immune effector cells (e.g., T cells or NK cells). These immune effector cell (e.g., T cell or NK cell) isolates may be expanded by methods known in the art and treated such that one or more CAR constructs of the

invention may be introduced, thereby creating a CAR-expressing cell (e.g., CAR T cell or CAR-expressing NK cell)of the invention. Subjects in need thereof may subsequently undergo standard treatment with high dose chemotherapy followed by peripheral blood stem cell transplantation. In certain aspects, following or concurrent with the transplant, subjects receive an infusion of the expanded CAR-expressing cells (e.g., CAR T cells or NK cells) of the present invention. In an additional aspect, expanded cells are administered before or following surgery.

In embodiments, lymphodepletion is performed on a subject, e.g., prior to administering one or more cells that express a CAR described herein, e.g., a BCMA-binding CAR described herein. In embodiments, the lymphodepletion comprises administering one or more of melphalan, cytoxan, cyclophosphamide, and fludarabine.

The dosage of the above treatments to be administered to a patient will vary with the precise nature of the condition being treated and the recipient of the treatment. The scaling of dosages for human administration can be performed according to art-accepted practices. The dose for CAMPATH, for example, will generally be in the range 1 to about 100 mg for an adult patient, usually administered daily for a period between 1 and 30 days. The preferred daily dose is 1 to 10 mg per day although in some instances larger doses of up to 40 mg per day may be used (described in U.S. Patent No. 6,120,766).

In one embodiment, the CAR is introduced into immune effector cells (e.g., T cells or NK cells), e.g., using in vitro transcription, and the subject (e.g., human) receives an initial administration of CAR immune effector cells (e.g., T cells or NK cells)of the invention, and one or more subsequent administrations of the CAR immune effector cells (e.g., T cells or NK cells) of the invention, wherein the one or more subsequent administrations are administered less than 15 days, e.g., 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 days after the previous administration. In one embodiment, more than one administration of the CAR immune effector cells (e.g., T cells or NK cells) of the invention are administered to the subject (e.g., human) per week, e.g., 2, 3, or 4 administrations of the CAR immune effector cells (e.g., T cells or NK cells) of the invention are administered per week. In one embodiment, the subject (e.g., human subject) receives more than one administration of the CAR immune effector cells (e.g., T cells or NK cells) per week (e.g., 2, 3 or 4 administrations per week) (also referred to herein as a cycle), followed by a week of no CAR immune effector cells (e.g., T cells or NK cells) administrations, and then one or more additional administration of the CAR immune effector cells (e.g., T cells or NK cells) (e.g., more than one administration of the CAR immune effector cells (e.g., T cells or NK cells) per week) is administered to the subject. In another embodiment, the subject (e.g., human subject) receives more than one cycle of CAR immune effector cells (e.g., T cells or NK cells), and the time between each cycle is less than 10, 9, 8, 7, 6, 5, 4, or 3 days. In one embodiment, the CAR

immune effector cells (e.g., T cells or NK cells) are administered every other day for 3 administrations per week. In one embodiment, the CAR immune effector cells (e.g., T cells or NK cells) of the invention are administered for at least two, three, four, five, six, seven, eight or more weeks.

In one aspect, BCMA CAR-expressing cells (e.g., BCMA CARTs or BCMA CAR-expressing NK cells) are generated using lentiviral viral vectors, such as lentivirus. CAR-expressing cells (e.g., CARTs or CAR-expressing NK cells) generated that way will have stable CAR expression.

In one aspect, CAR-expressing cells, e.g., CARTs, are generated using a viral vector such as a gammaretroviral vector, e.g., a gammaretroviral vector described herein. CARTs generated using these vectors can have stable CAR expression.

In one aspect, CAR-expressing cells (e.g., CARTs or CAR-expressing NK cells) transiently express CAR vectors for 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 days after transduction. Transient expression of CARs can be effected by RNA CAR vector delivery. In one aspect, the CAR RNA is transduced into the cell, e.g., T cell or NK cell, by electroporation.

A potential issue that can arise in patients being treated using transiently expressing CAR-expressing cells (e.g., CARTs or CAR-expressing NK cells) (particularly with murine scFv bearing CAR-expressing cells (e.g., CARTs or CAR-expressing NK cells)) is anaphylaxis after multiple treatments.

Without being bound by this theory, it is believed that such an anaphylactic response might be caused by a patient developing humoral anti-CAR response, i.e., anti-CAR antibodies having an anti-IgE isotype. It is thought that a patient's antibody producing cells undergo a class switch from IgG isotype (that does not cause anaphylaxis) to IgE isotype when there is a ten to fourteen day break in exposure to antigen.

If a patient is at high risk of generating an anti-CAR antibody response during the course of transient CAR therapy (such as those generated by RNA transductions), CAR-expressing cell (e.g., CART or CAR-expressing NK cell) infusion breaks should not last more than ten to fourteen days.

EXAMPLES

The invention is further described in detail by reference to the following experimental examples. These examples are provided for purposes of illustration only, and are not intended to be limiting unless otherwise specified. Thus, the invention should in no way be construed as being limited to the following examples, but rather, should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the compositions of the present invention and practice the claimed methods. The following working examples specifically point out various aspects of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

Example 1: BCMA-CART in Multiple Myeloma

CART-BCMA (MCM998) demonstrates potent anti-tumor activity in vivo

The level of tumor burden in a KMS11 tumor model following infusion of PBS, untransduced T cells ("UTD"), or T cells transduced with either a tool CAR ("J6MO"), BCMA-4, BCMA-9, BCMA-10 ("MCM998"), BCMA-13, or BCMA-15 was evaluated. BCMA-10 demonstrated the most potent anti-tumor activity (FIG. 14).

CART-BCMA in multiple myeloma clinical trial (NCT Number: NCT02546167; UPCC 14415)

An open-label, single-center, pilot study to assess the safety and feasibility of infusion of autologous T cells expressing BCMA-specific chimeric antigen receptors with tandem 4-1BB and CD3zeta signaling domains (referred to herein as "CART-BCMA") in adult patients with multiple myeloma (MM) was designed (FIG. 15).

Patients were divided into three groups (FIG. 15). Cohort 1 patients received 1-5x10^8 CART-BCMA cells given as a split dose infusion over 3 days. Cohort 2 patients received a cyclophosphamide infusion prior to administration of 1-5x10^7 CART-BCMA cells given as a split dose infusion over 3 days. Cohort 3 patients received a cyclophosphamide infusion prior to administration of 1-5x10^8 CART-BCMA cells given as a split dose infusion over 3 days. FIG. 16A provides patient disease characteristics. FIG. 16B provides information on presence of baseline lymphopenia due to disease and prior therapies.

CART-BCMA (MCM998) manufacturing and dosing

All the CART-BCMA products were successfully manufactured with minimum target threshold dose. Manufactured products had a median transduction efficiency of 22.5% (9.6 – 33.3%); a median fold expansion of 20.7 (7.9 – 60.4); median population doublings of 4.4 (2.98 – 5.92); median pheresis CD4/CD8 ratio of 1.03 (0.61 – 3.2); and median product CD4/CD8 ratio of 1.72 (0.84 – 3.9). Thirteen of the fourteen patients achieved max target dose of 5 x 10^8 or 5x10^7. Patient 2 of Cohort 1 received 1.9 x 10^8 cells, including 69% T cells in the product. Twelve of the fourteen patients received 100% of the planned dose. Patient 1 and Patient 3 of Cohort 1 only received the first two infusions (40%) due to

fevers on Day 2. These data demonstrate that CART-BCMA manufacturing is feasible in heavily pre-treated multiple myeloma patients.

Clinical outcomes

Clinical activity is shown in FIGs. 17A, 17B, and 17C for Cohorts 1, 2, and 3, respectively. The expansion of CART-BCMA was evaluated by flow cytometry (FIGs. 18A and 18B) and by PCR (FIGs. 19A and 19B). In vivo expansion of CART-BCMA may correlate with and predict response to therapy (FIGs. 20A and 20B). No correlation was observed between BCMA surface expression on multiple myeloma cells as determined by flow cytometry and clinical outcomes (data not show).

Example 2: Correlative analysis of clinical trial data

To identify biomarkers predictive of patient response to CART-BCMA treatment, the parameters listed in Table 28 were analyzed.

Table 28. Biomarker parameters

Parameter	**Sample type**	**Technology**
Release profile: QC and informational	Product	Several: Expansion, T cell count, CD4/CD8, CAR+, IFN-γ, cytotox
CART PK	Bone marrow (BM), blood	Flow, qPCR
Serum cytokines	Blood	MSD/Luminex
Immunophenotype	Apheresis and Product	Flow
Gene signature analysis	Apheresis and Product	RNAseq
TCR diversity	Apheresis and Product	Deep sequencing
Serum proteins	Serum: pre and post infusion	Somascan
Target expression (surface and soluble)	Bone marrow (BM), blood	ELISA: BCMA levels, soluble ligands
(CAR) T-cell tumor infiltration/suppression	Bone marrow (BM)	ISH/IHC

The fraction of CAR+ CD4/CD8 cells in patient samples was acquired at various time-points post-CART-BCMA infusion for Responders (patient having complete response (CR), very good partial response (VGPR), or partial response (PR)) and Non-Responders (patients having minor response (MR), stable disease (SD), or progressive disease (PD)) (FIGs. 21A, 21B, 21C, and 21D). These data demonstrate that Responders had greater persistence of CAR+ CD4/CD8 cell populations over time, as compared to Non-responders.

Evaluation of cytokine levels

The change in level of cytokine expression at various time points post infusion of CART-BCMA was evaluated (FIG. 22). These data demonstrate that the greatest changes from baseline (Day 0) occurred in the level of IL-6 (FIGs. 23A and 23B), IL-10, monokine induced by gamma interferon (MIG), and IFN-γ (FIGs. 24A and 24B). Importantly, IFN-γ may differentiate Responders to CART-BCMA treatment from Non-Responders.

Evaluation of BCMA levels in serum

The serum level of BCMA was evaluated in 14 normal donors and 12 myeloma patients (FIGs. 25A and 25B). BCMA was present in normal donors at a serum concentration of about 40 ng/mL, and in myeloma patients at a median serum concentration of 176 ng/mL at baseline. Serum levels of BCMA were also acquired at various time points post infusion of CART-BCMA (FIGs. 26A, 26B, 26C, and 26D). These data demonstrate that some patients with high baseline serum BCMA levels responded well to CART-BCMA treatment (FIG. 26A). In addition, serum BCMA levels could serve as a marker of response to CART-BCMA treatment (FIGs. 26C and 26D).

Evaluation of the percentage of CD4+ and CD8+ CART cells

The percentage of CD4+ and CD8+ CART cells was acquired at various time points post infusion of CART-BCMA in three patients (FIGs. 27A, 27B, and 27C). Responders as shown in FIGs. 27A and 27C had a dramatic expansion of CAR T cells as seen by high BBz copy numbers. Expansion was mainly driven by CD8+ CARTs. Although non-responders also had high BCMA levels, no expansion was seen (FIG. 27B).

Evaluation of CD4+ and CD8+ T cell subsets

The level of CD4+ and CD8+ T cell subsets of normal donors and multiple myeloma (MM) patients were compared (FIGs. 28A, 28B, 28C, and 28D). MM patients had a lower percentage of Tnl cells in comparison to normal donors. The level of Tscm and Te cells were similar in normal donors and MM patients. MM patients had a higher median percentage of Tem cells. The level of CD4+ and CD8+ T cell subsets in apheresis samples were also acquired from MM patients (FIGs. 28E and 28F).

T cell differentiation in apheresis samples was acquired from MM patients (FIG. 29). The level of CD4+ and CD8+ T cell subsets (e.g., CD4+ or CD8+ cells based on the expression of PD1, CD27, and/or GzB) were also determined in MM patients (FIGs. 30A and 30B).

Example 3: Predictive correlates of response to BCMA chimeric antigen receptor (CAR) T cell therapy in patients with multiple myeloma

This example describes studies that aimed to discover biomarkers that could predict the clinical response of subjects to treatment with CART-BCMA before the manufacturing of the CART-BCMA.

Peripheral blood samples were collected from a total of eight multiple myeloma (MM) human patients and were stained with a 14-parameter flow cytometry panel and analyzed on a flow cytometry instrument.

These MM patients received CART-BCMA treatment as described in Example 1. Based on clinical response at 28-days post infusion, patient samples were classified as Responders (R, defined as patients having CR, VGPR, or PR, $N_R = 3$) or Non-Responders (NR, defined as patients having MR, SD, or PD, $N_{NR} = 5$).

To identify a biomarker signature that correlated with clinical response, pre-gating was performed to limit analysis to viable, singlet, lymphocytes. Subsequently, pre-gated data was used for data mining and biomarker identification, using flowType (Aghaeepour et al. *Bioinformatics*. 28(7):1009-1016, 2012), a bio-statistical automated algorithm, based on R^+ (https://www.r-project.org/about.html). FlowType uses a simple threshold or clustering algorithm to partition every channel/marker density to a positive and a negative cell population based on the assumption that the expression of a marker is either on or off (*i.e.,* there are two distinct populations). These partitions are then combined to generate a set of multi-dimensional phenotypes. In addition, and to allow for exclusion of markers from subset identification, each marker could also be assigned a 'neutral' value (*i.e.,* that marker is excluded from a phenotype). This algorithm generates a total number of possible phenotypes of 3^N where N is the number of markers (N=14 in the present experiment).

The length of a phenotype was limited to a maximum of four markers to allow for the identification of biologically meaningful phenotypes, as too many markers may lead to the generation of phenotypes with very small cell counts that would be difficult to interpret. This process generated a set of 1,697 possible phenotypes. Beyond these exploratory phenotypes, a subset of combinations of the above phenotypes, such as CD4:CD8 ratio, Viable T cells (%), % Monocytes, and % B-cells were also considered.

To measure the predictive power of each phenotype, a T-test was used to evaluate the difference between the measured phenotypes' cell frequencies (the number of cells in that phenotype divided by the total number of cells in the parent population) among Responders (R) and Non-Responders (NR). The most statistically significant phenotypes were selected for manual confirmation using FlowJo.

The CD4:CD8 ratio was found to be a clear differentiator in the aphaeresis samples, in terms of clinical response (FIGs. 1A and 1B). The area that most likely separates Responders from Non-

Responders corresponds to a CD4:CD8 ratio range of between 1 and 1.6, suggesting that patients with higher levels of CD4 populations (e.g., a CD4:CD8 ratio of greater than or equal to 1.6) in their aphaeresis samples are likely to respond to the CART-BCMA treatment (FIG. 1B).

Higher levels of the CD8+ stem memory T cells (TSCM) populations HLADR-CD95+CD27+ (FIG. 2A), CD45RO-CD27+ (FIG. 2B), and CCR7+CD45RO-CD27+ (FIG. 2C) were also observed in Responders as compared to Non-Responders, suggesting that patients with higher levels of these TSCM populations in their aphaeresis samples are likely to respond to the CART-BCMA treatment.

The analysis, described above, of T cells in the pre-BCMA manufacturing apheresis samples from multiple myeloma patients demonstrated a high CD4:CD8 ratio in patients who later responded to the CART-BCMA therapy and a low CD4:CD8 ratio in Non-Responders. Thus, selecting for patients with a high CD4:CD8 ratio in their aphaeresis material may potentiate for a more efficacious treatment outcome. In addition, these data and the bioinformatics tools suggest that immunological biomarkers could be integrated as a means to identify which patients are most likely to respond to the CART-BCMA therapy, leading to an ideal personalized approach to cellular therapy.

Example 4: Analysis of Multiple Myeloma tumor biopsies

Bone marrow core biopsy samples were acquired from patients enrolled in the University of Pennsylvania clinical trial entitled "Pilot Study Of Redirected Autologous T Cells Engineered To Contain an Anti-BCMA scFv Coupled To TCRζ And 4-1BB Signaling Domains in Patients With Relapsed and/or Refractory Multiple Myeloma" (NCT Number: NCT02546167; UPCC 14415) for analysis. Bone marrow core biopsy samples were collected prior to administration ("Pretreatment" or "Pre") or on Day 28, Day 43, or Day 90 post-infusion. Biopsy samples were formalin fixed with Immunocal™ decalcification and embedded in paraffin; and sample processing quality was confirmed by in situ hybridization (ISH) to the house keeping gene PPIB RNA.

Analysis of CD138+ MM cell localization and BCMA expression

CD138+ MM cell localization data from bone marrow core biopsy samples from Patient 13, Patient 14, Patient 15, Patient 16, and patient 17 were acquired prior to administration ("Pretreatment" or "Pre"), and on Day 28 and Day 90 ("3 month") post-infusion (FIG. 3). Patient 13 had minimal CD138 expression in their pretreatment, Day 28, and Day 90 samples (FIG. 3). Patient 14 had an increased number of CD138+ MM cells in their Day 28 sample compared to their pretreatment sample (FIG. 3). Patient 15, Patient 16, and Patient 17 each had extensive infiltration of CD138+ MM cells at baseline, followed by a reduction in the Day 28 samples and an increase in the 3-month samples (FIG. 3).

Patient outcomes to treatment with CART-BCMA and estimated % CD138 infiltration are provided in Table 29.

Table 29. Patient outcomes to CART-BCMA treatment and estimated % CD138 infiltration

CD138 staining	**Estimated % CD138 infiltration**					
Patient	**Pre**	**Day 28**	**Day 90**	**D43**	**Response**	**Pregression free survival (PFS)**
Patient 7				50%	Partial regression (PR)	1.5
Patient 8	70%				Progressive disease (PD)	0.5
Patient 12		40%			Stable disease (SD)	1.5
Patient 13	1%	0%	0%		Minor response (MR)	4+
Patient 14	80%	90%			Stable disease (SD)	1.5
Patient 15	95%	5%	10%		Very good partial regression (VGPR)	
Patient 16	50%	5%	95%		Partial regression (PR)	2+
Patient 17	50%	5%	75%		Partial regression (PR)	2+

BCMA expression data from bone marrow core biopsy samples were similarly acquired and analyzed (FIG. 4).

Discordance between BCMA protein expression as measured by IHC and BCMA mRNA expression as measured by ISH was observed in Patient 13 and Patient 14 (FIG. 5).

In Patient 15, high BCMA protein and mRNA levels were observed in pretreatment samples, followed by a marked reduction in Day 28 samples and a recurrence in Day 90 samples (FIG. 6A). Rare CAR^{Lo} positive cells were observed in Day 28 and Day 90 samples (FIG. 6A). In Patient 16, a marked reduction in BCMA protein and mRNA signal was observed at Day 28, followed by an increase at Day 90 (FIG. 6B). Rare CAR^{Lo} positive cells were observed at Day 28 and Day 90 (FIG. 6B). In Patient 17, a reduction in the number of BCMA positive cells and a reduction in BCMA mRNA signal/cell were observed at Day 28 (FIG. 6C). BCMA mRNA signal/cell returned to base line level at Day 90 (FIG. 6C). Equivocal CAR^{Lo} mRNA signal was detected at Day 90 (FIG. 6C).

In summary, variability in BCMA protein and mRNA expression was observed at base line and appeared to correlate with response in the sample set examined. Decreased CD138 positive cell infiltration was observed in 3 of 5 patients at 28 days and was associated with decreased BCMA protein and mRNA expression. Increased CD138 positive cell infiltration was observed in these same patients at 3 months and was associated with a return of BCMA expression.

Analysis of IDO1, IFN-γ, and TGFβ mRNA levels

The expression of IDO1, IFN-γ, and TGFβ mRNA levels was determined by ISH in Pretreatment, Day 28, and Day 90 bone marrow core biopsy samples acquired from Patient 15 (FIG. 7A), Patient 16 (FIG. 7B), and Patient 17 (FIG. 7C).

In Patient 15, an increase in IDO1 mRNA levels was observed in the Day 28 and Day 90 samples as compared to the Pretreatment sample (FIG. 7A). Minimal change was observed in the level of IFN-γ mRNA in all tested samples (FIG. 7A). A reduction in TGFβ mRNA levels was observed in the Day 28 and Day 90 samples as compared to the Pretreatment sample, and this change may be due to a reduction in the level of MM cells (FIG. 7A).

In Patient 16, an increase in IDO1 mRNA levels was observed at the site of persistent MM cells (FIG. 7B). Rare IFN-γ mRNA positive cells were observed in the Day 28 and Day 90 samples, while a marked increase in TGFβ mRNA levels was observed in MM cells in the Day 90 sample over baseline (FIG. 7B).

In Patient 17, an increase in IDO1 mRNA levels was observed in the Day 28 sample as compared to the Pretreatment sample (FIG. 7C). A low level of IFN-γ mRNA was observed at all time points (FIG. 7C). A reduction in TGFβ mRNA levels was observed in the Day 28 sample as compared to the Pre sample, and this change may be due to a reduction in the level of MM cells (FIG. 7C).

These data show that a modest increase in IDO1 mRNA expression was observed in bone marrow at Day 28.

A similar ISH analysis was conducted in Pretreatment, Day 10, and Day 28 biopsy samples acquired from Patient 19 (FIG. 7D) and Patient 20 (FIG. 7E). An increase in IFN-γ and IDO1 mRNA expression was observed at Day 10.

Analysis of PD-L1, PD1, CD3, and FoxP3 protein expression levels

The level of PD-L1, PD1, CD3, and FoxP3 protein expression was determined by IHC in Pretreatment, Day 28, and Day 90 bone marrow core biopsies acquired from Patient 15 (FIG. 8A), Patient 16 (FIG. 8B), and Patient 17 (FIG.8C).

In Patient 15, an increase in PD-L1 stromal cell expression was observed at Day 90 (Fig. 8A). No change in PD1, CD3, or FoxP3 expression was observed in the tested samples (Fig. 8A).

In Patient 16, an increase in PD-L1 stromal cell expression was observed at Day 90 (Fig. 8B). No PD1+ cell infiltration was detected (Fig. 8B). No change in CD3+ or FoxP3+ cell number was detected (Fig. 8B).

In Patient 17, PD-L1 stromal cell expression was observed at all time points (Fig. 8C). No PD1+ cell infiltration was detected and no change in CD3 or FoxP3 expression was observed in the tested samples (Fig. 8C).

A similar IHC analysis was conducted in Pretreatment, Day 10, and Day 28 biopsy samples acquired from Patient 19 (FIG. 8D) and Patient 20 (FIG. 8E). These two patients showed an increase in PD1 or PD-L1 in Day 10 samples.

These data show that while consistent changes in PD-L1, PD1, CD3, and FoxP3 were not observed, up-regulation of PD-L1 and/or PD1 in some patients may represent a potential escape mechanism.

Analysis of CD19 protein expression levels

CD19 protein expression was determined by IHC in Pretreatment, Day 28, and Day 90 bone marrow core biopsies acquired from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17 (FIG. 9). An increase in the relative proportion of CD19 positive MM cells was observed in Patient 15 and Patient 17 at 28 days and 3 months (FIG. 9).

BCMA positive cells and CD19 positive cells were determined to be separate populations in the Pretreatment and Day 90 bone marrow core biopsies acquired from Patient 15 (FIGs. 11A and 11B).

CD19+ $CD34^{dim}$ cell population was present in the Pretreatment bone marrow core biopsies acquired from Patient 15 (FIG. 12A) and Patient 17 (FIG. 12B).

The CD19 population is variably CD138+ and CD138- in the Pretreatment samples acquired from Patient 15 (FIG. 13).

These data suggests that a combination therapy including a CART-BCMA and a CD19-targeted therapy may be beneficial in the treatment of MM patients.

Analysis of CD20 protein expression levels

CD20 protein expression was determined by IHC in bone marrow core biopsies acquired prior to administration, and on Day 28 and Day 90 post-infusion of CART-BCMA from Patient 13, Patient 14, Patient 15, Patient 16, and Patient 17 (FIG. 10). Pre-existing CD20 positive MM cells were observed in samples acquired from patient 14 (FIG. 10). An emergence of CD20 positive MM cells was observed in patient 15 and patient 17 (FIG. 10).

These data suggest that a combination therapy including a CART-BCMA and a CD20-targeted therapy may be beneficial in the treatment of MM patients.

Example 5: Clinical and biologic activity of B-cell Maturation Antigen-specific Chimeric Antigen Receptor T cells (CART-BCMA) in refractory multiple myeloma

Summary

Chimeric antigen receptor (CAR) T cells are emerging as a promising new therapy in hematologic malignancies. B-cell maturation antigen (BCMA) is a cell-surface receptor with expression largely restricted to plasma cells, making it a rational target for multiple myeloma (MM) therapy. A phase I study of autologous T cells transduced with a novel, fully human, BCMA-specific CAR containing CD3ζ and 4-1BB signaling domains (CART-BCMA) was conducted in subjects with relapsed/refractory MM after 3 or more prior lines of therapy. Reported here are mature results from Cohort 1 of this study, using a dose of 1-5 x 10^8 CART-BCMA cells administered without prior chemotherapy conditioning. Nine subjects with a median of 9 prior therapy lines were treated; all had high-risk cytogenetics. CAR T cells were successfully manufactured and were detectable post-infusion in all cases. Four subjects (44%) had an objective response (1 PR, 2 VGPR, 1 sCR), with median duration of response of 4 months, including 1 subject with ongoing stringent complete response 21 months after CART-BCMA treatment. Compared with non-responders, responders had greater magnitude of in vivo CART-BCMA expansion, which was in turn associated with pre-manufacturing CD4:CD8 ratio and magnitude of expansion during manufacturing. Cytokine release syndrome was the most frequent treatment-related adverse event, occurring in 8 of 9 subjects (3 grade 3/4). Grade 4 encephalopathy was observed in 2 subjects. Median overall survival is estimated at 551 days. CART-BCMA infusions given without lymphodepleting chemotherapy are clinically active in heavily-pretreated MM patients and represent a novel approach to MM therapy.

Results

Protocol design and enrolment

A phase I study (NCT02546167) was opened to evaluate the feasibility, safety, clinical activity, and biologic activity of manufacturing and administering CART-BCMA cells to relapsed/refractory myeloma patients. BCMA expression on myeloma cells was assessed by flow cytometry but no pre-specified level was required for enrolment. After a 2-week washout from therapy, subjects underwent steady-state leukapheresis to collect T cells for CART-BCMA manufacturing, typically a 3 to 4-week process. Anti-myeloma therapy could resume during manufacturing until 2 weeks prior to first CART-BCMA infusion. CART-BCMA cells were administered in an outpatient research unit over 3 days as split-dose intravenous infusions (10% of dose given on day 0; 30% on day 1, and 60% on day 2), as per prior adult CTL019 trials (Porter et al., Sci. Transl. Med. 7, 303ra139 (2015)). In cohorts 2 and 3 (described below), cyclophosphamide (Cy) was administered for lymphodepletion 3 days prior to first CART-BCMA infusion (FIG. 31).

Initially a standard 3+3 dose-escalation design was used, exploring 3 sequential cohorts: 1) 1-5 x 10^8 CART-BCMA cells alone; 2) Cy 1.5 g/m^2 + 1-5 x 10^7 CART-BCMA cells; and 3) Cy 1.5 g/m^2 + 1-5 x 10^8 CART-BCMA cells. The protocol was later amended to allow treatment of additional subjects in each cohort, in order to gain more information about the safety and efficacy of CART-BCMA cells

both with and without lymphodepleting conditioning (i.e. Cy), and at a higher (1-5 x 10^8) and lower (1-5 x 10^7) dose. Reported here are outcomes for the 9 subjects treated on Cohort 1 with CART-BCMA cells alone, now with mature follow-up. Enrollment and follow-up for Cohorts 2 and 3 are ongoing.

Twelve subjects consented during Cohort 1 enrollment; 2 never collected T cells (1 ineligible due to severe restrictive lung disease; 1 with rapid disease progression/clinical decline). Ten successfully manufactured CART-BCMA cells; 1 was never infused due to rapid progression/clinical decline, and 9 were infused between Nov. 2015 and Sept. 2016 (FIG. 37).

Subject and CART-BCMA product characteristics

Subject demographics, prior lines of therapy, and disease characteristics are summarized in Table 30, with individual details shown in Table 32. Median age of treated subjects was 57, with 67% male. These subjects had a median of 9 prior lines of therapy, and 8/9 (89%) were dual-refractory to at least 1 proteasome inhibitor and immunomodulatory agent. All had at least 1 high-risk cytogenetic abnormality; 67% had either deletion 17p or a *TP53* mutation. Baseline tumor burden was high (median 80% myeloma cells on pre-treatment bone marrow biopsy), and 2/9 (22%) had extramedullary disease. Median absolute lymphocyte count (ALC) and total CD3 count pre-leukapheresis were 830 and 325 cells/μL, respectively, and had declined to 500 and 258 cells/μL, respectively, by the time of CART-BCMA infusions, reflecting the advanced disease and extensive prior treatment in this cohort.

All 9 subjects successfully manufactured the minimum goal CART-BCMA cells (1 x 10^8), though 1 subject required 2 leukapheresis/manufacturing attempts. Median transduction efficiency was 22.2% (range 9.6 – 33.3%), with median 12.7-fold expansion of seeded cells during manufacturing. Final products were comprised of a median of 96% CD3+ T cells, with median CD4/CD8 ratio of 1.6. Six subjects received all 3 planned CART-BCMA infusions, with 3 (subjects 01, 03, and 15) receiving only 40% of planned dose (3rd infusion held due to fevers and signs of CRS). Further details of manufacturing, product characteristics, and dosing for each subject are shown in Table 33.

Clinical outcomes

Four of 9 subjects (44%) achieved a partial response (PR) or better, including 1 PR, 2 very good partial responses (VGPR), and 1 stringent complete response (sCR). Two additional subjects had minimal response (MR), and 3 had no response (FIG. 32A). Median time to first response was 14 days. Based on Kaplan-Meier estimates, median duration of response (for those with PR or better) was 120 days (range 29 – 665+); and median progression-free survival (PFS) was 65 days (range 13 – 679+). Three subjects had no detectable myeloma by flow cytometry (estimated sensitivity 10^{-5}) from marrow aspirates performed on day 28 (subjects 01, 15) or day 45 (subject 03) after CART-BCMA infusions. Subjects 03 and 15 achieved VGPR but progressed at 5 and 4 months, respectively. Subject 01 had 11 prior lines of therapy, was refractory to bortezomib, lenalidomide, carfilzomib and pomalidomide, and had deletion 17p along with mutations in *TP53* and *NRAS*, reflecting very poor-risk disease. He was

progressing rapidly prior to CART-BCMA therapy, with 70% marrow plasma cells, serum M-spike of 2.0 g/dL, 24-hour urine M-spike of 3900 mg, serum free kappa of 6794 mg/L, hypercalcemia and acute renal insufficiency (serum creatinine 1.82 mg/dL). He had gradual evolution of his response from PR (day 14) to VGPR (month 3), CR (month 6), and then to sCR (month 9), and remains in sCR 21 months after CART-BCMA infusion. One subject (03) with extramedullary involvement of paraspinal muscles and pleura had complete metabolic response on PET/CT 5 weeks after CART-BCMA infusion, including resolution of malignant pleural effusion (FIG. 32B), demonstrating ability of CART-BCMA cells to traffic outside blood and marrow compartments. The other subject (08) with extramedullary disease had no response. At time of data cutoff (9/11/17), 5 subjects had died, and estimated median overall survival (FIG. 32C) was 551 days (range 24 – 679+).

Safety

Grade 3 or higher adverse events were seen in 8/9 (88%) of subjects and are summarized in Table 31, with all adverse events for each subject listed in Table 34. Cytokine release syndrome (CRS), a well-described complication of CAR T cell therapy, was observed in 8 subjects: 1 grade 1, 4 grade 2, 3 grade 3, and 1 grade 4. Median time of CRS onset was 3.5 days after first infusion (range 1-8), with a median duration of 8 days (range 3 - 12), and median duration of hospitalization of 9 days (range 3 – 40). CRS was associated with elevations in ferritin and C-reactive protein. Four subjects received tocilizumab, the anti-IL6 receptor antibody, with 3 requiring a second administration (subjects 01, 03, 08), and 2 requiring care in the intensive care unit.

Neurotoxicity is a common adverse event after CAR T cell therapy, ranging from mild confusion or concentration defects to focal neurologic deficits, global encephalopathy, aphasia, seizures, and/or obtundation. Subject 01 had grade 1 confusion, which resolved without intervention, in the setting of grade 3 CRS. Two subjects (03 and 08) developed severe (grade 4) neurotoxicity following CART-BCMA infusions. Both had high tumor burden with extramedullary disease and rapid progression at time of treatment, and both had received tocilizumab for severe CRS. Subject 03 developed obtundation and recurrent seizures requiring intubation, in the setting of rising peripheral lymphocyte count suggesting rapid CART-BCMA proliferation. MRI of the brain on day 15 showed diffuse white matter enhancement most pronounced in the posterior lobes, with sulcal effacement suggestive of early cerebral edema. At the time cerebral edema had not yet been described as a consequence of CAR T cell therapy (Abbasi et al., JAMA 317, 2271 (2017)), and her clinical and radiologic picture was felt to be most consistent with posterior reversible encephalopathy syndrome (PRES). She received high-dose intravenous steroids (methylprednisolone 1 g/day x 3 days) without improvement, and then received cyclophosphamide 1.5 g/m2 on day 17, with rapid neurologic improvement within 48 hours, near complete resolution of abnormal enhancement on MRI day 23, and

no residual neurologic deficits. Further details are described separately (Garfall et al., Blood 128, 5702-5702 (2016), incorporated by reference in its entirety).

Subject 08 had rapidly progressive myeloma at time of CART-BCMA infusions, with 80% marrow plasma cells and extramedullary involvement of skin, lymph nodes, liver, adrenals, and kidneys, along with progressive renal dysfunction (Cr 2.87 g/dL). He developed grade 4 CRS on day 15 associated with worsening kidney injury, atrial fibrillation, hypoxia, hypotension, coagulopathy, delirium, and transaminitis. He had hemodynamic stabilization after tocilizumab, but had progressive grade 4 encephalopathy/obtundation requiring intubation day 17. MRI of the brain was unremarkable with no evidence of cerebral edema, but progressive myeloma in the base of skull was noted. He received steroids with improvement in mental status and was extubated on day 20. On day 22 he developed recurrent shock and hypoxia requiring intubation; blood cultures subsequently showed candidemia. Peripheral blood now showed 13% circulating plasma cells and labs confirmed progressive myeloma; in this setting his family opted for comfort care only and he expired on day 24. No other deaths occurred while on study.

Kinetics of CART-BCMA engraftment and persistence

All infused subjects had detectable CART-BCMA cells in peripheral blood by qPCR analysis, and CAR+ T cells were detectable in 8/9 subjects by flow cytometry (FIG. 33A; FIG. 38 for representative staining). Expansion peaked at day 10 for most subjects, with CART-BCMA cells comprising over 75% of all circulating CD3+ T cells in the two subjects (01, 03) with greatest expansion, corresponding to 5300 and 8700 circulating CART-BCMA cells per µL of blood, respectively, at the peak of expansion (FIG. 39). Despite a predominance of CD4+ T cells in the CART-BCMA product pre-infusion, CART-BCMA cells circulating in blood were predominantly CD8+, and were highly activated, with a median of 94% (range 33 – 98%) of CAR+CD3+ cells expressing HLA-DR during peak expansion (Table 35). CART-BCMA levels in marrow aspirates generally mirrored those in peripheral blood, and also were elevated in pleural fluid and cerebrospinal fluid for subject 03 (Table 36). CART-BCMA cells showed a limited duration of detection within blood in most subjects. In all but 2 subjects (01, 03), CART-BCMA cells were no longer detectable by flow cytometry after day 28 but remained detectable by qPCR to day 60 in 7/8 tested, including in subject 01 (in stringent CR), who continues to have detectable cells at 21 months (FIG. 33A). Responses were significantly associated with peak expansion by qPCR (median 102507 copies/µg DNA for ≥PR vs. 4187 copies/µg for <PR, p=0.016), as well as with persistence over the first 28 days, as measured by the area under the curve ($AUC_{0\text{-}28d}$) (median 885181 copies*days/µg DNA for ≥PR vs. 26183 copies*days/µg DNA for <PR, p=0.016) (FIG. 33B).

Changes in soluble factors post-CART-BCMA

A total of 30 cytokines were quantified in peripheral blood serum before and after CART-BCMA infusion. The most consistent changes from baseline (>5-fold increase) were seen for IL-6, IL-10, monokine induced by interferon-gamma (MIG, CXCL9), IP10, and IL-1 receptor alpha (FIG. 40). Cytokine increases were most pronounced in subjects with greatest expansion and response, peaking at time of peak expansion and with clinical manifestations of cytokine release syndrome, similar to patterns previously described with CD19-directed CAR T cells (Porter et al., Sci. Transl. Med. 7, 303ra139 (2015); Teachey et al., Cancer Discov. 6, 664-679 (2016)). The subjects with the deepest responses (01, 03, 15) all had peak IL-6, IL-10, and MIG concentrations >50-fold above baseline. The timing of CRS also was associated with response, with a median onset of 2 days (range 1-3) after first infusion in subjects with PR or better, compared with 4.5 days (range 4 – 8) in subjects without PR (p=0.029, Mann-Whitney test).

BCMA is shed from the surface of plasma cells by gamma-secretase-mediated cleavage (Laurent et al., Nat Commun 6, 7333 (2015)), leading to a soluble form (sBCMA) that is detectable in circulation. Elevated sBCMA levels are found in myeloma patients and higher concentrations of sBCMA are associated with poorer clinical outcomes (Sanchez et al., Br. J. Haematol. 158, 727-738 (2012)). The impact of CART-BCMA on serum concentration of sBCMA, as well as its ligands BAFF and APRIL, was serially assessed. Compared to a panel of healthy donors (HD, n=6, median sBCMA 41.6 ng/ml, range 25.2 – 84.4), most of the subjects had an elevated sBCMA concentration in blood at baseline (median 1532 ng/ml, range 78.2 – 6101.3), along with concomitant suppression of APRIL (median 0.04 ng/ml, range 0.01 – 0.96, compared to HD, median 5.69 ng/ml, range 3.07 – 6.24). BAFF concentrations (median 0.84 ng/ml, range 0.51 – 4.98) were not significantly different from HD (median 0.93 ng/ml, range 0.58 – 1.24). Baseline sBCMA concentration did not correlate with response (FIG. 41), but decline in sBCMA concentration after CART-BCMA was most pronounced in subjects with the deepest responses (01, 03, 15). sBCMA also started to rise again at time of progression for subjects 03, 07, 15 (FIG. 34), suggesting that sBCMA concentration in blood may be a useful biomarker for assessing myeloma disease burden.

All subjects had depressed frequencies of blood CD19+ B cells at baseline (median 1.9% of CD45+CD14- gate, range 0.1% - 4.5%), likely due to immune suppression from progressive myeloma and extensive prior therapy. However, in contrast to patients treated with CD19-directed CAR T cells, which cause prolonged B cell aplasia (Maude et al., N. Engl. J. Med. 371, 1507-1517 (2014)), 6 of 9 subjects treated with CART-BCMA cells had recovery of B cells, typically 2-3 months post-infusions. B cell recovery was most pronounced in subjects with the deepest responses (01, 03, 15), and was generally, though not always, associated with an increase in the concentration of serum BAFF and/or APRIL (FIG. 34), ligands known to promote normal B cell development, proliferation, and survival (Rickert et al., Immunol. Rev. 244, 115-133 (2011)). Importantly, B cell frequency remains normal in subject 01 despite prolonged persistence of circulating CART-BCMA cells, consistent with the previously-reported absence of BCMA expression on the majority of circulating B cells (Seckinger et al., Cancer Cell 31, 396-410 (2017); O'Connor et al., J. Exp. Med. 199, 91-98 (2004)).

BCMA expression on myeloma cells

Eight subjects were evaluable for BCMA expression by flow cytometry on myeloma cells prior to treatment, and all had detectable BCMA expression (FIG. 35) (see FIG. 42 for representative gating). Baseline intensity of BCMA varied from subject to subject, and did not appear to correlate with degree of CART-BCMA expansion or response (FIG. 43) in this small cohort. Post-treatment, 7 subjects had myeloma cells evaluable for BCMA expression. One subject (03) had significantly decreased BCMA staining intensity, relative to the fluorescence minus one (FMO) control, at time of progression (day 164) compared to pre-treatment, suggesting either downregulation of surface expression, immune selection of BCMA-dim/negative variants, and/or increased shedding from the cell surface.

Predictors of CART-BCMA expansion

As described above, and consistent with prior CAR T cell studies (Turtle et al., Sci. Transl. Med. 8, 355ra116 (2016); Porter et al., Sci. Transl. Med. 7, 303ra139 (2015); Ali et al., Blood 128, 1688-1700 (2016)), responding subjects had greater expansion and persistence of CART-BCMA cells, and more profound cytokine release, than non-responders. In order to explore pre-treatment characteristics potentially associated with strong expansion, features of the CART-BCMA product before, during, and at end of manufacturing were analyzed. It was found that a higher CD4/CD8 ratio in the leukapheresis product, as well as in the seed culture at the start of manufacturing (i.e. following the elutriation step to remove monocytes), was associated with greater CART-BCMA expansion in subjects (FIGs. 36A and 36B), while total CD3 T cell number in the leukapheresis product or seed culture, or CD4/CD8 ratio in final product at end of manufacturing was not (data not shown). Fold expansion of seeded cells during manufacturing also correlated with in vivo CART-BCMA expansion (FIG. 36C), suggesting that in vitro proliferative capacity may predict for in vivo activity. Finally, previous analyses in CLL patients receiving CD19-directed CAR T cells had demonstrated that better CAR T cell expansion and clinical responses were associated with a higher percentage of CD8+ T cells within the leukapheresis specimen expressing a CD27+CD45RO- phenotype (*24*). CD8+ T cells within the leukapheresis products of 9 subjects treated with CART-BCMA cells alone were examined and a similar correlation was found between the frequency of CD27+CD45RO- cells and CART-BCMA expansion in vivo (FIG. 36D).

Discussion

CAR T cell therapy is emerging as a promising therapeutic option for B-cell malignancies, with the potential for durable disease control following a single treatment, differentiating it from other therapies that require repeated and/or continuous administration. In this report, the potential of CAR T cell therapy in advanced and refractory myeloma is demonstrated, with 4/9 subjects achieving a partial response or better, including an ongoing stringent complete remission 21 months post-infusion, as well as 2 additional subjects with minor responses. This is notable given the highly adverse biological features of the enrolled subjects' myeloma, including high tumor burden, rapidly progressing disease, and high-risk genetics. CAR T cell products were successfully manufactured from all subjects, despite baseline T cell lymphocytopenia, and engraftment was seen in all subjects as well, though peak levels and persistence of CAR T cells varied significantly amongst subjects.

Myeloma has long been associated with quantitative and functional deficits in T cells, particularly in more advanced, refractory disease, with inverted CD4/CD8 T cell ratios, impaired ex vivo anti-tumor activity, and acquisition of an exhausted or senescent phenotype (Kay, et al., Blood 98, 23-28 (2001); Dhodapkar, et al., J. Exp. Med. 198, 1753-1757 (2003); Suen, et al., Leukemia 30, 1716-1724 (2016)). In this study responses correlated with degree of in vivo expansion, which in turn was associated with higher pre-manufacturing CD4/CD8 T cell ratio, pre-manufacturing frequency of

CD45RO-CD27+CD8+ T cells, and magnitude of in vitro proliferation during manufacturing. This suggests that more effective CART-BCMA products may be derived from subjects with a less differentiated, more "naïve-like" T cell compartment, as previously observed in a CLL trial using CD19-directed CAR T cells (Fraietta, et al., Blood 128, 57-57 (2016)). These findings suggest that pre-treatment phenotypic and/or functional T cell characteristics may eventually help predict subjects likely to respond or not to CART-BCMA therapy. They also suggest that treatment of patients earlier in the course of their disease, when T cells may be intrinsically "fitter," may be more effective.

The observed CAR T cell expansion and clinical activity is also notable due to the lack of any chemotherapy given as pre-infusion conditioning in this cohort. Chemotherapeutics such as cyclophosphamide have been demonstrated to enhance T cell-mediated anti-tumor immunity via multiple potential mechanisms, including reduction of cellular "sinks" leading to increased availability of IL-7 and IL-15; depletion of suppressor cell populations such as regulatory T cells; induction of mucosal damage with release of Toll-like receptor agonists which enhance maturation of antigen-presenting cells; and alteration of gut microbiota (Gattinoni, et al., Nat. Rev. Immunol. 6, 383-393 (2006); Viaud, et al., Science 342, 971-976 (2013)). Thus, adoptive transfer of tumor-specific T cells, including CAR T cells, in humans has most commonly followed some form of lymphodepleting conditioning (Porter, et al., Sci. Transl. Med. 7, 303ra139 (2015); Rapoport, et al., Nat. Med. 21, 914-921 (2015); Noonan, et al., Sci. Transl. Med. 7, 288ra278 (2015); Morgan, et al., Science 314, 126-129 (2006)), with some studies showing that incremental increases in the intensity of the conditioning leads to even better engraftment and clinical outcomes (Turtle, et al., Sci. Transl. Med. 8, 355ra116 (2016); Dudley, et al., J. Clin. Oncol. 26, 5233-5239 (2008)). Consistent with this, early studies of CAR T cell therapy given without lymphodepleting conditioning saw only low-level expansion and limited persistence of transferred T cells, though admittedly these studies used first-generation CAR constructs that lacked co-stimulatory domains and contained immunogenic sequences that also contributed to poor engraftment (Pule, et al., Mol. Ther. 15, 825-833 (2007); Park, et al., Mol. Ther. 15, 825-833 (2007); Till, et al., Blood 112, 2261-2271 (2008)).

This study clearly demonstrates, however, that at least in some patients (e.g. subject 01), chemotherapy conditioning is not required for robust and sustained CAR T cell engraftment and clinical efficacy. The conditions that may have contributed to this success include the inclusion of the 4-1BB co-stimulatory domain in the CAR construct, high tumor burden with widespread availability of antigen, and the significant baseline lymphopenia in the patient population. Nonetheless, given the known beneficial effects of chemotherapy conditioning as described above, it remains likely that lymphodepletion will increase the proportion of subjects who have successful CART-BCMA expansion and persistence, and perhaps clinical responses. This question will be addressed in Cohorts 2 and 3 which receive cyclophosphamide prior to CART-BCMA cells.

Together with the previous BCMA-specific CAR T cell trial reported by the NCI (Ali, et al., Blood 128, 1688-1700 (2016)), this study validates BCMA as a highly attractive target in myeloma. This has been reinforced further by the promising pre-clinical and early clinical activity noted with bispecific antibodies and antibody-drug conjugates targeting BCMA (Tai, et al., Blood 123, 3128-3138 (2014); Hipp, et al., Leukemia 31, 1743-1751 (2017); Cohen, et al., Blood 128, 1148-1148 (2016)). In addition, preliminary reports of two other studies of BCMA-specific CAR T cells, given in conjunction with lymphodepleting chemotherapy and in less-heavily pretreated patient populations, have shown even higher response rates, several of which were durable for >1 year at time of reporting (Fan, et al., J. Clin. Oncol. 35, abstr LBA3001 (2017); Berdeja, et al., J. Clin. Oncol. 35, abstr 3010 (2017)). Importantly, none of these studies reported any unexpected off-target or off-tumor toxicity, confirming the limited normal tissue expression of BCMA, and differentiating it from other potential CAR T cell targets in myeloma (e.g. CD138, CD38, CS1/SLAMF7) with more widespread expression (Jiang, et al., Mol. Oncol. 8, 297-310 (2014); Drent, et al., Haematologica 101, 616-625 (2016); Chu, et al., Clin. Cancer Res. 20, 3989-4000 (2014)).

An important unanswered question for BCMA-targeted CAR T cells is whether there is a threshold of BCMA expression on MM cells required for optimal recognition and killing. This study did not require any specific level of BCMA as an eligibility requirement, in contrast to the 3 other reported BCMA-specific CAR T cell studies, which required at least 50% of myeloma cells to express BCMA by immunohistochemistry (IHC) or flow cytometry (Ali, et al., Blood 128, 1688-1700 (2016); Fan, et al., J. Clin. Oncol. 35, abstr LBA3001 (2017); Berdeja, et al., J. Clin. Oncol. 35, abstr 3010 (2017)). In the NCI trial, only 52/85 (62%) of pre-screened bone marrow biopsies stained for BCMA by IHC met this threshold, meaning more than a third of potentially eligible MM patients would have been excluded (Ali, et al., Blood 128, 1688-1700 (2016)). While it remains possible that this approach may enrich for patients more likely to respond, it may also exclude those who could benefit, and at least in this initial cohort in this study, responses did not correlate with baseline BCMA expression by flow cytometry (FIG. 43). Larger datasets are needed to more fully address this question. Another question relates to potential downregulation of BCMA or selection of BCMA-dim/negative variants post-CAR T cell therapy, as observed in 1 patient each to date in both this study and the NCI study (Ali, et al., Blood 128, 1688-1700 (2016)). Larger studies and longer follow-up will help determine the true frequency of this phenomenon, but it suggests that it may be a means of MM cell escape.

The primary toxicities of CAR T cells remain cytokine release syndrome (CRS) and neurotoxicity. The frequency and severity of CRS in this cohort was similar to that reported in CD19-targeted CAR T cell trials (Maude, et al., N. Engl. J. Med. 371, 1507-1517 (2014); Porter, et al., Sci. Transl. Med. 7, 303ra139 (2015)), and fortunately was abrogated with IL-6 receptor blockade therapy. Given the apparent lack of impact of tocilizumab on expansion and persistence of infused CAR T cells,

studies are now underway (e.g. NCT02906371) exploring its use earlier post-infusion, even if CRS is only low-grade, which may limit the development of severe or life-threatening toxicity. Neurotoxicity has been reported in up to 50% of subjects in some CAR T cell trials (Turtle, et al., Sci. Transl. Med. 8, 355ra116 (2016); Turtle, et al., J. Clin. Invest. 126, 2123-2138 (2016); Kochenderfer, et al., J. Clin. Oncol. 33, 540-549 (2015)), and remains more of a challenge. It can occur concurrent with or subsequent to CRS, and often does not improve (or may worsen) after tocilizumab. The presence of CAR T cells within the central nervous system (CNS) (as assessed by analysis of cerebrospinal fluid) by itself does not necessarily predict for neurotoxicity, but neurotoxicity has been associated with early onset of CRS and rapid elevation of inflammatory cytokines (e.g. IL6, IFN-gamma) both within the serum and CNS, perhaps leading to increased CNS vascular permeability (Gust, et al., Cancer Discov., (2017)). Mild cases are treated supportively, with steroids usually administered for more severe cases. Fortunately, the majority of cases have been reversible and self-limiting, though fatal cases with cerebral edema have been reported (Abbasi, et al., JAMA 317, 2271 (2017); Gust, et al., Cancer Discov., (2017)). The experience in this study demonstrating rapid reversal of a PRES-like syndrome in subject 03 using cyclophosphamide suggests this may be a reasonable option to try in steroid-refractory cases, especially if symptoms are associated with extensive concomitant CAR T cell expansion.

In summary, autologous T cells expressing a fully human BCMA-specific CAR could expand and induce objective responses, even without lymphodepleting chemotherapy, in refractory MM patients. Subsequent cohorts exploring different dose levels in conjunction with cyclophosphamide conditioning will help further optimize the safety and efficacy of this approach.

Materials and methods

Subjects

Subjects had multiple myeloma that had relapsed or was refractory (defined as progressing on or within 60 days of most recent therapy) after at least 3 prior lines of therapy, or 2 prior lines if dual-refractory to a proteasome inhibitor and IMiD. Other key eligibility criteria included measurable disease; an ECOG performance status of 0-2; serum creatinine $\leq$ 2.5 mg/dL or estimated creatinine clearance $\geq$30 ml/min; absolute neutrophil count $\geq$1000/µl and platelet count $\geq$50,000/µl ($\geq$30,000/µl if bone marrow plasma cells are $\geq$50% of cellularity); SGOT $\leq$ 3x the upper limit of normal and total bilirubin $\leq$ 2.0 mg/dl (except for patients in whom hyperbilirubinemia is attributed to Gilbert's syndrome); left ventricular ejection fraction $\geq$ 45%; lack of active auto-immune disease; and lack of central nervous system involvement with myeloma. All subjects had a baseline MRI of the brain and serial evaluations by a designated study neurologist. Informed consent was obtained from each subject and the study was conducted with approval of University of Pennsylvania IRB in concordance with the Declaration of Helsinki.

Study design

This clinical trial was a phase 1 open-label study where the primary objective was safety. Toxicity grade was determined according to National Cancer Institute's Common Terminology Criteria for Adverse Events version 4.0, with the exception of cytokine release syndrome, which was graded as per the University of Pennsylvania CRS Grading System (Table 38), as described (Porter, et al., Sci. Transl. Med. 7, 303ra139 (2015)). The study was approved by the Recombinant DNA Advisory Committee, FDA, Abramson Cancer Center Clinical Trials Scientific Review Committee, and the Penn Institutional Biosafety Committee and Institutional Review Board. The trial was registered in clinicaltrials.gov under NCT02546167, and was conducted as described in "Protocol design and enrollment" in the Results section and in FIG. 31. Myeloma responses were assessed by updated International Myeloma Working Group criteria (Kumar, et al., Lancet Oncol. 17, e328-346 (2016), hereby incorporated herein by reference in its entirety). Data cutoff for this analysis was 9/11/17.

CART-BCMA manufacturing and infusions

Peripheral blood T cells were stimulated and transduced with a lentiviral vector encoding the CAR: human anti-BCMA single chain variable fragment fused to the hinge and transmembrane domain of CD8 and the human 4-1BB and CD3z intracellular signaling domains. CART-BCMA cells were manufactured at the Clinical Cell and Vaccine Production Facility at the University of Pennsylvania, which is FACT accredited (http://www.factwebsite.org), as previously described (Porter, et al., Sci. Transl. Med. 7, 303ra139 (2015); Kalos, et al., Sci. Transl. Med. 3, 95ra73 (2011)). The frequency of CD3, CD4, and CD8 cells was determined by flow cytometry within the leukapheresis product, in the seed culture at start of manufacturing (following elutriation to reduce monocytes) (Powell, et al., Cytotherapy 11, 923-935 (2009)), and at end of manufacturing. Fold expansion and population doublings of seeded cells was measured by cell counting on a Coulter Multisizer™. CART-BCMA cells were formulated and cryopreserved until time of infusion, then administered following performance of quality control testing and quality assurance review by intravenous infusion over 3 days, with 10%, 30%, and 60% of the dose given on each day.

Measurement of CART-BCMA expansion

Research sample processing, freezing, and laboratory analyses were performed in the Translational and Correlative Studies Laboratory at the University of Pennsylvania, using established standard operating procedures (SOPs) for sample receipt, processing, freezing, and analysis. CART-BCMA cells were quantified from peripheral blood or bone marrow samples obtained at protocol-specified time points. Samples were collected in lavender top (K2EDTA) or red top (no additive) Vacutainer tubes (Becton Dickinson). Lavender top tubes were delivered to the laboratory within 2 hours of the sample draw. Samples were processed within 16 hours of drawing according to the established SOP. PBMCs were purified, processed, and stored in the vapor phase of liquid nitrogen. Red

top tubes were processed within 2 hours of the draw including coagulation time, and serum was isolated by centrifugation, aliquoted, and stored at −80°C.

Cells were evaluated by flow cytometry directly after Ficoll-Paque processing. Immunophenotyping of PBMC was performed using about 2×10^5 to 5×10^5 total cells per condition depending on cell yield in samples. FMO (fluorescence minus one) secondary only controls were used for CART-BCMA and for BCMA evaluation. Reagents and protocols used for flow cytometry are described in the Supplementary Methods.

Genomic DNA was isolated directly from whole blood or marrow aspirate, and qPCR analysis was performed using ABI TaqMan technology and a validated assay to detect the integrated CAR transgene sequence as described (Kalos, et al., Sci. Transl. Med. 3, 95ra73 (2011)) using triplicates of 200 ng of genomic DNA per time point for peripheral blood and marrow samples. To determine copy number per unit DNA, an eight-point standard curve was generated consisting of 5 to 10^6 copies of lentivirus plasmid spiked into 100 ng of non-transduced control genomic DNA. The number of copies of plasmid present in the standard curve was verified using digital qPCR with the same primer/probe set and performed on a QuantStudio 3D digital PCR instrument (Life Technologies). Each datapoint (sample and standard curve) was evaluated in triplicate with a positive Ct value in three of three replicates with percent coefficient of variation of less than 0.95% for all quantifiable values. To control for the quality of interrogated DNA, a parallel amplification reaction was performed using 20 ng of genomic DNA and a primer/probe combination specific for a non-transcribed genomic sequence upstream of the CDKN1A (p21) gene as described (Kalos, et al., Sci. Transl. Med. 3, 95ra73 (2011)). These amplification reactions generated a correction factor to adjust for calculated versus actual DNA input. Copies of transgene per microgram of DNA were calculated according to the formula: copies per microgram of genomic DNA = (copies calculated from CART-BCMA standard curve) × correction factor/(amount DNA evaluated in nanograms) × 1000 ng.

Measurement of serum cytokines

Human cytokine magnetic 30-plex panel (LHC6003M) was from Life Technologies.

Serum samples collected 1 day prior to CART-BCMA infusion or from baseline and at scheduled time-points out until 28 days post-infusion were cryopreserved at -80°C. Batched samples were thawed and analyzed according to the manufacturers' protocols. Assay plates were measured using a FlexMAP 3D instrument, and data acquisition and analysis were done using xPONENT software. Data quality was examined based on the following criteria. The standard curve for each analyte has a 5P R^2 value > 0.95 with or without minor fitting using xPONENT software. To pass quality control, the results for an in-house control serum needed to be within the 95% of CI (confidence interval) derived from historical in-house control data for >25 of the tested analytes. No further tests were done on samples with results out of range low (<OOR). Samples with results that were out of

range high (>OOR) or greater than two times the standard curve maximum value (SC max) were re-tested at higher dilutions. Results that passed the above quality controls or retests were reported.

Measurement of soluble BCMA, BAFF, and APRIL

Antibody sets for human BCMA (DY193), APRIL (DY884B) and BAFF (DT124-05) were from R&D Systems. ELISA bead-strip and 4-column reservoir (SOW-A16735) were from Assay Depot. ELISA substrate ADHP (10010469) was from Cayman Chemical. Assay plates (OX1263) were from E&K Scientific. All ELISA reagents were prepared according to the protocols for DuoSet ELISA except for Color Reagent B, which was supplemented with ADHP at 100 uM. Due to limited volumes of sera and lack of availability of a Luminex assay for BCMA, APRIL and BAFF, the three analytes were measured using ELISA bead-strips. Instead of coating the capture antibody (cAB) to the wells of an ELISA plate, it was coated on the surfaces of macrospheres, which enabled the measurement of all three analytes using 100ul of serum. Assays were set up using bead-strips in assay plates based on an assay map following the protocol for antibody sets. At the end of the assay, one substrate plate per 12 bead-strips was prepared by adding 100 ul/well of substrate solution (1:1 of color reagent A and ADHP). Each bead-strip was placed in one column of the substrate plate according to the assay map. Color development was for 10 to 30 minutes. Plates were read on a FLUO STAR OMEGA instrument. Data quality control was performed as described for Luminex data.

Assessment of bone marrow myeloma cells, including BCMA expression

Flow cytometry assessment of bone marrow aspirate material was performed directly on aspirate following a brief ammonium chloride red blood cell lysis step. The procedure was adapted from the EuroFlow protocol as described in (Flores-Montero, et al., Leukemia 31, 2094-2103 (2017)). Briefly, up to 2mls of bone marrow aspirate was diluted with 48mls of Pharm Lyse solution (BD Biosciences Cat# 555899) and incubated for 15 minutes at room temperature on a shaking device. The cells were then collected by centrifugation for 10 minutes at 800g, washed twice with flow cytometry buffer (PBS with 1% fetal bovine serum), stained with L/D Aqua viability dye (Thermo Fisher Cat# L34957). Surface staining was done with a mixture of antibodies to CD45, CD19, CD138, CD38, CD14, CD56, CD20, CD3, CD269 (BCMA), CD274 (PD-L1). FMO (fluorescence minus one) secondary only controls were used for BCMA evaluation. Aliquots of normal donor PBMC cells were stained in parallel as controls. The cells were then washed before permeabilization/fixation using Cytofix/Cytoperm reagent (BD Biosciences) for 20 minutes at room temperature, washed, and stained with a mixture of antibodies to kappa and lambda immunoglobulin light chains. The samples were then washed before resuspension in PBS and acquisition on a 17-color LSR Fortessa Special Order Research Product flow cytometer (BD) equipped with a violet, blue, green, and red laser. List mode files were analyzed using either FlowJo (Treestar) or FCS Express.

Statistics

Statistical analysis of the study is primarily descriptive due to the pilot nature of the trial and small sample size of patients. Kaplan-Meier method was used to estimate duration of response, progression-free and overall survival and the associated median survival times. The Mann-Whitney test was used to evaluate significance of the association between response and peak CART-BCMA expansion, area under the curve for expansion over the first 28 days (AUC-28), baseline soluble BCMA levels, and baseline BCMA expression on MM cells. Spearman correlations were used to measure the correlations between two continuous variables. Significance of the Spearman correlation against the null hypothesis of no correlation was computed based on permutation. Analysis was performed using Graphpad Prism version 6.0.

Table 30. Subject characteristics

Characteristic (n=9)	**Median (range) or %**
Age	57 (44-70)
Gender	67% male; 33% female
Median time from diagnosis (years)	4.9 (1.8 – 9.6)
High-risk cytogenetics* Del 17p or *TP53* mutation	100% 67%
Prior lines of therapy	9 (4 – 11)
Len / Bort / Pom / Carf / Dara (% exposed)	100%/100%/100%/100%/44%
Len / Bort / Pom / Carf / Dara (% refractory)	78%/ 89%/ 89%/ 89%/ 44%
% Dual- / %Quad- / % Penta-refractory	100% / 56% / 33%
Autologous SCT	78%
Extramedullary disease	22%
% Bone marrow plasma cells	80 (15-95)
Day 0 absolute lymphocyte count (cells/µL) Day 0 absolute CD3 count (cells/µL)	500 (200 – 1420) 258 (117 – 1354)
Day 0 LDH (xx/xx)	175 (109 – 385)
Day 0 serum creatinine (mg/dL)	1.58 (0.83 – 2.87)
Day 0 hemoglobin (g/dL)	8.7 (6.4 – 11.3)
Day 0 platelets (x 10^3/ µL)	100 (13 – 221)

*Includes complex karyotype, gain 1q, deletion 17p, and/or t(4;14). Bort=bortezomib; Carf=carfilzomib; Dara=daratumumab; Del=deletion; Dual-refractory=refractory to both a proteasome inhibitor (PI) and immunomodulatory agent (IMiD); LDH=lactate dehyrdrogenase; Len=lenalidomide; Penta-refractory=refractory to 2 PIs, 2 IMiDs, and dara; Pom=pomalidomide; Quad-refractory=refractory to 2 PIs and 2 IMiDs; SCT=stem cell transplant.

Table 31. Grade 3 or higher adverse events

Event	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	All n (%)
Hypophosphatemia	4 (44%)	0	0	4 (44%)
Cytokine release syndrome	2 (22%)	1 (11%)	0	3 (33%)
Thrombocytopenia	2 (33%)	1 (11%)	0	3 (33%)
Neurotoxicity*	0	2 (22%)	0	2 (22%)
Anemia	2 (22%)	0	0	2 (22%)
Lung infection	0	2 (22%)	0	2 (22%)
Neutropenia	0	2 (22%)	0	2 (22%)
Hypocalcemia	1 (11%)	1 (11%)	0	2 (22%)
Hypokalemia	2 (22%)	0	0	2 (22%)
Death NOS**	0	0	1 (11%)	1 (11%)
Fatigue	1 (11%)	0	0	1 (11%)
Infection-other (candidemia)	0	1 (11%)	0	1 (11%)
Urinary tract infection	1 (11%)	0	0	1 (11%)
Alkaline phosphatase elevated	1 (11%)	0	0	1 (11%)
AST elevated	1 (11%)	0	0	1 (11%)
Fibrinogen decreased	1 (11%)	0	0	1 (11%)
Lymphopenia	0	1 (11%)	0	1 (11%)
Leukopenia	0	1 (11%)	0	1 (11%)
Hyponatremia	1 (11%)	0	0	1 (11%)
Pleural effusion	1 (11%)	0	0	1 (11%)
Hypertension	1 (11%)	0	0	1 (11%)

n=number of subjects who had the event. Highest grade toxicity experienced by subject is reported in table. *Neurotoxicity includes 1 subject with grade 3 seizures, grade 4 delirium, and grade 4 reversible posterior leukoencephalopathy syndrome (RPLS), also known as posterior reversible encephalopathy syndrome (PRES); and 1 subject with grade 3 delirium and grade 4 encephalopathy.
**Death NOS (not otherwise specified) in subject 08 with candidemia and rapidly progressive myeloma; family chose to pursue comfort measures only.

Supplementary Methods

Reagents and protocols for flow cytometry

Antibodies for T cell detection panels were anti-CD45 V450 (clone HI30), anti-CD14 V500 (clone M5E2), anti-CD56 Ax488 (clone B159), anti-CD4 PerCP-Cy5.5 (clone RPA-T4), anti-CD8 APC-H7 (clone SK1) (all from BD Bioscience). Also, anti-CD3 BV605 (clone OKT3), anti-HLA-DR BV711 (clone L243), anti-CD19 PE-Cy7 (clone H1B19) were used from Biolegend. CART-BCMA expression was assessed by using a bis-biotinylated BCMA-Fc recombinant protein and the secondary staining reagent Streptavidin-PE from BD Bioscience (cat#554061). Cells were resuspended in 100 µL PBS containing 1% fetal bovine serum, 0.02% sodium azide and bis-biotinylated BCMA-Fc and incubated for 30 min on ice, washed, resuspended in 100 µL PBS containing 1% fetal bovine serum, 0.02% sodium azide, surface antibodies and SA-PE, and incubated for 30 minutes on ice, washed,

resuspended in 250ul PBS containing 1% fetal bovine serum and 0.02% sodium azide and acquired using a Fortessa flow cytometer equipped with a violet (405 nm), blue (488 nm), a green (532 nm), and a red (628 nm) laser. Data were analyzed using FlowJo software (Version 10, Treestar). Compensation values were established using eBiosciene UltraComp eBeads (eBioscience cat#01-222-42) and DIVA software.

Table 32. Individual subject characteristics

Sub.	Age	Sex	Race	Yrs from Dx	Iso-type	Karyo-type	FISH	Mutation	# lines*	Last tx before pheresis, infusion**
01	66	M	white	9.6	IgGK	46XY	+11, -16q, -17p	*NRAS, TP53, TP53*	11	Pom/Dex Pom/Dex
02	68	M	white	6.3	IgAK	46XY	+1q, +4p, -17p	n/a	9	Carfilz/Len/Dex Carfilz/Cyclo/Dex
03	54	F	white	3.1	IgAL	n/a	+1q, t(4;14), -16q	n/a	4	D-PACE D-AC
07	44	M	white	1.8	K	n/a	+1q, -4, +11, -14, -16	*NRAS, TP53*	9	Carfilz/Pano Pom/Dex-ACE
08	70	M	white	3.3	IgAL	complex	+1q, -1p, -4, -17p	n/a	6	Carfilz/Pom/Dex Carfilz/Pom/Dex
09	61	M	white	6.6	K	46XY	t(11;14), -16q, -17p	none	9	Daratumumab Pulse Dex
10	47	M	white	4.9	IgGL	n/a	+1q, t(11;14)	*KRAS, SF3B1*	7	Pom/Dex Pom/Cyclo/Dex + plasma exchange
11	57	F	AA	6.3	IgGL	46XX	+1q, t(4;14), -17p	n/a	10	VDT-PACE VDT-PACE
15	51	F	Asian	4.7	IgAK	46XX	+1q, t(11;14)	*NRAS, KRAS, BIRC3, KIT*	7	Pembro/Pom/Dex Pom/Dex

*A line of therapy was defined as per IMWG criteria. Radiation was not counted as a line. **Most recent therapy received before T cell collection ("pheresis" – top line) and CART-BCMA infusion ("infusion" – bottom line). All therapy was held for at least 2 weeks prior to pheresis and again for at least 2 weeks prior to infusion.

Carfilz = carfilzomib; cyclo = cyclophosphamide; D-AC = dexamethasone + infusional doxorubicin and cyclophosphamide; D-PACE = dexamethasone + infusional cisplatinum, doxorubicin, cyclophosphamide, and etoposide; Dex = dexamethasone; Dx = diagnosis; Len = lenalidomide; Pano = panobinostat; Pembro = pembrolizumab; Pom = pomalidomide; Pom/Dex-ACE = pomalidomide, dexamethasone + infusional doxorubicin, cyclophosphamide, and etoposide; Tx = treatment; VDT-

PACE = bortezomib, dexamethasone, thalidomide + infusional cisplatinum, doxorubicin, cyclophosphamide, and etoposide; Yrs = years.

Table 33. CART-BCMA manufacturing and product details

Sub.	%CD3 + in aph	CD4: CD8 in aph	%CD3 + in seed culture	CD4: CD8 in seed culture	%CD3 + at harvest	CD4: CD8 at harvest	Fold exp	Pop dblgs	Trans Eff (%)	Total #CAR given (x 10^8)	Best re-sponse
01	28.4	3.20	52.6	2.04	98.4	2.40	43.5	4.54	9.6	2.0*	sCR
02	41.9	0.80	63	0.40	69.1	1.31	12.7	3.67	18.2	5.0	MR
03	25.2	2.33	58.4	2.47	97.6	1.72	17.9	4.16	25.9	2.0*	VGPR
07	10.2	2.18	20.3	1.47	94.9	1.60	38.9	5.28	24.2	5.0	PR
08	9.2	0.62	20.8	0.31	92.5	2.99	7.9	2.98	22.7	5.0	PD
09	54.6	0.77	86.8	0.49	87.5	1.69	10.0	3.33	22.2	5.0	SD
10	19.2	1.09	47.3	1.07	96.7	1.32	11.5	3.52	16.5	1.77	PD
11	5.56	1.14	21.4	0.81	96.9	1.20	8.7	3.11	19.4	5.0	MR
15	39.8	0.82	90.8	0.71	96	1.24	22.6	4.50	33.3	2.0*	VGPR

Frequency of total CD3+, CD3+CD4+, and CD3+CD8+ cells was assessed by flow cytometry in the apheresis product, at the start of manufacturing ("seed culture," after elutriation), and at the end of manufacturing ("at harvest"). Aph = apheresis product; fold exp = fold expansion; pop dblgs = population doublings; trans eff = transduction efficiency. MR = minimal response; PD = progressive disease; PR = partial response; sCR = stringent complete response; SD = stable disease; VGPR = very good partial response

*Subjects 01, 03, and 15 received only 40% of planned dose due to fevers/early CRS.

Table 34. Individual subject adverse events

Sub.	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
01	Dry eye Dry mouth Flu-like symptoms Metabolism disorder – other (iron deficiency) Myalgia Headache Ischemia cerebrovascular Nervous system disorder – other (confusion) Vascular disorder – other (edema)	DIC Vertigo Ileus Nausea Vomiting Fever Creatinine increased Thrombocytopenia Musculoskeletal disorder – other (generalized muscle aches) Urinary retention Respiratory disorder – other (pulmonary edema and atelectasis) Skin/SQ disorder – other (skin tear) Hypertension	Anemia Fatigue CRS Alk phos increased AST increased Hypocalcemia Hypokalemia Hypophosphatemia	Lymphopenia	
02	Sinus tachycardia		Thrombocytopenia		

	Gastrointestinal disorders – other (loose stool) Nausea Fatigue CRS Dizziness Headache Respiratory disorder – other (nasal and sinus congestion, cough)				
03	Sinus bradycardia Ear disorder – other (ears feel full, hard to hear) Eye disorder – other (difficulty reading) Constipation Edema Fever Hypokalemia Hypomagnesemia Bone pain Concentration impairment Headache Hoarseness Skin/SQ disorder – other (ecchymosis)	SVT Fatigue Infection – other (S. mitis/S. oralis bacteremia) Upper respiratory infection Lymphopenia Hypernatremia Musculoskeletal disorder – other (deconditioning, pain base of skull) Intracranial hemorrhage Respiratory disorder – other (post-nasal drip) Hypotension	CRS UTI Fibrinogen decreased Hypophosphatemia Seizure Pleural effusion Hypertension	Neutropenia Leukopenia Hypocalcemia RPLS Delirium	
07	Skin/SQ disorder – other (rash on face)	CRS Dyspepsia Hypoalbuminemia Hypocalcemia	Anemia Hypokalemia Hyponatremia		
08	Sinus tachycardia General disorder – other (rigors)		Lung infection Delirium	CRS Thrombocytopenia Encephalopathy Infection – other (fungemia)	Death NOS
09	Constipation Chills Fatigue Thrombocytopenia Anorexia Hypokalemia	Anemia Pericardial effusion CRS Neutropenia Hypocalcemia Headache			
10	Chills Fever	Thromobocytopenia			
11	Nausea Fatigue Thrombocytopenia Headache Respiratory disorder – other (cough, congestion)	CRS Infection – other (Clostridium difficile) Hypocalcemia	Hypophosphatemia		
15	Hypocalcemia Headache	Fatigue CRS	Thrombocytopenia	Neutropenia	

	Cough Dyspnea	Infection – other (positive test for Shiga toxin) Hypotension			

All events regardless of attribution are listed. If an event occurred more than once in same patient, highest grade is reported. Alk phos = alkaline phosphatase; AST = aspartate aminotransferase; CRS=cytokine release syndrome; DIC = disseminated intravascular coagulation; NOS = not otherwise specified; RPLS = reversible posterior leukoencephalopathy syndrome; SQ = subcutaneous; SVT = supraventricular tachycardia; UTI = urinary tract infection

Table 35. Characteristics of peripheral blood CART-BCMA+ cells at peak expansion

Sub.	Day of peak	%CAR+ of CD3+	%CAR+ of CD4+	%CAR+ of CD8+	%HLADR+ of CAR+	Best response
01	10	89.5	8.6	92.3	97	sCR
02	9	2.8	1.4	5.0	82	MR
03	14	76.2	13.7	85.9	97	VGPR
07	10	29.2	7.3	39.3	89	PR
08	16	9.3	0.4	16.9	95	PD
09	11*	*	*	*	*	SD
10	30	1.9	0.1	2.0	21	PD
11	8	18.2	14.6	25.2	94	MR
15	10	28.1	6.3	51.0	96	VGPR

CART-BCMA cells were assessed by flow cytometry as in FIG. 38. At day of peak expansion, the frequency of CAR+ cells within CD3+, CD4+, and CD8+ populations are listed. Activation status at peak expansion (as measured by % of CAR+ cells expressing HLA-DR) is also shown. MR = minimal response; PD = progressive disease; PR = partial response; sCR = stringent complete response; SD = stable disease; VGPR = very good partial response
*Peak determined by qPCR; CAR+ cells not detectable by flow.

Table 36. CART-BCMA engraftment by qPCR in blood, bone marrow, and other sites

Sub.	Day 28 blood	Day 28 BM	3 month blood	3 month BM	Other (site, day)
01	23447.33	10458.66	4373.95	n/a	n/a
02	454.57	383.62	334.90	n/a	n/a
03	220081.08*	109964.97*	9517.67	9934.97	CSF, D4: 3285.88 CSF, D16: 158038.74 Pleural fluid, D8: 23941.97 Pleural fluid, D18: 144516.62 BM, D164: 105.81
07	1757.60	2140.31	n/a	n/a	n/a
08	n/a	n/a	n/a	n/a	n/a
09	32.15	16.75	n/a	n/a	n/a
10	62.64	0	n/a	n/a	n/a
11	731.44		n/a	n/a	n/a
15	724.49	1084.16	32.58	99.48	n/a

CART-BCMA levels (copies/µg genomic DNA) were generally comparable in blood and marrow at tested timepoints. CART-BCMA was found at high levels in CSF and pleural fluid of subject 03. BM = bone marrow; CSF = cerebrospinal fluid. *Assays performed on day 45.

Table 37. Details of BCMA expression on myeloma cells

Sub.	Pre-tx %BCMA+	Pre-tx FMO MFI	Pre-tx BCMA MFI	Post-tx %BCMA+	Post-tx FMO MFI	Post-Tx BCMA MFI	Best response
01	95	568	10864	n/a	n/a	n/a	sCR
02	93	355	2375	97	483	3254	MR
03	84	265	1873	19 (d164)	78 (d164)	268	VGPR
07	n/a	n/a	n/a	84	273	1426	PR
08	99	124	6859	n/a	n/a	n/a	PD
09	28	50	103	93.7	204	1116	SD
10	83	192	1998	99	54	2140	PD
11	81	332	1844	62	49	831	MR
15	99	249	24842	100	362 (d90)	30685 (d90)	VGPR

Bone marrow myeloma cells were gated and BCMA expression analyzed. The % of myeloma cells expressing BCMA, as well as the mean fluorescence intensity (MFI) for BCMA and FMO negative control are depicted. n/a = not available. Pre-tx=pre-treatment. Post-tx = post-treatment, at day 28 timepoint unless otherwise specified.

Table 38. Penn grading system for Cytokine Release Syndrome (CRS)

University of Pennsylvania CRS Toxicity Grade				
1	**2**	**3**	**4**	**5**
Mild reaction: Treated with supportive care such as anti-pyretics, anti-emetics	Moderate reaction requiring IV fluids or parenteral nutrition; some signs of organ dysfunction (i.e., grade 2 creatinine or grade 3 liver function tests [LFTs] related to CRS and not attributable to any other condition). Hospitalization for management of CRS related symptoms including fevers with associated neutropenia.	More severe reaction: Hospitalization required for management of symptoms related to organ dysfunction including grade 4 LFTs or grade 3 creatinine related to CRS and not attributable to any other conditions. This excludes management of fever or myalgias. Includes hypotension treated with IVFs* or low-dose pressors, coagulopathy requiring fresh frozen plasma (FFP) or cryoprecipitate, and hypoxia requiring supplemental oxygen (nasal cannula oxygen, high flow oxygen, Continuous Positive Airway Pressure [CPAP] or Bilateral Positive Airway Pressure [BiPAP]). Patients admitted for management of suspected infection due to fevers and/or	Life-threatening complications such as hypotension requiring high dose pressors or hypoxia requiring mechanical ventilation.	Death

		neutropenia may have grade 2 CRS.		

*Defined as hypotension requiring multiple fluid boluses for blood pressure support.

Example 6: BCMA surface expression in B cell malignancies that are not multiple myeloma

Materials and methods

The following activated B cell subtype diffuse large B cell lymphoma (DLBCL) cell lines were tested: HBL-1, Oci-Ly3 and TMD-8. Additionally, the following germinal center B cell (GCB) subtype DLBCL lines were tested: SuDHL-4, SuDHL-6, and SuDHL-10. The multiple myeloma (MM) lines U266 and KMS11 served as positive controls and the acute lymphoblastic leukemia line Nalm6 as well as the chronic myelogenous leukemia (CML) line K562 were used as negative controls. Cells were stained with a PE-labeled anti-BCMA antibody (Biolegend, cat#357504) at 1:50 dilution. The antibody binding capacity (ABC) was determined with the Quantum Simply Cellular quantification kit (Bangs Laboratories, cat#815) according to the manufacturer's protocol. Cells were analyzed on a BD Fortessa flow cytometer and data was analyzed using FlowJo.

Results

FIG. 44A shows the histograms of BCMA expression and in FIG. 44B, the antibody binding capacity for each cell line is plotted. Both positive control lines showed high BCMA expression as seen in the histograms and by quantification (FIGs. 44A and 44B). All other lines showed significantly lower BCMA expression. However, all DLBCL lines tested, with the exception of Oci-Ly3, were distinctly BCMA positive. HBL-1 and SuDHL-6 showed the highest expression with an antibody binding capacity of >5,000.

Example 7: Predictors of T Cell Expansion and Clinical Responses following B-Cell Maturation Antigen-Specific Chimeric Antigen Receptor T cell therapy (CART-BCMA) for relapsed/refractory multiple myeloma (MM)

Background: Relapsed/refractory (rel/ref) MM is associated with progressive immune dysfunction, including reversal of CD4:CD8 T cell ratio and acquisition of terminally-differentiated T cell phenotypes. BCMA-directed CAR T cells have promising activity in MM, but the factors that predict for robust in vivo expansion and responses are not known. In a phase 1 study of CART-BCMA (autologous T cells expressing a human BCMA-specific CAR with CD3ζ/4-1BB signaling domains) in refractory MM patients (median 7 priors, 96% high-risk cytogenetics), partial response (PR) or better was observed in 12/25 (47%) (Cohen et al, ASH 2017, #505, herein incorporated by reference in its entirety). Recently, it was demonstrated in CLL patients receiving CD19-directed CAR T cells that certain T cell phenotypes prior to generation of the CAR T product were associated with improved in

vivo expansion and clinical outcomes (Fraietta et al, Nat Med 2018, herein incorporated by reference in its entirety). This study thus sought to identify pre-treatment clinical or immunological features associated with CART-BCMA expansion and/or response.

Methods: Three cohorts were enrolled: 1) 1-5 x 10^8 CART cells alone; 2) cyclophosphamide (Cy) 1.5 g/m^2 + 1-5 x 10^7 CART cells; and 3) Cy 1.5 g/m^2 + 1-5 x 10^8 CART cells. Phenotypic analysis of peripheral blood (PB) and bone marrow (BM) mononuclear cells, frozen leukapheresis aliquots, and phenotype and in vitro kinetics of CART-BCMA growth during manufacturing were performed by flow cytometry. CART-BCMA in vivo expansion was assessed by flow cytometry and qPCR. Responses were assessed by IMWG criteria.

Results: Responses (≥PR) were seen in 4/9 pts (44%, 1 sCR, 2 VPGR, 1 PR) in cohort 1; 1/5 (20%, 1 PR) in cohort 2; and 7/11 (64%, 1 CR, 3 VGPR, 3 PR) in cohort 3. As of 7/9/2018, 3/25 (12%) remain progression-free at 11, 14, and 32 months post-infusions. As previously described, responses were associated with both peak in vivo CART-BCMA expansion (p=0.002) as well as expansion over first month post-infusion (AUC-28, p=0.002). No baseline clinical or MM-related characteristic was significantly associated with expansion or response, including age, isotype, time from diagnosis, # prior therapies, being quad- or penta-refractory, presence of del 17p or *TP53* mutation, serum hemoglobin, BM MM cell percentage, MM cell BCMA intensity, or soluble BCMA concentration. Treatment regimen given before leukapheresis or CART-BCMA infusions also had no predictive value. It was found, however, that higher CD4:CD8 T cell ratios within the leukapheresis product were associated with greater in vivo CART-BCMA expansion (Spearman's r=0.56, p=0.005) and clinical response (PR or better; p=0.014, Mann-Whitney). In addition, and similar to CLL data, it was found that a higher frequency of CD8 T cells within the leukapheresis product with an "early-memory" phenotype of CD45RO-CD27+ was also associated with improved expansion (Spearman's r=0.48, p=0.018) and response (p=0.047). Analysis of manufacturing data confirmed that higher CD4:CD8 ratio at culture start was associated with greater expansion (r=0.41, p=0.044) and, to a lesser degree, responses (p=0.074), whereas absolute T cell numbers or CD4:CD8 ratio in final CART-BCMA product was not (p=NS). In vitro expansion during manufacturing did associate with in vivo expansion (r=0.48, p=0.017), but was not directly predictive of response. At the time of CART-BCMA infusion, the frequency of total T cells, CD8+ T cells, NK cells, B cells, and CD3+CD56+ cells within the PB or BM was not associated with subsequent CART-BCMA expansion or clinical response; higher PB and BM CD4:CD8 ratio pre-infusion correlated with expansion (r=0.58, p=0.004 and r=0.64, p=0.003, respectively), but not with response.

Conclusions: In this study, it was found that CART-BCMA expansion and responses in heavily-pretreated MM patients were not associated with tumor burden or other clinical characteristics, but did correlate with certain immunological features prior to T cell collection and manufacturing,

namely preservation of normal CD4:CD8 ratio and increased frequency of CD8 T cells with a CD45RO-CD27+ phenotype. This suggests that patients with less dysregulated immune systems may generate more effective CAR T cell products in MM, and has implications for optimizing patient selection, timing of T cell collection, and manufacturing techniques to try to overcome these limitations in MM patients.

Example 8: Clinical predictors of T cell fitness for CAR T cell manufacturing and efficacy in multiple myeloma

Introduction: The optimal clinical setting and cell product characteristics for chimeric antigen receptor (CAR) T cell therapy in multiple myeloma (MM) are uncertain. In CLL patients treated with anti-CD19 CAR T cells (CART19), prevalence of an early memory (early-mem) T cell phenotype (CD27+ CD45RO- CD8+) at time of leukapheresis was predictive of clinical response independently of other patient- or disease-specific factors and was associated with enhanced capacity for in vitro T cell expansion and CD19-responsive activation (Fraietta et al. Nat Med 2018, herein incorporated by reference in its entirety). T cell fitness is therefore a major determinant of response to CAR T cell therapy. In this study, leukapheresis samples from MM patients obtained at completion of induction therapy (post-ind) was compared with those obtained in relapsed/refractory (rel/ref) patients for frequency of early-mem T cells, CD4/CD8 ratio, and in vitro T cell expansion.

Methods: Cryopreserved leukapheresis samples were analyzed for the percentage of early-mem T cells and CD4/CD8 ratio by flow cytometry and in vitro expansion kinetics during anti-CD3/anti-CD28 bead stimulation. Post-ind samples were obtained between 2007 and 2014 from previously reported MM trials in which ex-vivo-expanded autologous T cells were infused post-ASCT to facilitate immune reconstitution (NCT01245673, NCT01426828, NCT00046852); rel/ref samples were from MM patients treated in a phase-one study of CART-BCMA (NCT02546167).

Results: The post-ind cohort includes 38 patients with median age 55y (range 41-68) and prior exposure to lenalidomide (22), bortezomib (21), dexamethasone (38), cyclophosphamide (8), vincristine (2), thalidomide (8), and doxorubicin (4); median time from first systemic therapy to leukapheresis was 152 days (range 53-1886) with a median of 1 prior line of therapy (range 1-4). The rel/ref cohort included 25 patients with median age 58y (range 44-75), median 7 prior lines of therapy (range 3-13), and previously exposed to lenalidomide (25), bortezomib (25), pomalidomide (23), carfilzomib/oprozomib (24), daratumumab (19), cyclophosphamide (25), autologous SCT (23), allogeneic SCT (1), and anti-PD1 (7). Median marrow plasma cell content at leukapheresis was lower in the post-ind cohort (12.5%, range 0-80, n=37) compared to the rel/ref cohort (65%, range 0-95%). Percentage of early-mem T cells was higher in the post-ind vs rel/ref cohort (median 43.9% vs 29.0%,

p=0.001, FIG. 45A). Likewise, CD4/CD8 ratio was higher in the post-ind vs rel/ref cohort (median 2.6 vs 0.87, p<0.0001, FIG. 45B). Magnitude of in vitro T cell expansion during manufacturing (measured as population doublings by day 9, or PDL9), which correlated with response to CART19 in CLL, was higher in post-ind vs rel/ref cohort (median PDL9 5.3 vs 4.5, p=0.0008, FIG. 45C). Pooling data from both cohorts, PDL9 correlated with both early-mem T cell percentage (Spearman's rho 0.38, multiplicity adjusted p=0.01) and CD4/CD8 ratio (Spearman's rho 0.42, multiplicity adjusted p=0.005). Within the post-ind cohort, there was no significant association between early-mem T cell percentage and time since MM diagnosis, duration of therapy, exposure to specific therapies (including cyclophosphamide, bortezomib, or lenalidomide), or bone marrow plasma cell content at time of apheresis. However, in the post-ind cohort, there was a trend of toward lower percentage early-mem phenotype (29% vs 49%, p=0.07) and lower CD4/CD8 ratio (median 1.4 vs 2.7, p=0.04) among patients who required >2 lines of therapy prior to apheresis (n=3) compared to the rest of the cohort (n=35).

Conclusion: In MM patients, frequency of the early-mem T cell phenotype, a functionally validated biomarker of fitness for CAR T cell manufacturing, was significantly higher in leukapheresis products obtained after induction therapy compared to the relapsed/refractory setting, as was CD4/CD8 ratio and magnitude of in vitro T cell expansion. This result suggests that CAR T cells for MM would yield better clinical responses at early points in the disease course, at periods of relatively low disease burden and before exposure to multiple lines of therapy.

Example 9: PD-1 inhibitor combinations as salvage therapy for relapsed/refractory multiple myeloma (MM) patients progressing after BCMA-directed CART cells

Background: Autologous T cells expressing a chimeric antigen receptor (CAR) specific for B-cell maturation antigen (CART-BCMA cells) show activity in refractory MM, but relapses remain common. Anti-PD-1 antibodies (Abs) augment CART cell activity pre-clinically, and induced CART cell re-expansion and responses in DLBCL patients progressing after CD19-specific CART cells (Chong et al, Blood 2017, herein incorporated by reference in its entirety). The IMiDs lenalidomide (len) and pomalidomide (pom) may enhance efficacy, but also toxicity, of both CART cells and PD-1 inhibitors in MM. Elotuzumab (elo) has clinical anti-MM activity in combination with IMiDs and dexamethasone (dex), and synergizes with anti-PD-1 Ab in pre-clinical models.

Methods: Outcomes of 25 subjects enrolled in a phase 1 study of CART-BCMA cells in relapsed/refractory MM were previously described (Cohen et al, ASH 2017, #505, herein incorporated by reference in its entirety). Five subjects were identified and retrospectively reviewed who progressed after CART-BCMA and received a PD-1 inhibitor (pembrolizumab (pembro)) combination as their next therapy. Responses were assessed by IMWG criteria. CART-BCMA levels were assessed by flow

cytometry and qPCR pre-treatment, 2-4 weeks after first pembro dose, then q4 weeks until progression. Pembro dosing was 200mg every 3 weeks; dex dosing was 20-40mg/week.

Results: Characteristics of five subjects are shown in Table 39. Median prior lines were 9; all had high-risk cytogenetics. All were refractory to pom, 2 to pembro/pom/dex, and 1 to elo. Best response to CART-BCMA was PR in 2, MR in 2, and PD in 1. Median time from CART-BCMA to pembro-based therapy was 117 days. All patients still had CART-BCMA cells detectable by qPCR, with 2 (pts. 07 and 21) still detectable by flow, at initiation of salvage therapy. The first pt. (02) received pembro/pom/dex and had MR but progressed at 2 months, with no detectable CART-BCMA re-expansion. The second pt. (07) had rapidly-progressing kappa light chain MM 2 months post-CART-BCMA and had previously progressed on pembro/pom/dex. He started elo/pembro/pom/dex and had MR at day 12 (free kappa 1446 to 937 mg/L), associated with robust expansion of CART-BCMA cells (875.64 to 20505.07 copies/µg DNA by qPCR; 0.7% to 6.4% of peripheral CD3+ cells by flow). Re-expanded CART-BCMA cells were predominantly CD8+ and highly activated (89% HLA-DR+, up from 18% pre-therapy). This response was short-lived, however, with progression 1 week later, and return of CART-BCMA levels to baseline at week 5. Three subsequent subjects then received elo/pembro/dex with either len or pom; with 2 MR and 1 SD, and PFS of 3 to 4 months. None had re-expansion of CART-BCMA cells. Non-specific immune modulation was observed and included altered CD4:CD8 T cell ratio (n=5), increased NK cell/decreased T cell frequency (n=4), and HLA-DR upregulation on CAR-negative T cells (n=2). More detailed phenotyping of CART and other immune cells, including PD-1 expression, is ongoing. With regard to toxicity, pt. 02 had self-limiting low-grade fevers and myalgias 4 weeks after pembro/pom/dex, associated with mild elevation in ferritin/CRP, suggestive of mild CRS. No other CRS was noted, including pt. 07 despite CART-BCMA re-expansion. One patient (17) developed recurrent expressive aphasia starting 2 months after elo/pembro/pom/dex, without signs of CRS and no observed expansion of CART-BCMA cells in blood or CSF. This resolved with stopping therapy and brief steroid taper.

Conclusions: This study demonstrates that a PD1-inhibitor combination can induce CART cell re-expansion and anti-MM response in a MM patient progressing after CART-BCMA therapy. Since this patient previously progressed on pembro/pom/dex, the observed clinical activity was likely related to the CART cells, with elotuzumab also possibly contributing. This proof-of-principle observation suggests that a subset of patients may respond to checkpoint blockade or other immune-modulating approaches following BCMA CART cell therapy, meriting further study.

Table 39. Patient characteristics

Pt	Age/Sex	Cohort	Best CART Response	CART D0 to Pembro D0	Pembro Regimen	Best Pembro Response	PFS post-Pembro (Days)	CART qPCR pre-	Peak CART qPCR post-Pembro^

				(Days)				Pembro^	
2	68/M	1	MR	117	Pembro/Pom/Dex	MR	67	331.59	128.82
7	44/M	1	PR	51	Elo/Pembro/Pom/Dex	MR	18	875.64	20505.07
13	59/M	2	MR	149	Elo/Pembro/Len/Dex	MR	105	50.34	50.72
17	64/F	3	PR	134	Elo/Pembro/Pom/Dex	MR	130	405.56	320.61
21	73/M	3	PD	34	Elo/Pembro/Len/Dex	SD	83	8372.96	433.28

Cohort 1==5x10^8 CART-BCMA cells alone; Cohort 2=1.5 g/m^2 Cy and 5x10^7 cells; Cohort 3=1.5 g/m^2 Cy and 5x10^8 cells
Pembro=Pembrolizumab; Elo=Elotuzumab; Pom=Pomalidomide; Len=Lenalidomide; Dex=Dexamethasone; Cy= cyclophosphamide
SD=stable disease; MR=minimal response; PR=partial response; PD=progressive disease; PFS=progression-free survival;
^units are copies/µg genomic DNA

Example 10: Clinical and biologic activity of B-cell Maturation Antigen-specific Chimeric Antigen Receptor T cells (CART-BCMA) in refractory multiple myeloma: a single-centre, open-label, phase 1 trial

Abstract

Background: Chimeric antigen receptor (CAR) T cells are a promising new therapy for hematologic malignancies. B-cell maturation antigen (BCMA) is a cell-surface receptor with expression largely restricted to plasma cells, making it a rational target for multiple myeloma (MM) therapy. *Methods:* A phase I study of autologous T cells lentivirally-transduced with a novel, fully human, BCMA-specific CAR containing CD3ζ and 4-1BB signaling domains (CART-BCMA), were conducted in subjects with relapsed/refractory MM. Twenty-five subjects were treated in 3 dose cohorts: 1) 1-5 x 10^8 CART-BCMA cells alone; 2) Cyclophosphamide (Cy) 1.5 g/m^2 + 1-5 x 10^7 CART-BCMA cells; and 3) Cy 1.5 g/m^2 + 1-5 x 10^8 CART-BCMA cells. No pre-specified BCMA expression level was required. *Findings:* Subjects had a median of 7 prior therapy lines; 96% were dual-refractory to a proteasome inhibitor and immunomodulatory drug; 96% had high-risk cytogenetics. CAR T cells were successfully manufactured in all cases. Toxicities included cytokine release syndrome and neurotoxicity, which were grade 3/4 in 8 (32%) and 3 (12%) subjects, respectively, and reversible. CART-BCMA cells expanded in all subjects, most consistently in cohort 3. Clinical responses were seen in 4/9 (44%) in cohort 1, 1/5 (20%) in cohort 2, and 7/11 (63%) in cohort 3, including 5 partial, 5 very good partial, and 2 complete responses. Three subjects had ongoing responses at 11, 14, and 32 months. Decreased BCMA expression on residual MM cells was noted in responders; expression increased at progression in most. Responses were associated with CART-BCMA expansion, which was associated with CD4:CD8 T cell ratio

and frequency of CD45RO-CD27+CD8+ T cells in the pre-manufacturing leukapheresis product. *Interpretation:* CART-BCMA infusions given with or without lymphodepleting chemotherapy are clinically active in heavily-pretreated MM patients and represent a novel approach to MM therapy.

This study provides further clinical validation of BCMA as a rational target for myeloma therapy, and characterises the safety and efficacy of a novel, fully human BCMA-specific CAR construct containing a 4-1BB co-stimulatory domain. This study further describes biologic and clinical activity of BCMA-specific CAR T cells both with and without lymphodepleting chemotherapy; demonstrates dynamic BCMA expression on myeloma cells post-infusion, particularly in responding patients; and identifies potential novel biomarkers of CAR T cell expansion and clinical response.

Methods

Study Design and Participants

Eligible subjects had relapsed and/or refractory MM after at least 3 prior regimens, or 2 prior regimens if dual-refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD). Other key eligibility criteria at screening included ECOG (Eastern Cooperative Oncology Group) performance status of 0-2; serum creatinine $\leq$ 2.5 mg/dL or estimated creatinine clearance $\geq$30 ml/min; absolute neutrophil count $\geq$1000/µl and platelet count $\geq$50,000/µl ($\geq$30,000/µl if bone marrow plasma cells were $\geq$50% of cellularity); SGOT $\leq$ 3 times upper limit of normal and total bilirubin $\leq$ 2.0 mg/dl; left ventricular ejection fraction $\geq$ 45%; lack of active auto-immune disease; and lack of central nervous system involvement with myeloma. No pre-specified level of BCMA expression on MM cells was required.

This clinical trial (NCT02546167) was a phase 1, single-centre, open-label study. Initially a standard 3+3 dose-escalation design was used, exploring 3 sequential cohorts: 1) 1-5 x 10^8 CART-BCMA cells alone; 2) Cyclophosphamide (Cy) 1.5 g/m^2 + 1-5 x 10^7 CART-BCMA cells; and 3) Cy 1.5 g/m^2 + 1-5 x 10^8 CART-BCMA cells. The protocol was amended to expand each cohort to 9 treated subjects, to gain more information about the safety and efficacy of CART-BCMA cells both with and without lymphodepleting conditioning and at a higher (1-5 x 10^8) and lower (1-5 x 10^7) dose. A subsequent amendment stopped enrollment in cohort 2 after 5 subjects due to suboptimal efficacy, and allowed up to 13 subjects in cohort 3; however, funding limitations ultimately ended enrollment after 11 treated Cohort 3 subjects (total n=25 treated).

Procedures

After a 2-week washout from therapy (4 weeks for monoclonal antibodies), subjects underwent steady-state leukapheresis to collect T cells for CART-BCMA manufacturing. Anti-myeloma therapy could resume during manufacturing until 2 weeks prior to first CART-BCMA infusion. CART-BCMA cells were administered intravenously over 3 days (10% of dose on day 0; 30% on day 1, and 60% on day 2), as described in Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139. The 30% or 60% dose could be held if subjects developed signs of CRS. Cy was administered 3 days prior to first CART-BCMA infusion. Clinical and laboratory assessments were performed as per FIG. 46.

CART-BCMA cells were manufactured in the FACT-accredited Clinical Cell and Vaccine Production Facility at the University of Pennsylvania, as described in Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139; Kalos M, et al., Sci Transl Med 2011; 3(95): 95ra73. The frequency of CD3, CD4, and CD8 cells was determined by flow cytometry in the seed culture at beginning and end of manufacturing. Fold expansion and population doubling of seeded cells was measured by cell counting on a Coulter Multisizer™. After manufacturing and quality control testing, CART-BCMA cells were cryopreserved until time of infusion.

Data on adverse events (AEs) were collected from time of first CART-BCMA infusion (or Cy administration for cohorts 2 and 3). Toxicity grade was determined according to National Cancer Institute's Common Terminology Criteria for Adverse Events version 4.0, with the exception of cytokine release syndrome, which was graded as per the University of Pennsylvania CRS Grading System (Table 38) (Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139). Myeloma responses were assessed by updated International Myeloma Working Group criteria (Kumar S, et al., Lancet Oncol 2016; 17(8): e328-46).

Research sample processing, freezing, and laboratory analyses were performed in the Translational and Correlative Studies Laboratory at the University of Pennsylvania, as described (Maude SL, et al., N Engl J Med 2014; 371(16): 1507-17; Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139; Kalos M, et al., Sci Transl Med 2011; 3(95): 95ra73). CART-BCMA cells were quantified from peripheral blood or bone marrow samples by flow cytometry and quantitative PCR. Reagents and protocols for flow cytometry are described in the Supplementary Methods. Genomic DNA was isolated directly from whole blood or marrow aspirate, and qPCR analysis was performed using ABI TaqMan technology and a

validated assay to detect the integrated CAR transgene sequence as per Supplementary Methods and described in Kalos M, et al., Sci Transl Med 2011; 3(95): 95ra73.

Serum cytokine levels were assessed on batched cryopreserved samples using the human cytokine magnetic 30-plex panel (LHC6003M) from Life Technologies, as described in Maude SL, et al., N Engl J Med 2014; 371(16): 1507-17. Measurement of soluble BCMA, BAFF, and APRIL concentrations in serum was performed by ELISA using antibody sets for human BCMA (DY193), APRIL (DY884B) and BAFF (DT124-05) from R&D Systems. See Supplementary Methods for details.

Flow cytometric assessment of MM cells, including BCMA expression, on fresh bone marrow aspirate material was adapted from the EuroFlow protocol as described in Flores-Montero J, et al., Leukemia 2017; 31(10): 2094-103 and in Supplementary Methods. Flow cytometric assessment of T cell phenotype in cryopreserved leukapheresis specimens was performed and analyzed as described in Fraietta JA, et al., Nat Med 2018; 24(5): 563-71.

Outcomes

The primary objective was to evaluate the safety of CART-BCMA in patients with relapsed/refractory myeloma. The primary endpoint was incidence of study-related grade 3 or higher AEs, including dose-limiting toxicities (DLTs). A DLT was defined as a serious AND unexpected AE whose relationship to study therapy could not be ruled out, occurring within 4 weeks of receiving protocol therapy. Hematologic toxicity was not considered a DLT due to the refractory nature of the underlying disease and expected myelosuppression from cyclophosphamide. In addition, any death related to protocol treatment, as well as any expected grade 4 organ toxicity or grade 4 neurologic toxicity that did not resolve or improve to grade 2 or less within 4 weeks of onset, despite medical management, was also considered a DLT. Secondary objectives were to assess feasibility of manufacturing CART-BCMA cells, and clinical activity. Secondary endpoints were frequency of successful manufacturing, and clinical outcomes, including response rates, progression-free survival, and overall survival. Exploratory endpoints included CART-BCMA expansion and persistence *in vivo*; changes in concentration of serum cytokines and soluble BCMA, and expression of BCMA on MM cells.

Statistical analysis

Statistical analysis of the study is primarily descriptive due to the pilot nature of the trial and small sample size of each cohort. Kaplan-Meier method was used to estimate duration of response, progression-free and overall survival and the associated median survival times.

Association between a binary endpoint (e.g. response) and a continuous factor (e.g. CAR T cell numbers) was evaluated using the Mann-Whitney test. Association between a binary endpoint and a categorical factor (e.g. presence or absence of deletion 17p) was evaluated using Fisher's Exact test. Spearman correlations were used to measure the correlations between two continuous variables. Significance of the Spearman correlation against the null hypothesis of no correlation was computed based on permutation. Because the statistical analyses performed here are exploratory and hypothesis-generating in nature, no adjustment of the p-values was made for multiple comparisons. Exact p-values are reported when applicable. Analysis was performed using Graphpad Prism version 6.0.

Results

From November 2015 – December 2017, 34 subjects consented and 29 were eligible and commenced manufacturing, with 25 receiving CART-BCMA infusions. Four were not treated due to rapid disease progression/clinical deterioration during manufacturing and bridging therapy (FIG. 52). Baseline characteristics and prior lines of therapy are summarized in Table 40, with individual details shown in Table 42. Subjects had a median of 7 prior lines of therapy, with 96% dual refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMID), 72% refractory to daratumumab, and 44% penta-refractory to 2 PIs, 2 IMIDs, and daratumumab. Ninety-six % had at least 1 high-risk cytogenetic abnormality; 68% had either deletion 17p or a *TP53* mutation. Baseline tumor burden was high (median 65% myeloma cells on bone marrow biopsy), and 28% had extramedullary disease.

Table 40. Subject characteristics

Characteristic (n=25)	Median (range) or %
Age	58 (44 - 75)
Gender	68% male; 32% female
Median time from diagnosis (years)	4.6 (1.8 – 14.5)
High-risk cytogenetics* Del 17p or *TP53* mutation	96% 68%
Prior lines of therapy	7 (3 - 13)
Len / Bort / Pom / Carf** / Dara (% exposed)	100%/100%/92%/96%/76%
Len / Bort / Pom / Carf / Dara (% refractory)	76%/ 88%/ 88%/ 80%/ 72%
% Dual- / %Quad- / % Penta-refractory	96% / 56% / 44%
Prior Autologous SCT	92%
Extramedullary disease	28%
% Bone marrow plasma cells	65 (0 – 95)
Absolute CD3+ T cell count (cells/μL) pre-leukapheresis***	538 (151 – 1529)
Day 0 LDH (units/L)	175 (75 – 385)
Day 0 serum creatinine (mg/dL)	0.93 (0.55 – 2.87)
Day 0 hemoglobin (g/dL)	9.1 (6.4 – 12.4)
Day 0 platelets (x 10^3/ μL)	128 (13 – 316)

*Includes complex karyotype, gain 1q, deletion 17p, t(14;16), and/or t(4;14). **Includes 1 patient who received oprozomib. ***n=23 (subjects 01 and 02 did not have pre-pheresis T cell counts done). Normal range = 900 – 3245 cells/μL
Bort=bortezomib; Carf=carfilzomib; Dara=daratumumab; Del=deletion; Dual-refractory = refractory to both a proteasome inhibitor (PI) and immunomodulatory agent (IMiD); LDH=lactate dehyrdrogenase; Len=lenalidomide; Penta-refractory=refractory to 2 PIs, 2 IMiDs, and dara; Pom=pomalidomide; Quad-refractory=refractory to 2 PIs and 2 IMiDs; SCT=stem cell transplant.

All subjects successfully manufactured minimum target goal of CART-BCMA cells, though 1 subject required 2 leukaphereses and manufacturing attempts. Final products were comprised of a median of 97% CD3+ T cells, with median CD4/CD8 ratio of 1.7. Twenty-one subjects received all 3 planned CART-BCMA infusions, with 4 receiving 40% of planned dose (3rd infusion held due to early CRS). Further details of manufacturing, product characteristics, and dosing for each subject are shown in Table 43.

Grade 3 or higher adverse events, regardless of attribution, were seen in 24/25 subjects (96%) and are summarized in Table 41, with individual adverse events for each subject listed in Table 44. Cytokine release syndrome (CRS) was observed in 22/25 subjects (88%), and was grade 3/4 on Penn grading scale (Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139) (Table 38) in 8 (32%), all of whom were treated at the 1-5 x 10^8 dose. Median time to CRS onset was 4 days (range 1-11), with a median duration of 6 days (range 1 - 18), and median

duration of hospitalization of 7 days (range 0 – 40). CRS was associated with elevations in ferritin and C-reactive protein, as described previously (Maude SL, et al., N Engl J Med 2014; 371(16): 1507-17). Seven subjects (28%) received IL-6 blockade with either tocilizumab (n=6) or siltuximab (n=1).

Table 41. Grade 3 or higher adverse events, regardless of attribution

Event	Grade 3 n	Grade 4 n	Grade 5 n	All n (%)
Leukopenia	3	8	0	11 (44%)
Neutropenia	2	9	0	11 (44%)
Lymphopenia	3	6	0	9 (36%)
Cytokine release syndrome	7	1	0	8 (32%)
Thrombocytopenia	3	4	0	7 (28%)
Hypophosphatemia	7	0	0	7 (28%)
Febrile neutropenia	6	0	0	6 (24%)
Hyponatremia	6	0	0	6 (24%)
Anemia	4	1	0	5 (20%)
Hypocalcemia	3	2	0	5 (20%)
AST increased	2	1	0	3 (12%)
Hypokalemia	2	1	0	3 (12%)
Neurotoxicity*	1	2	0	3 (12%)
Hypertension	3	0	0	3 (12%)
Lung infection	2	0	0	2 (8%)
Hypoalbuminemia	2	0	0	2 (8%)
Supraventricular tachycardia	1	0	0	1(4%)
Papilledema	1	0	0	1 (4%)
Abdominal pain	1	0	0	1 (4%)
Death NOS**	0	0	1	1 (4%)
Fatigue	1	0	0	1 (4%)
Infections – other (fungemia)	0	1	0	1 (4%)
Sepsis	0	1	0	1 (4%)
Urinary tract infection	1	0	0	1 (4%)
Alk phos increased	1	0	0	1 (4%)
Ejection fraction decreased	1	0	0	1 (4%)
Fibrinogen decreased	1	0	0	1 (4%)
Hyperglycemia	0	1	0	1 (4%)
Hypoglycemia	1	0	0	1 (4%)
Pleural effusion	1	0	0	1 (4%)
Pleural hemorrhage	0	1	0	1 (4%)

Highest grade toxicity experienced by subject is reported in table. n=number of subjects who had the event; Alk phos = alkaline phosphatase; AST = aspartate aminotransferase. *Neurotoxicity includes 1 subject with grade 3 seizures, grade 4 delirium, and grade 4 reversible posterior leukoencephalopathy syndrome (RPLS) (also known as posterior reversible encephalopathy syndrome (PRES)); 1 subject with grade 3 delirium and grade 4 encephalopathy; and 1 subject with grade 3 encephalopathy. **Death

NOS (not otherwise specified) in subject 08 with candidemia and rapidly progressive myeloma; family chose to pursue comfort measures only.

Neurotoxicity was seen in 7/25 subjects (28%), and was mild (grade 1/2) in 4 (transient confusion and/or aphasia). Three (12%) had grade 3/4 encephalopathy including 1 subject (03) in cohort 1 with a DLT of PRES (posterior reversible encephalopathy syndrome) with severe obtundation, recurrent seizures and mild cerebral edema on MRI (magnetic resonance imaging) that fully resolved after treatment with high-dose methylprednisolone (1 g/day x 3) and cyclophosphamide 1.5 g/m^2. The others had no objective changes on MRI. All 3 subjects with severe neurotoxicity had high tumor burden (2 with extramedullary disease); had received a dose of 5 x 10^8 CART-BCMA cells; and had grade 3 or 4 CRS. The only other DLT was grade 3 cardiomyopathy and grade 4 pleural hemorrhage/spontaneous hemothorax in subject 27 (cohort 3) in the setting of CRS, coagulopathy, thrombocytopenia, and extensive myelomatous rib lesions; all these toxicities fully resolved. One subject (08) who had grade 4 encephalopathy and CRS initially improved with tocilizumab and steroids, then developed candidemia and progressive myeloma/evolving plasma cell leukemia. Family opted for comfort care and he expired at day 24. No other deaths occurred on study. No unexpected off-target toxicities were observed.

Regarding clinical outcomes, objective responses (partial response (PR) or better) were confirmed in 4/9 subjects (44%) in cohort 1, 1/5 (20%) in cohort 2, and 7/11 (63%) in cohort 3 (FIGs. 47A-47C), including 5 PR, 5 very good partial responses (VGPR), 1 complete response (CR), and 1 stringent complete response (sCR). Thus overall response rate was 12/25 (48%), and was 11/20 (55%) at the more effective dose of 1-5 x 10^8 CART-BCMA cells. Five additional subjects had minimal response (MR). Four of 7 subjects with extramedullary disease responded (FIG. 32B). Four subjects (01, 03, 15, 19) had no detectable myeloma (i.e. MRD-negative) by flow cytometry (estimated sensitivity 10^{-5}) from post-infusion marrow aspirates at months 1 and/or 3. Median time to first response was 14 days. Based on Kaplan-Meier estimates, median duration of response (for PR or better) was 124.5 days (range 29 – 939+) (FIG. 53A). At time of data cut-off, 3 subjects (01, 19, 33) remained progression free at 953, 427, and 322 days (roughly 32, 14, and 11 months), respectively. All other subjects have progressed, and median progression-free survival (PFS) is 65, 57, and 125 days for cohorts 1, 2, and 3, respectively (FIG. 53C). At time of data cut-off, 13 subjects had expired, with median

overall survival of 502 days for all subjects (FIG. 53B), and 359 days, 502 days, and not reached for cohorts 1, 2, and 3, respectively (FIG. 47D).

All infused subjects had detectable CART-BCMA cells in peripheral blood by qPCR (FIGs. 48A-48C), and 24/25 had detectable CAR+ T cells by flow cytometry (FIGs. 54A-54C; FIG. 38 for representative staining). Expansion generally peaked at day 10-14, and appeared most uniform in cohort 3 with Cy conditioning and the higher dose of CART-BCMA cells, while it was more heterogeneous in cohorts 1 and 2, though this difference did not meet statistical significance (FIG. 48D). Despite a predominance of CD4+ T cells in the infused product, CART-BCMA cells circulating in blood were predominantly CD8+, and were highly activated, with a median of 94% (range 21 – 94%) of CAR+CD3+ cells expressing HLA-DR during peak expansion (Table 45). CART-BCMA levels in marrow aspirates generally mirrored those in peripheral blood, and also were elevated in pleural fluid and cerebrospinal fluid for subject 03, and pleural fluid from subject 27, demonstrating widespread trafficking (Table 46). Following peak expansion, CART-BCMA cell levels by qPCR declined in a log-linear fashion in the majority of patients (FIGs. 48A-48C), and were still detectable at 3 months post-infusion in 20/20 (100%) subjects tested, and at 6 months in 14/17 (82%) tested. Subject 01 (in stringent CR) continued to have detectable cells by qPCR when last tested at 2.5 years post-infusion.

Thirty cytokines were quantified in peripheral blood serum before and after CART-BCMA infusion. Nineteen of these were increased >5-fold over baseline in more than 1 subject, with the most frequent increases observed for IL-6, IL-10, monokine induced by interferon-gamma (MIG, CXCL9), IP-10, IL-8, GM-CSF, and IL-1 receptor antagonist (IL-1RA) (FIG. 55). More severe CRS (Grade 3/4, or Grade 2 receiving tocilizumab) was associated with increases in multiple cytokines (Table 47), most significantly with IL-6, IFN-γ, IL-2 receptor alpha (IL2-Rα), macrophage inflammatory protein 1 alpha (MIP-1α), and IL-15 (FIGs. 49A-49E). Neurotoxicity was most strongly associated with increases in IL-6, IFN-γ, IL-1RA and MIP-1α, (FIGs. 49F-49I, see Table 48 for full analysis). Significant differences were not observed in peak fold cytokine increases between Cohorts 1 and 3, which received the same dose of CART-BCMA cells with or without Cy conditioning, respectively (FIG. 55).

Serum concentration of sBCMA, as well as its ligands BAFF and APRIL, were also assessed. Compared to a panel of healthy donors (HD), enrolled subjects had significantly elevated sBCMA and reduced APRIL levels at baseline, with high variability amongst subjects

(FIG. 50A). BAFF concentrations in subjects were not significantly different from HD. Serial assessments of serum sBCMA showed decreases following CART-BCMA infusions, which were more pronounced in responding compared to non-responding subjects (FIG. 50B), and which increased as subjects developed progressive disease, suggesting that serum sBCMA concentration may be a useful adjunctive biomarker for assessing myeloma disease burden.

Twenty subjects were evaluable for BCMA surface expression on MM cells by flow cytometry performed on fresh marrow aspirates prior to treatment, and all had detectable BCMA expression, though intensity varied (median mean fluorescence intensity (MFI)=3741, range 206 – 24842; see FIG. 42 for representative gating). Of 18 subjects with evaluable serial BCMA expression (FIG. 50C), either at 1 month (n=16), 3 months (n=8), and/or 5.5 months (n=1), 12 (67%) had a decline in BCMA intensity at least at 1 post-infusion time-point, including 8/9 responders and 4/9 non-responders (FIG. 50D). BCMA intensity was lowest on residual MM cells 1 month post-CART-BCMA, and increased back toward baseline in most, but not all, subjects with subsequent testing. Individual subject details are provided in Table 49.

Responses were significantly associated with peak expansion by qPCR (median 75339 copies/µg DNA for ≥PR vs. 6368 copies/µg for <PR, p=0.0002), as well as with persistence over the first 28 days, as measured by the area under the curve ($AUC_{0\text{-}28d}$) (median 561796 copies*days/µg DNA for ≥PR vs. 52391 copies*days/µg DNA for <PR, p=0.0002) (FIGs. 51A-51B). Both expansion and response were more likely in the setting of more severe CRS (grade 3/4 or grade 2 requiring tocilizumab) (FIGs. 51C-51D). Neither expansion nor response were significantly associated with age, years from diagnosis, number of prior lines of therapy, presence of del17p or *TP53* mutation, being penta-refractory, most recent therapy pre-pheresis, bone marrow MM cell percentage, baseline serum sBCMA concentration, or MM cell BCMA intensity (FIGs. 56A-56L and 57A-57L).

In order to explore other pre-treatment characteristics potentially associated with expansion and/or response, features of the CART-BCMA product before, during, and at end of manufacturing were analyzed. It was found that a higher CD4/CD8 T cell ratio in the leukapheresis product, pre-manufacturing, was associated with greater *in vivo* CART-BCMA expansion (FIG. 51E), and to a lesser degree, response (FIG. 51F), while absolute CD3+, CD4+, or CD8+ T cell numbers in the leukapheresis product, or CD4/CD8 ratio in the final CART-BCMA product at end of manufacturing was not (data not shown). Fold expansion of

seeded cells during manufacturing also correlated with *in vivo* CART-BCMA expansion (FIG. 51G), suggesting that *in vitro* proliferative capacity may predict for *in vivo* activity. Finally, CD8+ T cells within the leukapheresis products in subjects treated with CART-BCMA cells were examined and it was found that subjects with higher frequencies of CD27+CD45RO-CD8+ T cells were more likely to have robust *in vivo* expansion and clinical response (FIGs. 51H-51I).

Discussion

CAR T cell therapy is emerging as a promising therapeutic option for B-cell malignancies, with the potential for durable disease control following a single treatment, differentiating it from other therapies that require repeated and/or continuous administration. In this report, the potential of CAR T cell therapy was demonstrated in advanced refractory myeloma, with 12/25 subjects (48%) achieving a partial response or better, including 7/11 (63%) treated at optimal doses (>10^8 CART-BCMA cells) following lymphodepleting chemotherapy. Three subjects had ongoing remissions >11 months after CART-BCMA therapy, including one ongoing sCR at 2.5 years. This is notable given the highly adverse biological features of the enrolled subjects' myeloma, including high tumor burden, rapidly progressing disease, and high-risk genetics. This clinical activity further validates BCMA as a highly attractive target in myeloma. Importantly, this activity was seen despite the fact that this study, unlike the previous study, did not exclude patients with low BCMA expression or high tumor burden, and used either no lymphodepletion or Cy alone, compared with Cy + fludarabine in the prior study (Ali SA, et al., Blood 2016; 128(13): 1688-700; Brudno JN, et al., J Clin Oncol 2018; 36(22): 2267-80). CAR T cell products were successfully manufactured from all subjects, despite baseline T cell lymphocytopenia, and engraftment was seen in all as well, though peak levels and persistence of CAR T cells varied significantly amongst subjects.

In this study, responses correlated with degree of *in vivo* expansion, which in turn was associated with higher pre-manufacturing CD4/CD8 T cell ratio, pre-manufacturing frequency of CD45RO-CD27+CD8+ T cells, and magnitude of *in vitro* proliferation during manufacturing. This suggests that more effective CART-BCMA products may be derived from subjects with a less differentiated, more naïve and/or stem cell memory-like T cell compartment. These data suggest that pre-treatment phenotypic and/or functional T cell characteristics may aid in the prediction of response to CART-BCMA therapy. They also suggest that treatment of patients earlier in the course of their disease, when T cells may be

intrinsically "fitter," or modifying manufacturing techniques to generate more phenotypically favorable CAR+ T cells, may be more effective.

Successful adoptive transfer of tumor-specific T cells, including CAR T cells, in humans has most commonly followed some form of lymphodepleting conditioning (Turtle CJ, et al., Sci Transl Med 2016; 8(355): 355ra116; Maude SL, et al., N Engl J Med 2014; 371(16): 1507-17; Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139; Dudley ME, et al., J Clin Oncol 2008; 26(32): 5233-9), which has been demonstrated to enhance T cell-mediated anti-tumor immunity via multiple potential mechanisms, including reduction of cellular "sinks" leading to increased availability of homeostatic cytokines, and depletion of suppressor cell populations such as regulatory T cells, among others (Gattinoni L, et al., Nat Rev Immunol 2006; 6(5): 383-93). This study demonstrates that lymphodepletion is not absolutely required for robust and sustained CAR T cell expansion and clinical activity, as seen with subjects 01 and 03 in Cohort 1. However, short-term expansion was observed more consistently in Cohort 3, where subjects received Cy conditioning, compared to Cohort 1 (FIGs. 48A and 48C), demonstrating an effect of lymphodepletion on CAR-T cell kinetics following adoptive transfer. It is possible that modifying the lymphodepletion (e.g. adding fludarabine to Cy) may further augment the activity of CART-BCMA cells.

An important unanswered question for BCMA-targeted CAR T cells is whether there is a threshold of BCMA expression on MM cells required for optimal recognition and killing. In the previously-reported NCI trial, 52/85 (62%) of pre-screened bone marrow biopsies stained for BCMA by IHC met their pre-specified threshold for eligibility, meaning more than a third of potentially eligible MM patients would have been excluded (Ali SA, et al., Blood 2016; 128(13): 1688-700). This study did not require any specific level of BCMA as an eligibility requirement, and identified MM cell BCMA expression by flow cytometry in all subjects, consistent with recent data that flow cytometry is more sensitive than IHC for this purpose (Salem DA, et al., Leuk Res 2018; 71: 106-11). Baseline BCMA intensity by flow cytometry did not correlate with either expansion or response in this study (FIGs. 56A-56L and 57A-57L), suggesting that excluding patients based on baseline BCMA expression is likely not necessary.

The observed dynamics of BCMA surface expression on MM cells, with the residual MM cells from several subjects in this study having significantly diminished BCMA intensity following CAR T cell therapy (FIGs. 50A-50D), highlights an important area for future research into resistance to CART-BCMA therapy. Down-modulation of BCMA expression

was also observed in at least 1 subject in the NCI study (Brudno JN, et al., J Clin Oncol 2018; 36(22): 2267-80), suggesting that it may be a common means of MM cell escape from BCMA-directed CAR-T cell therapies. Surface BCMA expression subsequently increased in most subjects upon progression, suggesting a transcriptional or post-translational mechanism, such as increased shedding from the cell surface. Alternatively, there may be immune selection for BCMA-dim/negative clonal variants, which are subsequently outcompeted by residual BCMA+ clones upon loss of CART-BCMA cells. This suggests that most patients progressing after CART-BCMA will remain candidates for additional BCMA-targeted therapies.

The primary toxicities of CAR T cells remain cytokine release syndrome (CRS) and neurotoxicity. The frequency and severity of CRS in this study was similar to that reported in CD19-targeted CAR T cell trials (Maude SL, et al., N Engl J Med 2014; 371(16): 1507-17; Porter DL, et al., Sci Transl Med 2015; 7(303): 303ra139), and was abrogated with IL-6 receptor blockade therapy. Though patient numbers are small, peak serum cytokine increases did not appear to differ significantly with or without Cy lymphodepletion, when CAR T cell dose was kept the same (Cohort 1 vs. 3, FIG. 55). Interestingly, however, median peak fold-increases of IL-6 and several other cytokines (e.g. IFN-γ, IL-10, GMCSF, IL-17) in this study were 1 to 2 orders of magnitude lower than that reported in the NCI BCMA CAR T cell study (Brudno JN, et al., J Clin Oncol 2018; 36(22): 2267-80), despite a higher tumor burden in this study. One explanation for this difference may be the co-stimulatory domains used within the 2 CAR constructs, since CD28 domains, such as that used in the NCI CAR construct, have been associated with more rapid CAR T cell proliferation and cytokine release than 4-1BB domains (Milone MC, et al., Mol Ther 2009; 17(8): 1453-64), as used in this CAR construct. However, the small numbers of patients and multiple differences between the studies with regards to inclusion criteria, dose, schedule, and lymphodepletion regimen preclude definitive conclusions.

Neurotoxicity has been reported in up to 50% of subjects in some CAR T cell trials (Turtle CJ, et al., Sci Transl Med 2016; 8(355): 355ra116; Turtle CJ, et al., J Clin Invest 2016; 126(6): 2123-38; Kochenderfer JN, et al., J Clin Oncol 2015; 33(6): 540-9); can occur concurrently with or subsequent to CRS; often does not improve with tocilizumab; and is reversible in most, but not all, cases. Neurotoxicity has been associated with early onset of CRS and rapid elevation of inflammatory cytokines both within the serum and CNS, perhaps leading to increased CNS vascular permeability (Gust J, et al., Cancer Discov 2017).

Consistent with this, this study identified peak serum increases of IL-6, IFN-γ, and MIP-1α as most associated with neurotoxicity in this study (FIGs. 49A-49I). Interestingly, neurotoxicity was also associated with peak fold increase in IL-1RA, an endogenous inhibitor of the pro-inflammatory effects of IL-1α and IL-1β, which have been implicated in CAR T cell-associated neurotoxicity (Giavridis T, et al., Nat Med 2018; 24(6): 731-8; Norelli M, et al., Nat Med 2018; 24(6): 739-48). This perhaps reflects induction of an (ultimately ineffective) feedback mechanism in patients with neurotoxicity, and suggests that augmenting IL-1 blockade via the recombinant IL-1RA anakinra may have therapeutic benefit in this setting, as demonstrated in pre-clinical models (Giavridis T, et al., Nat Med 2018; 24(6): 731-8; Norelli M, et al., Nat Med 2018; 24(6): 739-48). This study demonstrating rapid reversal of a PRES-like syndrome in subject 03 suggests that cyclophosphamide may also be an option in steroid-refractory cases.

In summary, autologous T cells expressing a fully human BCMA-specific CAR could expand and induce objective responses, both with and without lymphodepleting chemotherapy, in subjects with advanced, refractory MM, and represent a promising new therapeutic approach. The toxicity profile appears similar to that seen with CD19-directed CAR T cells in B-cell malignancies. Challenges include disease progression during manufacturing, potential for antigen escape due to changes in BCMA expression, and durability of responses. Subsequent studies exploring less heavily-pretreated/refractory patient populations, dual-antigen-targeting CAR constructs, novel lymphodepletion regimens or manufacturing protocols, and off-the-shelf CART products may further optimize the safety and long-term efficacy of this approach.

Supplementary Methods

Reagents and protocols for flow cytometry: Antibodies for CAR T cell detection panels were anti-CD45 V450 (clone HI30), anti-CD14 V500 (clone M5E2), anti-CD56 Ax488 (clone B159), anti-CD4 PerCP-Cy5.5 (clone RPA-T4), anti-CD8 APC-H7 (clone SK1) (all from BD Bioscience). Also, anti-CD3 BV605 (clone OKT3), anti-HLA-DR BV711 (clone L243), anti-CD19 PE-Cy7 (clone H1B19) were used from Biolegend. CART-BCMA expression was assessed by using a bis-biotinylated BCMA-Fc recombinant protein and the secondary staining reagent Streptavidin-PE from BD Bioscience (cat#554061). Cells were resuspended in 100 µL PBS containing 1% fetal bovine serum, 0.02% sodium azide and bis-biotinylated BCMA-Fc and incubated for 30 min on ice, washed, resuspended in 100 µL PBS containing 1% fetal bovine serum, 0.02% sodium azide, surface antibodies and SA-PE, and incubated for 30

minutes on ice, washed, resuspended in 250ul PBS containing 1% fetal bovine serum and 0.02% sodium azide and acquired using a Fortessa flow cytometer equipped with a violet (405 nm), blue (488 nm), a green (532 nm), and a red (628 nm) laser. Data were analyzed using FlowJo software (Version 10, Treestar). Compensation values were established using eBioscience UltraComp eBeads (eBioscience cat#01-222-42) and DIVA software.

Quantitative PCR: Genomic DNA was isolated directly from whole blood or marrow aspirate, and qPCR analysis was performed using ABI TaqMan technology and a validated assay to detect the integrated CAR transgene sequence as described in Kalos M, et al., Sci Transl Med 2011; 3(95): 95ra73 using triplicates of 200 ng of genomic DNA per time point for peripheral blood and marrow samples. To determine copy number per unit DNA, an eight-point standard curve was generated consisting of 5 to 106 copies of lentivirus plasmid spiked into 100 ng of non-transduced control genomic DNA. The number of copies of plasmid present in the standard curve was verified using digital qPCR with the same primer/probe set and performed on a QuantStudio 3D digital PCR instrument (Life Technologies). Each datapoint (sample and standard curve) was evaluated in triplicate with a positive Ct value in three of three replicates with percent coefficient of variation of less than 0.95% for all quantifiable values. To control for the quality of interrogated DNA, a parallel amplification reaction was performed using 20 ng of genomic DNA and a primer/probe combination specific for a non-transcribed genomic sequence upstream of the CDKN1A (p21) gene as described in Kalos M, et al., Sci Transl Med 2011; 3(95): 95ra73. These amplification reactions generated a correction factor to adjust for calculated versus actual DNA input. Copies of transgene per microgram of DNA were calculated according to the formula: copies per microgram of genomic DNA = (copies calculated from CART-BCMA standard curve) × correction factor/(amount DNA evaluated in nanograms) × 1000 ng.

Measurement of serum cytokines: Human cytokine magnetic 30-plex panel (LHC6003M) was from Life Technologies. Serum samples collected at baseline and at scheduled time-points out until 28 days post-infusion were cryopreserved at -80°C. Batched samples were thawed and analyzed according to the manufacturers' protocols. Assay plates were measured using a FlexMAP 3D instrument, and data acquisition and analysis were done using xPONENT software. Data quality was examined based on the following criteria. The standard curve for each analyte has a 5P R^2 value > 0.95 with or without minor fitting using xPONENT software. To pass quality control, the results for an in-house control serum needed

to be within the 95% of CI (confidence interval) derived from historical in-house control data for >25 of the tested analytes. No further tests were done on samples with results out of range low (<OOR). Samples with results that were out of range high (>OOR) or greater than two times the standard curve maximum value (SC max) were re-tested at higher dilutions. Results that passed the above quality controls or retests were reported.

Measurement of soluble BCMA, BAFF, and APRIL: Antibody sets for human BCMA (DY193), APRIL (DY884B) and BAFF (DT124-05) were from R&D Systems. ELISA bead-strip and 4-column reservoir (SOW-A16735) were from Assay Depot. ELISA substrate ADHP (10010469) was from Cayman Chemical. Assay plates (OX1263) were from E&K Scientific. All ELISA reagents were prepared according to the protocols for DuoSet ELISA except for Color Reagent B, which was supplemented with ADHP at 100 uM. Due to limited volumes of sera and lack of availability of a Luminex assay for BCMA, APRIL and BAFF, the three analytes were measured using ELISA bead-strips. Instead of coating the capture antibody (cAB) to the wells of an ELISA plate, it was coated on the surfaces of macrospheres, which enabled the measurement of all three analytes using 100ul of serum. Assays were set up using bead-strips in assay plates based on an assay map following the protocol for antibody sets. At the end of the assay, one substrate plate per 12 bead-strips was prepared by adding 100 ul/well of substrate solution (1:1 of color reagent A and ADHP). Each bead-strip was placed in one column of the substrate plate according to the assay map. Color development was for 10 to 30 minutes. Plates were read on a FLUO STAR OMEGA instrument. Data quality control was performed as described for Luminex data.

Assessment of bone marrow myeloma cells, including BCMA expression: Flow cytometry assessment of bone marrow aspirate material was performed directly on aspirate following a brief ammonium chloride red blood cell lysis step. The procedure was adapted from the EuroFlow protocol as described in Flores-Montero J, et al., Leukemia 2017; 31(10): 2094-103. Briefly, up to 2mls of bone marrow aspirate was diluted with 48mls of Pharm Lyse solution (BD Biosciences Cat# 555899) and incubated for 15 minutes at room temperature on a shaking device. The cells were then collected by centrifugation for 10 minutes at 800g, washed twice with flow cytometry buffer (PBS with 1% fetal bovine serum), stained with L/D Aqua viability dye (Thermo Fisher Cat# L34957). Surface staining was done with a mixture of antibodies to CD45, CD19, CD138, CD38, CD14, CD56, CD20, CD3, CD269 (BCMA), CD274 (PD-L1). FMO (fluorescence minus one) secondary only controls were used for

BCMA evaluation. Aliquots of normal donor PBMC cells were stained in parallel as controls. The cells were then washed before permeabilization/fixation using Cytofix/Cytoperm reagent (BD Biosciences) for 20 minutes at room temperature, washed, and stained with a mixture of antibodies to kappa and lambda immunoglobulin light chains. The samples were then washed before resuspension in PBS and acquisition on a 17-color LSR Fortessa Special Order Research Product flow cytometer (BD) equipped with a violet, blue, green, and red laser. List mode files were analyzed using either FlowJo (Treestar) or FCS Express.

Table 42. Individual subject characteristics

Sub.	Age	Sex	Race	Yrs from Dx	Iso-type	Karyo-type	FISH	Mutation	# lines *	Last tx before pheresis, infusion**
Cohort 1										
01	66	M	white	9.6	IgGK	46XY	+11, -16q, -17p	*NRAS, TP53, TP53*	11	Pom/Dex Pom/Dex
02	68	M	white	6.3	IgAK	46XY	+1q, +4p, -17p	n/a	9	Carfilz/Len/Dex Carfilz/Cyclo/Dex
03	54	F	white	3.1	IgAL	n/a	+1q, t(4;14), -16q	n/a	4	D-PACE D-AC
07	44	M	white	1.8	K	n/a	+1q, -4, +11, -14, -16	*NRAS, TP53*	9	Carfilz/Pano Pom/Dex-ACE
08	70	M	white	3.3	IgAL	complex	+1q, -1p, -4, -17p	n/a	6	Carfilz/Pom/Dex Carfilz/Pom/Dex
09	61	M	white	6.6	K	46XY	t(11;14), -16q, -17p	none	9	Daratumumab Pulse Dex
10	47	M	white	4.9	IgGL	n/a	+1q, t(11;14)	*KRAS, SF3B1*	7	Pom/Dex Pom/Cyclo/Dex + plasma exchange
11	57	F	AA	6.3	IgGL	46XX	+1q, t(4;14), -17p	n/a	10	VDT-PACE VDT-PACE
15	51	F	Asian	4.7	IgAK	46XX	+1q, t(11;14)	*NRAS, KRAS, BIRC3, KIT*	7	Pembro/Pom/Dex Pom/Dex
Cohort 2										
12	51	F	white	2.8	IgAL	46XX	+1q,	*TET2*	5	CyBorD CyBorD

							-1p, t(4;14), +17p			
13	59	M	white	9.4	IgGL	46XY	+11, -16q, -17p	n/a	10	Salvage ASCT VD-CE
14	54	F	white	4.9	IgGK	46XX	t(11;14), -16q, -17p	n/a	7	Venetoclax none
16	54	M	white	4.1	IgGK	complex	+1q, -16q, -17p	*BRAF*	7	D-CE D-CE + radiation
22	45	M	white	2.7	IgGL	46XY	t(11;14), +1q, -17p	*n/a*	7	D-ACE none
Cohort 3										
17	64	F	white	5.0	IgAK	46XX	t(14;16), +1q, -1p, +11	n/a	7	CPI-610 D-AC
19	58	M	white	4.1	L	46XY	r(11;14), +1q, +17, -17p	n/a	5	Dara/Ixa/Pom/Dex Dara/Ixa/Pom/Dex
20	61	M	white	2.6	IgGL	n/a	t(4;14), +1q, -17p	n/a	6	Carfilz/cyclo/pom/dex VD-AC
21	73	M	white	2.5	IgAK	46XY	+1q, +14, +17, -17p	*TET2*	5	Dara/Pom/Dex Bort/Pom/Dex
23	63	M	white	2.3	IgGK	46XY	none	none	6	Carfilz/Pom/Dex/Nelfin VD-PCE
25	51	M	AA	4.5	IgGK	46XY	t(11;14), +1q	*FLT3*	7	Selinexor/Dex Bort/Venetoclax/Dex + XRT
27	58	F	AA	10.3	IgGK	complex	t(11;14), +1q, -1p, -16, -17p	*BRAF, TET2*	13	Carfilz/Venetoclax/Dex Carfilz/Venetoclax/Dex
29	60	F	white	1.8	IgGK	45X,-X	none	*TET2, RB1, TP53*	3	VDT-PACE none
32	65	F	white	14.5	IgGL	46XX	t(4;14), +1q, -17	*TET2, TET2*	6	Carfilz/Cyclo/Dex Carfilz/Cyclo/Dex

33	75	M	white	8.8	IgGK	hyperdi p	+5, +9, +11, +15, -17p	*RAD21*	5	Pembro/Len/Dex none
34	47	M	white	2.0	IgGL	46XY	+1q, -1p, +14q	*MYCN, TPMT*	4	Carfilz/Pom/Dex VD-PACE

*A line of therapy was defined as per IMWG criteria. Radiation was not counted as a line. **Most recent therapy received before T cell collection ("pheresis" – top line) and CART-BCMA infusion ("infusion" – bottom line). All therapy was held for at least 2 weeks prior to pheresis and again for at least 2 weeks prior to infusion (4 weeks for monoclonal antibodies). AA = African-American; ASCT = autologous stem cell transplant; Bort = bortezomib; Carfilz = carfilzomib; cyclo = cyclophosphamide; CPI-610 = investigational BET inhibitor; CyBorD = cyclophosphamide, bortezomib, dexamethasone; D-AC = dexamethasone + infusional doxorubicin and cyclophosphamide; D-ACE = dexamethasone + infusional doxorubicin, cyclophosphamide, and etoposide; D-CE: dexamethasone + infusional cyclophosphamide and etoposide; D-PACE = dexamethasone + infusional cisplatinum, doxorubicin, cyclophosphamide, and etoposide; Dara = daratumumab; Dex = dexamethasone; Dx = diagnosis; hyperdip = hyperdiploid; ixa = ixazomib; K = kappa light chain; L = lambda light chain; Len = lenalidomide; Nelfin = nelfinavir; Pano = panobinostat; Pembro = pembrolizumab; Pom = pomalidomide; Pom/Dex-ACE = pomalidomide, dexamethasone + infusional doxorubicin, cyclophosphamide, and etoposide; Tx = treatment; VD-AC = bortezomib, dexamethasone + infusional doxorubicin and cyclophosphamide; VD-CE = bortezomib, dexamethasone + infusional cyclophosphamide and etoposide; VD-PCE = bortezomib, dexamethasone + infusional cisplatinum, cyclophosphamide, etoposide; VDT-PACE = bortezomib, dexamethasone, thalidomide + infusional cisplatinum, doxorubicin, cyclophosphamide, and etoposide; Yrs = years.

Table 43. CART-BCMA manufacturing and product details

Sub.	%CD3+ in seed culture	CD4: CD8 in seed culture	%CD3+ at harvest	CD4: CD8 at harvest	Fold exp	Pop dblgs	Trans Eff (%)	Total #CAR+ given (x 10^8)	Best re-sponse
Cohort 1									
01	52.6	2.04	98.4	2.40	43.5	4.54	9.6	2.0*	sCR
02	63	0.40	69.1	1.31	12.7	3.67	18.2	5.0	MR
03	58.4	2.47	97.6	1.72	17.9	4.16	25.9	2.0*	VGPR
07	20.3	1.47	94.9	1.60	38.9	5.28	24.2	5.0	PR
08	20.8	0.31	92.5	2.99	7.9	2.98	22.7	3.5	PD
09	86.8	0.49	87.5	1.69	10.0	3.33	22.2	5.0	SD
10	47.3	1.07	96.7	1.32	11.5	3.52	16.5	1.77	PD
11	21.4	0.81	96.9	1.20	8.7	3.11	19.4	5.0	MR
15	90.8	0.71	96	1.24	22.6	4.50	33.3	2.0*	VGPR
Cohort 2									
12	80	0.38	96.2	3.23	31.7	4.98	21.7	0.5	SD
13	72	0.50	86.9	1.72	14.0	3.84	24.2	0.5	MR
14	94.6	0.81	98.9	2.21	60.4	5.92	31.8	0.5	SD

16	50.9	1.06	98.1	0.84	30.6	4.94	21.9	0.5	PR
22	65.1	0.46	98.4	1.39	49.3	5.62	11	0.5	SD
Cohort 3									
17	84.4	0.59	97.3	1.87	56.8	5.83	27.4	5.0	PR
19	88.1	0.91	94.9	2.09	16.8	4.07	13.7	5.0	CR
20	70	0.70	97.4	2.17	32.3	5.02	8.4	5.0	VGPR
21	83.5	0.46	98.9	3.26	45.9	5.52	7.5	5.0	SD
23	74.7	0.42	97.6	1.46	45.1	5.77	11	5.0	MR
25	69.2	0.54	99	0.93	23.7	4.57	10.7	2.0*	PR
27	69	0.91	97.9	0.90	25.1	4.65	15	5.0	VGPR
29	29.8	2.49	91.7	4.55	23.0	4.52	8.3	5.0	SD
32	71	1.23	98.3	1.87	40.0	5.32	8.9	5.0	MR
33	83.6	0.33	96.5	1.78	31.1	4.96	8.6	5.0	PR
34	62.7	1.73	96.4	4.02	29.3	4.87	14.7	5.0	VGPR

Frequency of total CD3+, CD3+CD4+, and CD3+CD8+ cells was assessed by flow cytometry at the start of manufacturing ("seed culture," after elutriation), and at the end of manufacturing ("at harvest"). Aph = apheresis product; fold exp = fold expansion; pop dblgs = population doublings; trans eff = transduction efficiency. MR = minimal response; PD = progressive disease; PR = partial response; sCR = stringent complete response; SD = stable disease; VGPR = very good partial response

*Subjects 01, 03, 15, and 25 received only 40% of planned dose due to fevers/early CRS.

Table 44. Individual subject adverse events

Sub.	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Cohort 1					
01	Dry eye Dry mouth Vomiting Flu-like symptoms Metabolism disorder – other (iron deficiency) Myalgia Headache Ischemia cerebrovascular Nervous system disorder – other (confusion) Vascular disorder – other (edema)	DIC Vertigo Ileus Nausea Fever Lung infection Creatinine increased Thrombocytopenia Musculoskeletal disorder – other (generalized muscle aches) Urinary retention Respiratory disorder – other (pulmonary edema and atelectasis) Skin/SQ disorder – other (skin tear) Hypertension	Anemia Fatigue CRS Alk phos increased AST increased Hypocalcemia Hypokalemia Hypophosphatemia	Lymphopenia	
02	Sinus tachycardia Gastrointestinal disorders – other (loose stool) Nausea Fatigue CRS		Thrombocytopenia		

	Dizziness Headache Respiratory disorder – other (nasal and sinus congestion, cough)				
03	Sinus bradycardia Ear disorder – other (ears feel full, hard to hear) Eye disorder – other (difficulty reading) Constipation Edema Fever Hypokalemia Hypomagnesemia Bone pain Concentration impairment Headache Hoarseness Skin/SQ disorder – other (ecchymosis)	SVT Fatigue Infection – other (S. mitis/S. oralis bacteremia) Upper respiratory infection Lymphopenia Hypernatremia Musculoskeletal disorder – other (deconditioning, pain base of skull) Intracranial hemorrhage Respiratory disorder – other (post-nasal drip) Hypotension	CRS UTI Fibrinogen decreased Hypophosphatemia Seizure Pleural effusion Hypertension	Neutropenia Leukopenia Hypocalcemia RPLS Delirium	
07	Infection – other (upper respiratory infection) Skin/SQ disorder – other (rash on face)	CRS Dyspepsia Hypoalbuminemia Hypocalcemia Respiratory, thoracic disorders – other (hemothorax)	Anemia Hypokalemia Hyponatremia		
08	Sinus tachycardia General disorder – other (rigors)		Lung infection Delirium	CRS Thrombocytopenia Encephalopathy Infection – other (fungemia)	Death NOS
09	Constipation Chills Fatigue Thrombocytopenia Anorexia Hypokalemia	Anemia Pericardial effusion CRS Neutropenia Hypocalcemia Headache	Lung infection		
10	Chills Fever	Thromobocytopenia			
11	Nausea Fatigue Thrombocytopenia Headache Respiratory disorder – other (cough, congestion)	CRS Infection – other (Clostridium difficile) Hypocalcemia	Hypophosphatemia		
15	Hypocalcemia Hypokalemia Headache Cough Dyspnea	Fatigue CRS Infection – other (positive test for Shiga toxin)	Thrombocytopenia Hypoglycemia	Neutropenia	

	Respiratory disorders – other (nasal congestion) Alopecia	Alk phos increased Hypotension			
Cohort 2					
12	Anemia Vomiting Fatigue Fever Hypocalcemia	Infection – other (adenovirus)	Febrile neutropenia	Sepsis Neutropenia Leukopenia	
13	Diarrhea Fatigue ALT increased AST increased Anorexia Dizziness Pruritis Skin/subcutaneous tissue disorder – other (lesions on bilateral ears)	Upper respiratory infection	Neutropenia		
14	Back pain Pain in extremity	CRS	Anemia Febrile neutropenia	Neutropenia Leukopenia	
16	Colitis Hypocalcemia Hypokalemia Hypomagnesemia Paresthesia Confusion Hoarseness Sore throat Hypotension	Flu-like symptoms CRS Hypoalbuminemia Epistaxis	Febrile neutropenia	Lymphopenia Neutropenia Thrombocytopenia Leukopenia	
22	Fatigue Myalgia Insomnia	Nausea CRS	Febrile neutropenia	Lymphopenia Leukopenia	
Cohort 3					
17	Diarrhea Hypocalcemia Hypokalemia Back pain Headache Peripheral sensory neuropathy Insomnia	Chills CRS Arthralgia		Neutropenia Leukopenia	
19	Nausea Chills	Ear and labyrinth disorders – other (seasonal allergies) Gastrointestinal disorders – other (food poisoning) Fever Sinusitis Upper respiratory infection	CRS Lymphopenia Hypophosphatemia Hypertension		
20	Constipation Diarrhea	Fatigue ALT increased	CRS Hyponatremia	AST increased	

	Vomiting Chills CPK increased Hypokalemia Back pain Allergic rhinitis	Hypophosphatemia Dysphasia Lethargy Confusion Hypotension			
21	Alk phos increased Hypocalcemia Hyponatremia Epistaxis	CRS Skin disorders – other (cellulitis)	Lymphopenia Neutropenia Thrombocytopenia Leukopenia		
23	Anal hemorrhage Nausea Edema limbs Hypoalbuminemia Hypocalcemia Tremor	CRS Abdominal pain Colitis Diarrhea Vomiting Pain Thrombocytopenia Hypokalemia	Febrile neutropenia		
25	Nausea Facial pain Fatigue Hypomagnesemia Headache Peripheral sensory neuropathy	Hypoalbuminemia Hypokalemia Hypercalcemia	CRS Hypocalcemia Papilledema		
27	Diarrhea Nausea Oral pain Fatigue Pain Infections – other (upper respiratory infection) Back pain Myalgia Pain in extremity Dry skin Hematoma	Sinus bradycardia Edema limbs Urinary tract infection Creatinine increased Neutropenia Hypernatremia Wheezing	CRS SVT AST increased Ejection fraction decreased Lymphopenia Leukopenia Hypoalbuminemia Hyponatremia Encephalopathy Hypertension	Anemia Thrombocytopenia Hyperglycemia Hypocalcemia Hypokalemia Pleural hemorrhage	
29	Nausea Fatigue Pain Respiratory disorders – Other (scratchy throat, slight cough)	Chills CRS Hypoalbuminemia	Abdominal pain Hyponatremia Hypophosphatemia	Lymphopenia Leukopenia	
32	Nausea Fatigue Alopecia	Diarrhea Encephalopathy Allergic rhinitis	Anemia CRS Neutropenia Hypoalbuminemia Hypocalcemia Hyponatremia Hypophosphatemia	Lymphopenia Thrombocytopenia Leukopenia	
33	Oral pain Diarrhea Fatigue Flu-like symptoms Arthralgia	Chills CRS Hypoalbuminemia	Febrile neutropenia	Neutropenia	

	Flank pain Allergic rhinitis				
34	Diarrhea Nausea Sinus tachycardia Confusion ALT increased	CRS Thrombocytopenia Hypocalcemia Flu-like symptoms AST increased	Leukopenia Hypophosphatemia Hyopnatremia	Lymphopenia Neutropenia	

All events regardless of attribution are listed. If an event occurred more than once in same patient, highest grade is reported. Alk phos = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CPK = creatine phosphokinase; CRS=cytokine release syndrome; DIC = disseminated intravascular coagulation; NOS = not otherwise specified; RPLS = reversible posterior leukoencephalopathy syndrome (also known as posterior reversible encephalopathy syndrome (PRES)); SQ = subcutaneous; SVT = supraventricular tachycardia; UTI = urinary tract infection

Table 45. Characteristics of peripheral blood CART-BCMA+ cells at peak expansion

Sub.	Day of peak	%CAR+ of CD3+	%CAR+ of CD4+	%CAR+ of CD8+	%HLADR+ of CAR+	Best response
Cohort 1						
01	10	89.5	8.6	92.3	97	sCR
02	9	2.8	1.4	5.0	82	MR
03	14	76.2	13.7	85.9	97	VGPR
07	10	29.2	7.3	39.3	89	PR
08	16	9.3	0.4	16.9	95	PD
09	11*	*	*	*	*	SD
10	30	1.9	0.1	2.0	21	PD
11	8	18.2	14.6	25.2	94	MR
15	10	28.1	6.3	51.0	96	VGPR
Cohort 2						
12	10	2.0	0.8	2.3	76	SD
13	13	8.4	2.9	13.2	92	MR
14	10	7.8	3.5	10.6	95	SD
16	14	47.1	12.1	50.3	98	PR
22	9	4.3	0.6	8.6	94	SD
Cohort 3						
17	9	22.1	10.4	27.4	96	PR
19	15	9.7	8.9	10.2	87	CR
20	15	59.2	22.4	65.1	99	VGPR
21	9	16.0	9.2	19.9	97	SD
23	10	13.8	6.6	17.3	93	MR
25	10	5.1	3.8	5.9	85	PR
27	14	42.9	4.9	47.3	88	VGPR
29	7	4.1	2.8	15.0	77	SD
32	10	36.2	6.1	46.4	97	MR
33	11	41.8	29.8	46.9	91	PR
34	**	**	**	**	**	VGPR

CART-BCMA cells were assessed by flow cytometry as in Fig. 38. At day of peak expansion, the frequency of CAR+ cells within CD3+, CD4+, and CD8+ populations are listed. Activation status at peak expansion (as measured by % of CAR+ cells expressing HLA-DR) is also shown.

MR = minimal response; PD = progressive disease; PR = partial response; sCR = stringent complete response; SD = stable disease; VGPR = very good partial response
*Peak determined by qPCR; CAR+ cells not detectable by flow. **No sample available between days 10-21 so peak could not be determined.

Table 46. CART-BCMA engraftment by qPCR in blood, bone marrow, and other sites

Sub.	Day 28 blood	Day 28 BM	3 month blood	3 month BM	Other (site, day)
Cohort 1					
01	23447.33	10458.66	4373.95	n/a	n/a
02	454.57	383.62	334.90	n/a	n/a
03	220081.08*	109964.97*	9517.67	9934.97	CSF, D4: 3285.88 CSF, D16: 158038.74 Pleural fluid, D8: 23941.97 Pleural fluid, D18: 144516.62
07	1757.60	2140.31	n/a	n/a	n/a
08	n/a	n/a	n/a	n/a	n/a
09	32.15	16.75	n/a	n/a	n/a
10	62.64	0.00	n/a	n/a	n/a
11	731.44	n/a	218.26	n/a	n/a
15	724.49	1084.16	32.58	99.48	n/a
Cohort 2					
12	140.60	25.59	n/a	n/a	n/a
13	193.80	43.64	94.70	27.04	n/a
14	66.69	255.76	8.80	0.00	n/a
16	25919.10	22077.89	n/a	n/a	n/a
22	34.56	22.09	77.71	63.76	n/a
Cohort 3					
17	1639.98	1398.82	1392.25	649.69	n/a
19	12987.83	6578.03	153.88	117.53	n/a
20	43463.65	28086.46	4107.95	5223.76	n/a
21	8372.96	1161.92	96.11	n/a	n/a
23	5946.81	n/a	102.68	n/a	n/a
25	256.33	259.97	149.20	160.33	n/a
27	51014.95	41242.37	14271.48	9634.66	Pleural fluid, D15: 58511.99
29	738.84	210.05	n/a	n/a	n/a
32	6983.98	7055.94	58.15	15.72	n/a
33	7539.99	5142.13	230.66	39.09	n/a
34	5199.07	1512.03	n/a	n/a	n/a

CART-BCMA levels (copies/µg genomic DNA) were generally comparable in blood and marrow at tested timepoints. CART-BCMA was found at high levels in CSF and pleural fluid of subject 03, and pleural fluid of subject 27. BM = bone marrow; CSF = cerebrospinal fluid. n/a = not available. *Assays performed on day 45.

Table 47. Peak fold increase in serum cytokines and severity of cytokine release syndrome (CRS)

Cytokine	**Median peak fold increase: CRS Gr 0-2**	**Median peak fold increase: CRS Gr 3-4 or Gr 2 + toci**	**p-value**
IL-6	3.88	76.26	<0.0001

IFN-γ	1.26	11.95	<0.0001
IL-2Rα	4.13	18.40	<0.0001
MIP-1α	1.35	3.47	<0.0001
IL-15	1.71	12.81	0.0004
IL-1RA	2.33	19.68	0.0036
MCP-1	2.11	6.99	0.0044
GM-CSF	2.69	36.27	0.0052
IL-1β	1.28	2.23	0.0052
MIG	6.81	39.14	0.008
MIP-1β	1.49	2.39	0.013
IL-5	2.84	35.32	0.019
VEGF	1.93	3.68	0.022
IL-17	1.16	3.13	0.026
IL-7	2.24	6.18	0.10
IP-10	6.63	10.97	0.10
IL-8	8.65	30.72	0.20
IL-4	1.29	1.95	0.24
IL-10	13.84	15.82	0.53

Serum cytokine concentrations in pg/ml through day 28 were measured by Luminex assay. The median peak fold increase over baseline for each cytokine listed for subjects with no CRS, grade 1 CRS, or grade 2 CRS not receiving tocilizumab (CRS gr 0-2) was compared to median peak fold increase for subjects with grade 3-4 CRS or grade 2 CRS receiving tocilizumab (CRS Gr 3-4 or Gr 2 + toci). Exact p-value by Mann-Whitney test is listed when applicable.

Table 48. Peak fold increase in serum cytokines and neurotoxicity

Cytokine	Median peak fold increase: No neurotox	Median peak fold increase: Any neurotox	p-value
IL-6	3.92	76.26	0.0002
IFN-γ	1.28	15.77	0.0002
IL-1RA	2.33	19.68	0.0015
MIP-1α	1.53	3.47	0.006
GM-CSF	3.46	36.27	0.013
IL-15	1.76	10.54	0.016
IL-1β	1.32	3.70	0.018
IP-10	5.80	20.44	0.019
IL-7	3.29	10.28	0.019
IL-2Rα	4.46	20.86	0.019
VEGF	1.93	3.68	0.050
MIP-1β	1.56	2.24	0.056
MIG	7.17	39.14	0.057
MCP-1	2.13	6.41	0.066
IL-8	8.65	36.77	0.12
IL-17	1.32	1.57	0.19
IL-5	5.15	8.54	0.26
IL-4	1.47	2.20	0.40
IL-10	13.70	27.51	0.41

Serum cytokine concentrations in pg/ml through day 28 were measured by Luminex assay. The median peak fold increase over baseline for each cytokine listed for subjects with no

neurotoxicity (neurotox) was compared to median peak fold increase for subjects with any grade neurotoxicity. Exact p-value by Mann-Whitney test is listed.

Table 49. Details of BCMA expression on myeloma cells

Sub	Pre % +	Pre FMO MFI	Pre BCMA MFI	D28 % +	D28 FMO MFI	D28 BCMA MFI	D90 %+	D90 BCMA MFI	D90 BCMA MFI	Best response
Cohort 1										
01	95	568	10864	n/a	n/a	n/a	n/a	n/a	n/a	sCR
02	93	355	2375	97	483	3254	n/a	n/a	n/a	MR
03	84	265	1873	n/a	n/a	n/a	19*	78*	268*	VGPR
07	n/a	n/a	n/a	84	273	1426	n/a	n/a	n/a	PR
08	99	124	6859	n/a	n/a	n/a	n/a	n/a	n/a	PD
09	28	53	206	94	204	1116	n/a	n/a	n/a	SD
10	83	192	1998	99	54	2140	n/a	n/a	n/a	PD
11	81	332	1844	62	49	832	n/a	n/a	n/an	MR
15	99	249	24842	n/a	n/a	n/a	100	362	30685	VGPR
Cohort 2										
12	100	-142	6755	100	187	7268	n/a	n/a	n/a	SD
13	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	MR
14	99	192	4317	98	172	2388	n/a	n/a	n/a	SD
16	97	366	4039	48	394	850	93	488	3819	PR
22	100	321	5947	99	271	4947	100	126	5599	SD
Cohort 3										
17	87	646	2667	27	295	784	76	350	1543	PR
19	98	429	2923	65	316	992	n/a	n/a	n/a	CR
20	89	394	2643	29	369	944	36	185	377	VGPR
21	99	314	2704	86	252	1108	n/a	n/a	n/a	SD
23	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	MR
25	97	283	4000	54	259	833	92	223	2501	PR
27	100	618	6548	74	242	964	70	159	616	VGPR
29	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	SD
32	92	176	3482	85	169	1472	n/a	n/a	n/a	MR
33	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	PR
34	100	303	17109	92	1607	5001	100	309	11232	VGPR

Bone marrow myeloma cells were gated and BCMA expression analyzed as per FIG. 55. The percentage of myeloma cells expressing BCMA (% +), as well as the mean fluorescence intensity (MFI) for BCMA and FMO (fluorescence minus one) negative control are depicted. n/a = not available. Pre=pre-treatment. D28 = day 28 post-treatment. D90 = day 90 post-treatment. Sub = subject. *actually D164.

EQUIVALENTS

The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to specific aspects, it is apparent that other aspects and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention. The appended claims are intended to be construed to include all such aspects and equivalent variations.

What is claimed is:

1. A method of evaluating or predicting a subject's responsiveness to a BCMA CAR-expressing cell therapy, wherein the subject has a disease associated with the expression of BCMA, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

(a) an increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased responsiveness of the subject to the BCMA CAR-expressing cell therapy; or

(b) a decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy,

thereby evaluating or predicting the subject's responsiveness to the BCMA CAR-expressing cell therapy.

2. The method of claim 1, wherein the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

3. The method of claim 1 or 2, wherein the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

4. The method of any one of claims 1-3, wherein the value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) comprises a ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells), e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

5. The method of claim 4, wherein the ratio being:

(1) greater than or equal to 1 (e.g., between 1 and 5, e.g., between 1 and 3.5); or

(2) greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5),

is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

6. The method of claim 4 or 5, wherein the ratio being less than 1 (e.g., between 0.001 and 1) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

7. The method of any one of claims 1-6, wherein the value for the level or activity of CD8+ Tscm (stem cell memory T cells) comprises the percentage of CD8+ Tscm (stem cell memory T cells) among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

8. The method of any one of claims 1-7, wherein the value for the level or activity of HLADR-CD95+CD27+CD8+ cells comprises the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

9. The method of claim 8, wherein the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being greater than or equal to 25% (e.g., between 30% and 90%, e.g., between 35% and 85%, e.g., between 40% and 80%, e.g., between 45% and 75%, e.g., between 50% and 75%) is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

10. The method of claim 8 or 9, wherein the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being less than 25% (e.g., between 0.1% and 25%, e.g., between 0.1% and 22%, e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%)) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

11. The method of any one of claims 1-10, wherein the value for the level or activity of CD45RO-CD27+CD8+ cells comprises the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

12. The method of claim 11, wherein the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 20% (e.g., between 20% and 90%, e.g., between 20% and 80%, e.g., between 20% and 70%, e.g., between 20% and 60%) is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

13. The method of claim 11 or 12, wherein the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 20% (e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

14. The method of any one of claims 1-13, wherein the value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells comprises the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

15. The method of claim 14, wherein the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 15% (e.g., between 15% and 90%, e.g., between 15% and 80%, e.g., between 15% and 70%, e.g., between 15% and 60%, e.g., between 15% and 50%) is indicative or predictive of one, two, three, or all of:

(a) increased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

16. The method of claim 14 or 15, wherein the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 15% (e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%, e.g., between 0.1% and 8%) is indicative or predictive of one, two, or all of:

(a) decreased responsiveness of the subject to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

17. The method of any one of claims 1-16, wherein the value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy comprises the fold expansion of seeded cells from the subject during manufacturing (e.g., total cell counts at the end of manufacturing relative to at the start of manufacturing) of the BCMA CAR-expressing cell therapy, e.g., as measured by an assay disclosed herein, e.g., as measured by cell counting.

18. The method of any one of claims 1-17, further comprising performing:

manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, the BCMA CAR-expressing cell therapy to the subject, when:

(a) the subject was indicated or predicted to have increased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject was indicated or predicted as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject was indicated or predicted as suitable for the BCMA CAR-expressing cell therapy; or

(d) the BCMA CAR-expressing cell therapy was indicated or predicted to have increased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per μg DNA using qPCR.

19. The method of any one of claims 1-17, further comprising performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of the BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not the BCMA CAR-expressing cell therapy) to the subject;

administering the BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of the BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and

administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject, when:

(a) the subject was indicated or predicted to have decreased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject was indicated or predicted as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) the BCMA CAR-expressing cell therapy was indicated or predicted to have decreased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per μg DNA using qPCR.

20. A method of treating a subject having a disease associated with the expression of BCMA, comprising:

responsive to an increased value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of a BCMA CAR-expressing cell therapy,

as compared to a reference value, e.g., a non-responder reference value, performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject,

thereby treating the subject having the disease associated with the expression of BCMA.

21. A method of treating a subject having a disease associated with the expression of BCMA, comprising:

responsive to a decreased value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of a BCMA CAR-expressing cell therapy,

as compared to a reference value, e.g., a responder reference value, performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or

CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject,

thereby treating the subject having the disease associated with the expression of BCMA.

22. The method of claim 20, comprising: responsive to an increased value for one, two, three, four, five, or all of (i)-(vi), identifying or predicting one, two, three, or all of:

(a) the subject as having increased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject as a responder of the BCMA CAR-expressing cell therapy;

(c) the subject as suitable for the BCMA CAR-expressing cell therapy; or

(d) the BCMA CAR-expressing cell therapy as having increased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

23. The method of claim 21, comprising: response to a decreased value for one, two, three, four, five, or all of (i)-(vi), identifying or predicting one, two, or all of:

(a) the subject as having decreased responsiveness to the BCMA CAR-expressing cell therapy;

(b) the subject as a non-responder of the BCMA CAR-expressing cell therapy; or

(c) the BCMA CAR-expressing cell therapy as having decreased expansion in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

24. The method of any one of claims 20-23, wherein the value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) comprises a ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells), e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

25. The method of claim 24, comprising:

responsive to the ratio being:

(1) greater than or equal to 1 (e.g., between 1 and 5, e.g., between 1 and 3.5); or

(2) greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

26. The method of claim 24 or 25, comprising:

responsive to the ratio being less than 1 (e.g., between 0.001 and 1), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

27. The method of any one of claims 20-26, wherein the value for the level or activity of CD8+ Tscm (stem cell memory T cells) comprises the percentage of CD8+ Tscm (stem cell memory T cells) among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

28. The method of any one of claims 20-27, wherein the value for the level or activity of HLADR-CD95+CD27+CD8+ cells comprises the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

29. The method of claim 28, comprising:

responsive to the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being greater than or equal to 25% (e.g., between 30% and 90%, e.g., between 35% and 85%, e.g., between 40% and 80%, e.g., between 45% and 75%, e.g., between 50% and 75%), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

30. The method of claim 28 or 29, comprising:

responsive to the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells being less than 25% (e.g., between 0.1% and 25%, e.g., between 0.1% and 22%, e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

31. The method of any one of claims 20-30, wherein the value for the level or activity of CD45RO-CD27+CD8+ cells comprises the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

32. The method of claim 31, comprising:

responsive to the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 20% (e.g., between 20% and 90%, e.g., between 20% and 80%, e.g., between 20% and 70%, e.g., between 20% and 60%), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

33. The method of claim 31 or 32, comprising:

responsive to the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 20% (e.g., between 0.1% and 20%, e.g., between 0.1% and 18%, e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T

cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

34. The method of any one of claims 20-33, wherein the value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells comprises the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

35. The method of claim 34, comprising:

responsive to the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being greater than or equal to 15% (e.g., between 15% and 90%, e.g., between 15% and 80%, e.g., between 15% and 70%, e.g., between 15% and 60%, e.g., between 15% and 50%), performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject.

36. The method of claim 34 or 35, comprising:

responsive to the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells being less than 15% (e.g., between 0.1% and 15%, e.g., between 0.1% and 12%, e.g., between 0.1% and 10%, e.g., between 0.1% and 8%), performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy

using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject.

37. The method of any one of claims 20-36, wherein the value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy comprises the fold expansion of seeded cells from the subject during manufacturing (e.g., total cell counts at the end of manufacturing relative to at the start of manufacturing) of the BCMA CAR-expressing cell therapy, e.g., as measured by an assay disclosed herein, e.g., as measured by cell counting.

38. A method of evaluating or predicting the potency of a BCMA CAR-expressing cell therapy in a subject, wherein the subject has a disease associated with the expression of BCMA and wherein the BCMA CAR-expressing cell therapy is manufactured using cells (e.g., T cells) from the subject, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of

the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

(a) an increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased potency of the BCMA CAR-expressing cell therapy in the subject; or

(b) a decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased potency of the BCMA CAR-expressing cell therapy in the subject,

thereby evaluating or predicting the potency of the BCMA CAR-expressing cell therapy.

39. The method of claim 38, wherein the increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, is indicative or predictive of increased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

40. The method of claim 38 or 39, wherein the decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, is indicative or predictive of decreased expansion of the BCMA CAR-expressing cell therapy in the subject, e.g., as measured by an assay disclosed herein, e.g., as measured by the copy number of CAR transgenes per µg DNA using qPCR.

41. A method of manufacturing a BCMA CAR-expressing cell therapy, wherein the BCMA CAR-expressing cell therapy is manufactured using cells (e.g., T cells) from a subject, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

responsive to an increase in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a non-responder reference value, manufacturing the BCMA CAR-expressing cell therapy using cells from the subject.

42. A method of manufacturing a BCMA CAR-expressing cell therapy, wherein the BCMA CAR-expressing cell therapy is manufactured using cells (e.g., T cells) from a subject, comprising:

acquiring a value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the

start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy, e.g., as measured by population doublings by day 9 (PDL9), wherein:

responsive to a decrease in the value of one, two, three, four, five, or all of (i)-(vi), as compared to a reference value, e.g., a responder reference value, performing one, two, three, or all of:

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of the BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g.,

between 1.6 and 5, e.g., between 1.6 and 3.5), and manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject.

43. The method of any one of claims 38-42, wherein the value for the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) comprises a ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells), e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

44. The method of any one of claims 38-43, wherein the value for the level or activity of CD8+ Tscm (stem cell memory T cells) comprises the percentage of CD8+ Tscm (stem cell memory T cells) among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

45. The method of any one of claims 38-44, wherein the value for the level or activity of HLADR-CD95+CD27+CD8+ cells comprises the percentage of HLADR-CD95+CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

46. The method of any one of claims 38-45, the value for the level or activity of CD45RO-CD27+CD8+ cells comprises the percentage of CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

47. The method of any one of claims 38-46, wherein the value for the level or activity of CCR7+CD45RO-CD27+CD8+ cells comprises the percentage of CCR7+CD45RO-CD27+CD8+ cells among CD8+ T cells, e.g., as measured by an assay disclosed herein, e.g., flow cytometry.

48. The method of any one of claims 38-47, the value for the proliferation of seeded cells from the subject during manufacturing of the BCMA CAR-expressing cell therapy comprises the fold expansion of seeded cells from the subject during manufacturing (e.g., total cell counts at the end of manufacturing relative to at the start of manufacturing) of the BCMA CAR-expressing cell therapy, e.g., as measured by an assay disclosed herein, e.g., as measured by cell counting.

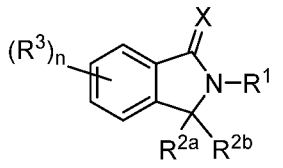
49. The method of any one of claims 1-48, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with one, two, or all of:

(1) an agent that increases the efficacy of the cell comprising the CAR nucleic acid or CAR polypeptide;

(2) an agent that ameliorates one or more side effects associated with administration of the cell comprising the CAR nucleic acid or CAR polypeptide;

(3) an agent that treats the disease associated with the expression of BCMA.

50. The method of any one of claims 1-49, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a compound of Formula (I) (COF1), wherein the COF1 is:



(I)

or a pharmaceutically acceptable salt, ester, hydrate, solvate, or tautomer thereof, wherein:

X is O or S;

R^1 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl, each of which is optionally substituted by one or more R^4;

each of R^{2a} and R^{2b} is independently hydrogen or C_1-C_6 alkyl; or R^{2a} and R^{2b} together with the carbon atom to which they are attached form a carbonyl group or a thiocarbonyl group;

each of R^3 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, $-C(O)R^A$, $-C(O)OR^B$, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, $-S(O)_xR^E$, $-S(O)_xN(R^C)(R^D)$, or $-N(R^C)S(O)_xR^E$, wherein each alkyl, alkenyl, alkynyl, and heteroalkyl is independently and optionally substituted with one or more R^6;

each R^4 is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, halo, cyano, oxo, $-C(O)R^A$, $-C(O)OR^B$, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, $-S(O)_xR^E$, $-S(O)_xN(R^C)(R^D)$, $-N(R^C)S(O)_xR^E$, carbocyclyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, heteroalkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently and optionally substituted with one or more R^7;

each of R^A, R^B, R^C, R^D, and R^E is independently hydrogen or C_1-C_6 alkyl;

each R^6 is independently C_1-C_6 alkyl, oxo, cyano, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, $-N(R^C)C(O)R^A$, aryl, or heteroaryl, wherein each aryl and heteroaryl is independently and optionally substituted with one or more R^8;

each R^7 is independently halo, oxo, cyano, $-OR^B$, $-N(R^C)(R^D)$, $-C(O)N(R^C)(R^D)$, or $-N(R^C)C(O)R^A$;

each R^8 is independently C_1-C_6 alkyl, cyano, -OR^B, -$N(R^C)(R^D)$, -$C(O)N(R^C)(R^D)$, or -$N(R^C)C(O)R^A$;

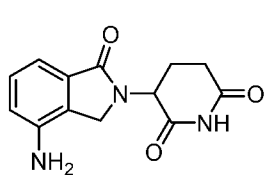
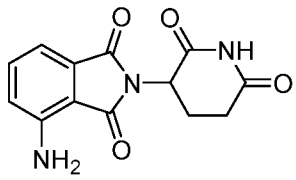
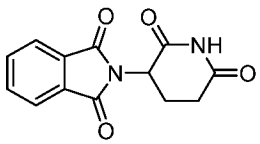
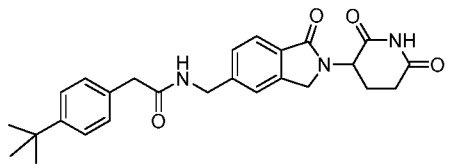
n is 0, 1, 2, 3 or 4; and

x is 0, 1, or 2, optionally wherein:

(1) the COF1 is an immunomodulatory imide drug (IMiD), or a pharmaceutically acceptable salt thereof;

(2) the COF1 is selected from the group consisting of lenalidomide, pomalidomide, thalidomide, and 2-(4-(tert-butyl)phenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)acetamide, or a pharmaceutically acceptable salt thereof;

(3) the COF1 is selected from the group consisting of:


,

,

, and

, or a pharmaceutically acceptable salt thereof; or

(4) the COF1 is lenalidomide, or a pharmaceutically acceptable salt thereof.

51. The method of any one of claims 1-50, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a kinase inhibitor, e.g., a BTK inhibitor, e.g., ibrutinib.

52. The method of any one of claims 1-51, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a second CAR-expressing cell therapy, optionally wherein the second CAR-expressing cell therapy is:

(1) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019, optionally wherein the CD19 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(2) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein, optionally wherein the CD20 CAR-expressing cell therapy is administered after the

administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(3) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein, optionally wherein the CD22 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(4) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein), optionally wherein the second CAR is selected from the group consisting of a CD19 CAR (e.g., a CD19 CAR disclosed herein), a CD20 CAR (e.g., a CD20 CAR disclosed herein), and a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(5) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to a first antigen and a second antigen, wherein the first antigen is BCMA, optionally wherein the second antigen is selected from the group consisting of CD19, CD20, and CD22.

53. The method of any one of claims 1-52, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a CD19 inhibitor, e.g., a CD19 inhibitor disclosed herein, optionally wherein the CD19 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

54. The method of any one of claims 1-53, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a CD20 inhibitor, e.g., a CD20 inhibitor disclosed herein, optionally wherein the CD20 inhibitor is a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338, optionally wherein the CD20 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

55. The method of any one of claims 1-54, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a CD22 inhibitor, e.g., a CD22 inhibitor disclosed herein, optionally wherein the CD22 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

56. The method of any one of claims 1-55, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a molecule that binds to Fc receptor like 2 (FCRL2) or Fc receptor like 5 (FCRL5), optionally wherein the molecule is:

(1) a CAR-expressing cell therapy comprising a cell expressing a CAR that binds to FCRL2 or FCRL5; or

(2) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to a first antigen and a second antigen, wherein the first antigen is FCRL2 or FCRL5, optionally wherein the second antigen is CD3.

57. The method of any one of claims 1-56, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an interleukin-15 (IL-15) polypeptide, an interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both an IL-15 polypeptide and an IL-15Ra polypeptide, e.g., hetIL-15.

58. The method of any one of claims 1-57, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an inhibitor of TGF beta.

59. The method of any one of claims 1-58, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an $EGFR^{mut}$-tyrosine kinase inhibitor (TKI), e.g., EGF816.

60. The method of any one of claims 1-59, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an adenosine A2AR antagonist, optionally wherein:

(1) the adenosine A2AR antagonist is selected from the group consisting of PBF509, CPI444, AZD4635, Vipadenant, GBV-2034, and AB928; or

(2) the adenosine A2AR antagonist is selected from the group consisting of 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine.

61. The method of any one of claims 1-60, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an anti-CD73 antibody molecule, e.g., an anti-CD73 antibody molecule disclosed herein.

62. The method of any one of claims 1-61, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with a check point inhibitor, optionally wherein the check point inhibitor is:

(1) a PD-1 inhibitor, optionally wherein the PD-1 inhibitor is selected from the group consisting of PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, and AMP-224, optionally wherein the PD-1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject;

(2) a PD-L1 inhibitor, optionally wherein the PD-L1 inhibitor is selected from the group consisting of FAZ053, Atezolizumab, Avelumab, Durvalumab, and BMS-936559, optionally wherein the PD-L1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject;

(3) a LAG-3 inhibitor, optionally wherein the LAG-3 inhibitor is selected from the group consisting of LAG525, BMS-986016, TSR-033, MK-4280 and REGN3767; or

(4) a TIM-3 inhibitor, optionally wherein the TIM-3 inhibitor is selected from the group consisting of MGB453, TSR-022, and LY3321367.

63. The method of any one of claims 1-62, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an antibody molecule that binds to CD32B.

64. The method of any one of claims 1-63, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an antibody molecule that binds to IL-17, e.g., an antagonistic antibody molecule that binds to IL-17, e.g., CJM112.

65. The method of any one of claims 1-64, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an antibody molecule that binds to IL-1 beta.

66. The method of any one of claims 1-65, comprising administering the BCMA CAR-expressing cell therapy to the subject in combination with an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO), e.g., an IDO1 inhibitor, optionally wherein the inhibitor of IDO and/or TDO is chosen from:

(1) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(2) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan.

67. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is:

(1) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019, optionally wherein the CD19 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(2) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein, optionally wherein the CD20 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(3) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein, optionally wherein the CD22 CAR-expressing cell therapy is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(4) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein), optionally wherein the second CAR is selected from the group consisting of a CD19 CAR (e.g., a CD19 CAR disclosed herein), a CD20 CAR (e.g., a CD20 CAR disclosed herein), and a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(5) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR that binds to a first antigen and a second antigen, wherein the first antigen is BCMA, optionally wherein the second antigen is selected from the group consisting of CD19, CD20, and CD22.

68. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is:

(1) a CD19 inhibitor, e.g., a CD19 inhibitor disclosed herein, optionally wherein the CD19 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after

CD19 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy;

(2) a CD20 inhibitor, e.g., a CD20 inhibitor disclosed herein, optionally wherein the CD20 inhibitor is a multispecific antibody molecule, e.g., a bispecific antibody molecule that binds to CD20 and CD3, e.g., THG338, optionally wherein the CD20 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD20 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy; or

(3) a CD22 inhibitor, e.g., a CD22 inhibitor disclosed herein, optionally wherein the CD22 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after CD22 expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

69. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is a molecule that binds to Fc receptor like 2 (FCRL2) or Fc receptor like 5 (FCRL5), optionally wherein the molecule is:

(1) a CAR-expressing cell therapy comprising a cell expressing a CAR that binds to FCRL2 or FCRL5; or

(2) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to a first antigen and a second antigen, wherein the first antigen is FCRL2 or FCRL5, optionally wherein the second antigen is CD3.

70. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an inhibitor of TGF beta.

71. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an $EGFR^{mut}$-tyrosine kinase inhibitor (TKI), e.g., EGF816.

72. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an adenosine A2AR antagonist, optionally wherein:

(1) the adenosine A2AR antagonist is selected from the group consisting of PBF509, CPI444, AZD4635, Vipadenant, GBV-2034, and AB928; or

(2) the adenosine A2AR antagonist is selected from the group consisting of 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine.

73. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an anti-CD73 antibody molecule, e.g., an anti-CD73 antibody molecule disclosed herein.

74. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is a check point inhibitor, optionally wherein the check point inhibitor is:

(1) a PD-1 inhibitor, optionally wherein the PD-1 inhibitor is selected from the group consisting of PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, and AMP-224, optionally wherein the PD-1 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of PD-1 or PD-L1 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy, optionally wherein the PD-1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject;

(2) a PD-L1 inhibitor, optionally wherein the PD-L1 inhibitor is selected from the group consisting of FAZ053, Atezolizumab, Avelumab, Durvalumab, and BMS-936559, optionally wherein the PD-L1 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of PD-1 or PD-L1 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy, optionally wherein the PD-L1 inhibitor increases expansion of BCMA CAR-expressing cells in the subject;

(3) a LAG-3 inhibitor, optionally wherein the LAG-3 inhibitor is selected from the group consisting of LAG525, BMS-986016, TSR-033, MK-4280 and REGN3767, optionally wherein the LAG-3 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy,

e.g., after the expression of LAG-3 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy; or

(4) a TIM-3 inhibitor, optionally wherein the TIM-3 inhibitor is selected from the group consisting of MGB453, TSR-022, and LY3321367, optionally wherein the TIM-3 inhibitor is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after the expression of TIM-3 is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

75. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an antibody molecule that binds to CD32B.

76. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an antibody molecule that binds to IL-17, e.g., an antagonistic antibody molecule that binds to IL-17, e.g., CJM112.

77. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an antibody molecule that binds to IL-1 beta.

78. A method of treating a subject having a disease associated with the expression of BCMA, comprising administering a BCMA CAR-expressing cell therapy and a second therapy to the subject, wherein the second therapy is an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO), e.g., an IDO1 inhibitor, optionally wherein the inhibitor of IDO and/or TDO is chosen from:

(1) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(2) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, optionally wherein:

the inhibitor of IDO and/or TDO is administered after the administration of the BCMA CAR-expressing cell therapy, e.g., after IDO and/or TDO expression is increased in the subject following the administration of the BCMA CAR-expressing cell therapy.

79. The method of any one of claims 67-78, wherein the second therapy is administered prior to, concurrently with, or subsequent to the administration of the BCMA CAR-expressing cell therapy.

80. A method of treating a subject having a disease associated with the expression of BCMA, wherein the subject has received or is receiving a BCMA CAR-expressing cell therapy, comprising:

responsive to an increase in a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy, relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

81. A method of treating a subject having a disease associated with the expression of BCMA, wherein the subject has received or is receiving a BCMA CAR-expressing cell therapy, comprising:

acquiring a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy,

responsive to an increase in the value relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

82. A method of treating a subject having a disease associated with the expression of BCMA, comprising:

administering a BCMA CAR-expressing cell therapy to the subject,

responsive to an increase in a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy, relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

83. A method of treating a subject having a disease associated with the expression of BCMA, comprising:

administering a BCMA CAR-expressing cell therapy to the subject,

acquiring a value of the level or activity of an antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), at at least one time point after the subject began receiving the BCMA CAR-expressing cell therapy,

responsive to an increase in the value relative to a reference value, wherein the reference value is:

(i) the level or activity of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), prior to the at least one time point (e.g., the level or activity of the antigen in the subject before the subject began receiving the BCMA CAR-expressing cell therapy, or the level or activity of the antigen in the subject after the subject began receiving the BCMA CAR-expressing cell therapy but prior to the at least one time point);

(ii) the level or activity of the antigen in a different subject having the disease associated with the expression of BCMA; or

(iii) an average level or activity of the antigen in a population of subjects having the disease associated with the expression of BCMA,

administering an inhibitor of the antigen to the subject, wherein:

(1) the antigen is CD19 and the inhibitor of the antigen is a CD19 inhibitor, optionally wherein the CD19 inhibitor is:

(a) a CD19 CAR-expressing cell therapy, e.g., a CD19 CAR-expressing cell therapy disclosed herein, e.g., CTL119 or CTL019;

(b) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD19 CAR (e.g., a CD19 CAR disclosed herein); or

(c) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD19,

(2) the antigen is CD20 and the inhibitor of the antigen is a CD20 inhibitor, optionally wherein the CD20 inhibitor is:

(d) a CD20 CAR-expressing cell therapy, e.g., a CD20 CAR-expressing cell therapy disclosed herein;

(e) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD20 CAR (e.g., a CD20 CAR disclosed herein);

(f) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD20; or

(g) a multispecific antibody molecule, e.g., a bispecific antibody molecule, that binds to CD20 and CD3, e.g., THG338,

(3) the antigen is CD22 and the inhibitor of the antigen is a CD22 inhibitor, optionally wherein the CD22 inhibitor is:

(h) a CD22 CAR-expressing cell therapy, e.g., a CD22 CAR-expressing cell therapy disclosed herein;

(i) a CAR-expressing cell therapy comprising a cell expressing a first CAR and a second CAR, wherein the first CAR is a BCMA CAR (e.g., a BCMA CAR disclosed herein) and the second CAR is a CD22 CAR (e.g., a CD22 CAR disclosed herein); or

(j) a CAR-expressing cell therapy comprising a cell expressing a multispecific CAR, e.g., a bispecific CAR, that binds to BCMA and CD22,

(4) the antigen is PD1 or PD-L1 and the inhibitor of the antigen is an anti-PD1 antibody molecule or an anti-PD-L1 antibody molecule, optionally wherein the inhibitor of the antigen is:

(k) PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224; or

(l) FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559,

(5) the antigen is IDO or TDO and the inhibitor of the antigen is an inhibitor of IDO and/or TDO, optionally wherein the inhibitor of IDO and/or TDO is:

(m) INCB24360, indoximod, NLG919, epacadostat, NLG919, or F001287; or

(n) (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine, 1-methyl-D-tryptophan, α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol, or the D isomer of 1-methyl-tryptophan, or

(6) the antigen is TGF-beta and the inhibitor of the antigen is a TGF beta inhibitor.

84. The method of any one of claims 80-83, wherein the value of the level or activity of the antigen comprises the expression level of the antigen in the subject, e.g., in a sample from the subject (e.g., a biopsy sample, e.g., a bone marrow biopsy sample), as measured by an assay described herein, e.g., immunohistochemistry.

85. The method of any one of claims 80-84, wherein the at least one time point is 5, 10, 15, 20, 25, 28, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, or 90 days after the subject began receiving the BCMA CAR-expressing cell therapy.

86. The method of any one of claims 80-85, wherein the subject experiences a decrease in BCMA expression after the subject began receiving the BCMA CAR-expressing cell therapy.

87. The method of any one of claims 1-86, wherein the BCMA CAR-expressing cell therapy comprises a cell expressing a BCAM CAR, wherein:

(i) the BCMA CAR comprises one or more of (e.g., all three of) heavy chain complementary determining region 1 (HCDR1), HCDR2, and HCDR3 listed in Table 3 or 5 and/or one or more of (e.g., all three of) light chain complementary determining region 1 (LCDR1), LCDR2, and LCDR3 listed in Table 4 or 5, or a sequence with 95-99% identify thereof;

(ii) the BCMA CAR comprises a heavy chain variable region (VH) listed in Table 2 or 5 and/or a light chain variable region (VL) listed in Table 2 or 5, or a sequence with 95-99% identify thereof;

(iii) the BCMA CAR comprises a BCMA scFv domain amino acid sequence listed in Table 2 or 5 (e.g., SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, and SEQ ID NO: 149), or a sequence with 95-99% identify thereof;

(iv) the BCMA CAR comprises a full-length BCMA CAR amino acid sequence listed in Table 2 or 5 (e.g., residues 22-483 of SEQ ID NO: 109, residues 22-490 of SEQ ID NO: 99, residues 22-488 of SEQ ID NO: 100, residues 22-487 of SEQ ID NO: 101, residues 22-493 of SEQ ID NO: 102, residues 22-490 of SEQ ID NO: 103, residues 22-491 of SEQ ID NO: 104, residues 22-482 of SEQ ID NO: 105, residues 22-483 of SEQ ID NO: 106, residues 22-485 of SEQ ID NO: 107, residues 22-483 of SEQ ID NO: 108, residues 22-490 of SEQ ID NO: 110, residues 22-483 of SEQ ID NO: 111, residues 22-484 of SEQ ID NO: 112, residues 22-485 of SEQ ID NO: 113, residues 22-487 of SEQ ID NO: 213, residues 23-489 of SEQ ID NO: 214, residues 22-490 of SEQ ID NO: 215, residues 22-484 of SEQ ID NO: 216, residues 22-485 of SEQ ID NO: 217, residues 22-489 of SEQ ID NO: 218, residues 22-497 of SEQ ID NO: 219, residues 22-492 of SEQ ID NO: 220, residues 22-490 of SEQ ID NO: 221, residues 22-485 of SEQ ID NO: 222, residues 22-492 of SEQ ID NO: 223, residues 22-492 of SEQ ID NO: 224, residues 22-483 of SEQ ID NO: 225, residues 22-490 of SEQ ID NO: 226, residues 22-485 of SEQ ID NO: 227, residues 22-486 of SEQ ID NO: 228, residues 22-492 of SEQ ID NO: 229, residues 22-488 of SEQ ID NO: 230, residues 22-488 of SEQ ID NO: 231, residues 22-495 of SEQ ID NO: 232, residues 22-490 of SEQ ID NO: 233), or a sequence with 95-99% identify thereof; or

(v) the BCMA CAR is encoded by a nucleic acid sequence listed in Table 2 or 5 (e.g., SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, SEQ ID NO: 169, SEQ ID NO: 170), or a sequence with 95-99% identify thereof.

88. The method of any one of claims 1-87, wherein the disease associated with the expression of BCMA is cancer, optionally wherein the cancer is a hematological cancer.

89. The method of any one of claims 1-88, wherein the disease associated with the expression of BCMA is an acute leukemia chosen from one or more of B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant

lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia; a prostate cancer (e.g., castrate-resistant or therapy-resistant prostate cancer, or metastatic prostate cancer), pancreatic cancer, lung cancer; or a plasma cell proliferative disorder (e.g., asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammapathy of undetermined significance (MGUS), Waldenstrom's macroglobulinemia, plasmacytomas (e.g., plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, and POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome)), or a combination thereof.

90. The method of any one of claims 1-89, wherein the disease associated with the expression of BCMA is ALL, CLL, DLBCL, or multiple myeloma.

91. The method of any one of claims 1-90, wherein the subject is a human patient.

92. A BCMA CAR-expressing cell therapy for use in a method of treatment of a subject having a disease associated with the expression of BCMA, the method comprising:

responsive to an increased value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of a BCMA CAR-expressing cell therapy,

as compared to a reference value, e.g., a non-responder reference value, performing:

manufacturing a BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject and administering the BCMA CAR-expressing cell therapy to the subject; or

administering, e.g., initiating administering or continuing administering, a BCMA CAR-expressing cell therapy to the subject,

thereby treating the subject having the disease associated with the expression of BCMA.

93. A BCMA CAR-expressing cell therapy for use in a method of treatment of a subject having a disease associated with the expression of BCMA, the method comprising:

responsive to a decreased value for one, two, three, four, five, or all of:

(i) the level or activity of CD4+ immune effector cells (e.g., CD4+ T cells) relative to the level or activity of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), in a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy,

(ii) the level or activity of CD8+ Tscm (stem cell memory T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iii) the level or activity of HLADR-CD95+CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(iv) the level or activity of CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)),

(v) the level or activity of CCR7+CD45RO-CD27+CD8+ cells in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample) or a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or

(vi) the proliferation of seeded cells from the subject during manufacturing of a BCMA CAR-expressing cell therapy,

as compared to a reference value, e.g., a responder reference value, performing one, two, three, four, five, six, seven, or all of:

administering an altered dosing regimen of a BCMA CAR-expressing cell therapy (e.g., a dosing regimen with a higher dose and/or more frequent administration than a reference dosing regimen) to the subject;

administering a second therapy (e.g., a second therapy that is not a BCMA CAR-expressing cell therapy) to the subject;

administering a BCMA CAR-expressing cell therapy and a second therapy to the subject;

discontinuing administration of a BCMA CAR-expressing cell therapy and optionally administering a second therapy to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD4+ immune effector cells (e.g., CD4+ T cells) relative to CD8+ immune effector cells (CD8+ T cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of a BCMA CAR-expressing cell therapy, e.g., enriching for CD8+ Tscm (e.g., HLADR-CD95+CD27+CD8+ cells, CD45RO-CD27+CD8+ cells, or CCR7+CD45RO-CD27+CD8+ cells) prior to introducing a nucleic acid encoding a BCMA CAR, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject;

modifying a manufacturing process of the BCMA CAR-expressing cell therapy, e.g., increasing the proliferation of seeded cells from the subject during the manufacturing of the BCMA CAR-expressing cell therapy, and administering the BCMA CAR-expressing cell therapy generated by the modified manufacturing process to the subject; or

administering a pretreatment to the subject, wherein the pretreatment increases the ratio of the amount of CD4+ immune effector cells (e.g., CD4+ T cells) to the amount of CD8+ immune effector cells (e.g., CD8+ T cells) in the subject, e.g., in a sample from the subject (e.g., an apheresis sample (e.g., a leukapheresis sample), a seed culture at the start of the manufacturing of a BCMA CAR-expressing cell therapy (e.g., a leukapheresis sample after monocytes are removed using elutriation)), or in the subject's peripheral blood and/or bone marrow prior to the administration of the BCMA CAR-expressing cell therapy, e.g., the pretreatment increases the ratio to greater than or equal to 1.6 (e.g., between 1.6 and 5, e.g., between 1.6 and 3.5), manufacturing the BCMA CAR-expressing cell therapy using cells (e.g., T cells) from the subject, and administering the BCMA CAR-expressing cell therapy to the subject,

thereby treating the subject having the disease associated with the expression of BCMA.

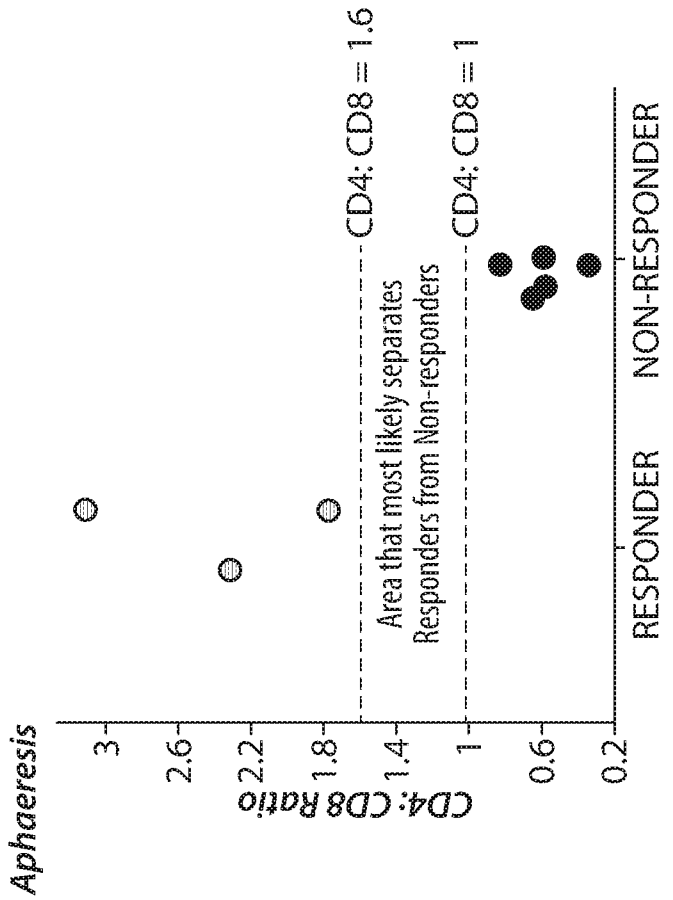

Aphaeresis
CD4: CD8 Ratio
3
2.6
2.2
1.8
1.4
1
0.6
0.2
CD4; CD8 = 1.6
Area that most likely separates
Responders from Non-responders
CD4; CD8 = 1
RESPONDER
NON-RESPONDER

FIG. 1B

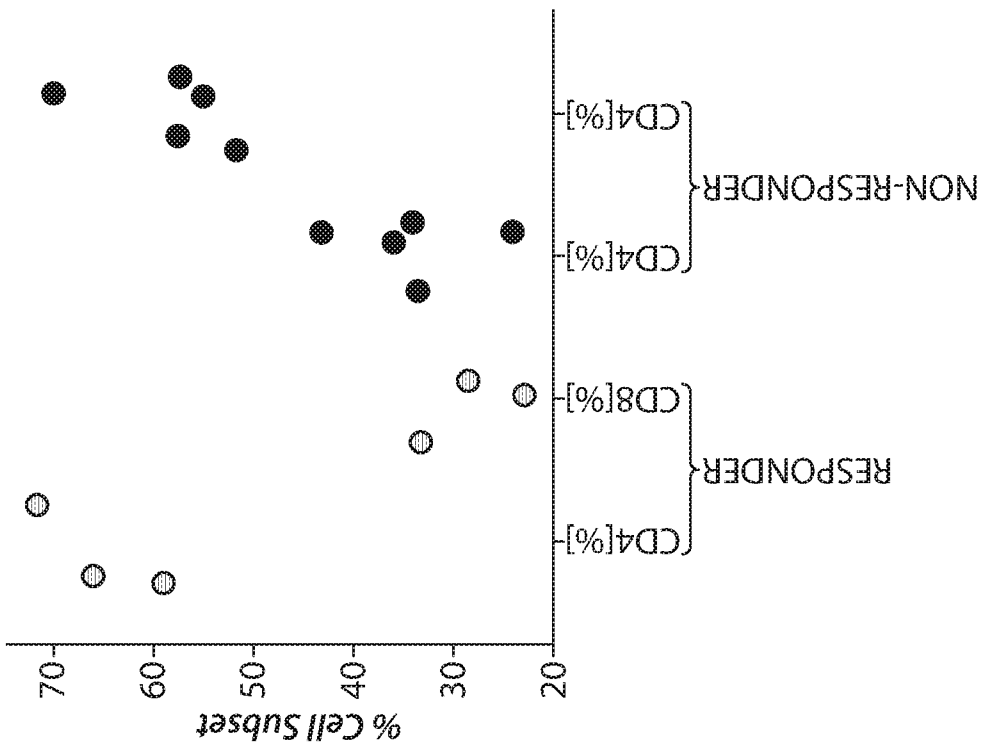

% Cell Subset
70
60
50
40
30
20
RESPONDER
CD4[%]
CD8[%]
NON-RESPONDER
CD4[%]
CD4[%]

FIG. 1A

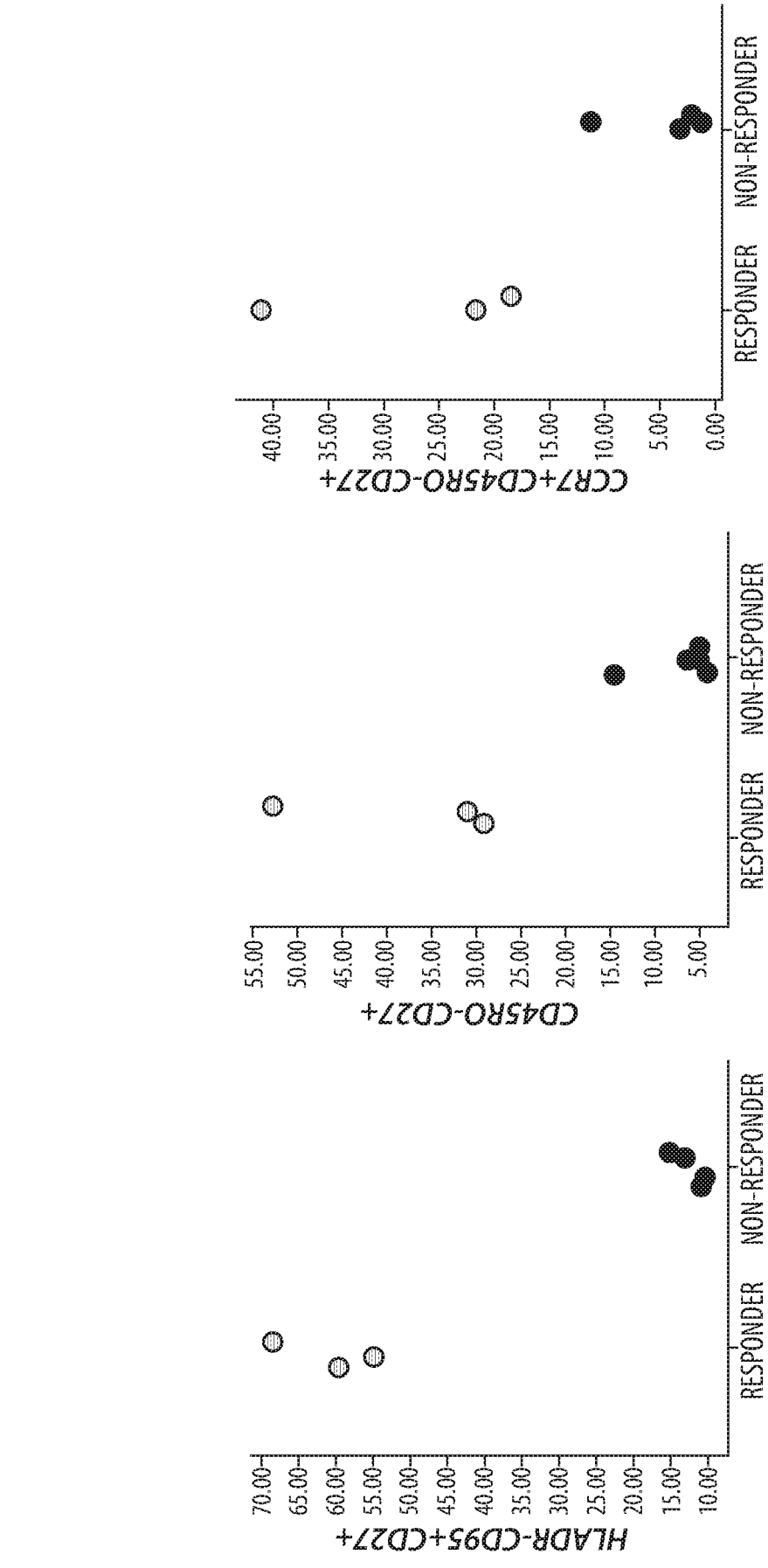


FIG. 2A

FIG. 2B

FIG. 2C

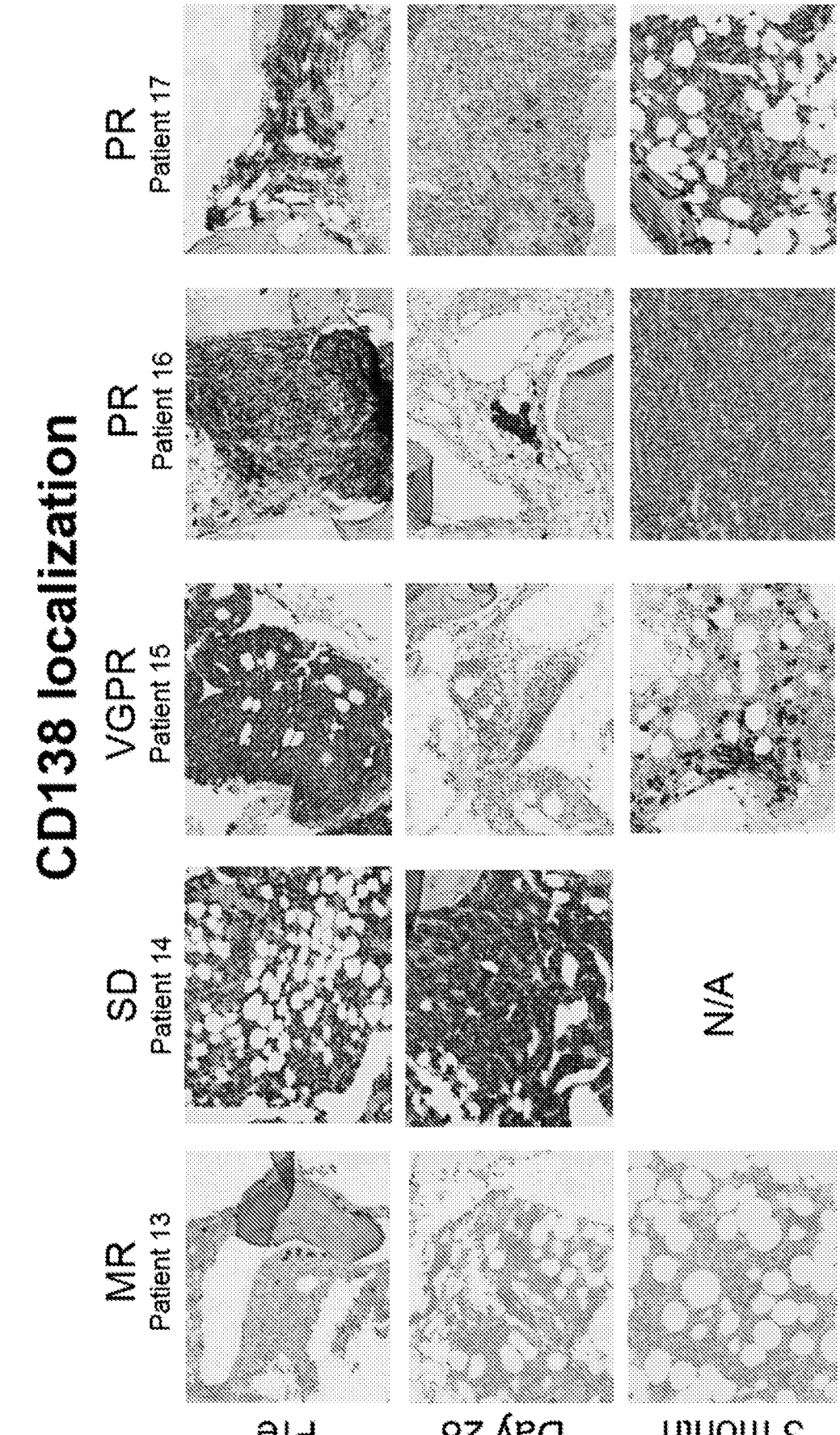

CD138 localization
MR
Patient 13
SD
Patient 14
VGPR
Patient 15
PR
Patient 16
PR
Patient 17
Pre
Day 28
3 month
Minimal CD138 expression detected at all time points in patient 13
Increased numbers of CD138 MM cells were observed at 28 days in patient 14
N/A
Extensive infiltration of CD138 MM cells at base line was observed in patients 15, 16 and 17 followed by reductions at 28 days and increased numbers at 3 months

FIG. 3

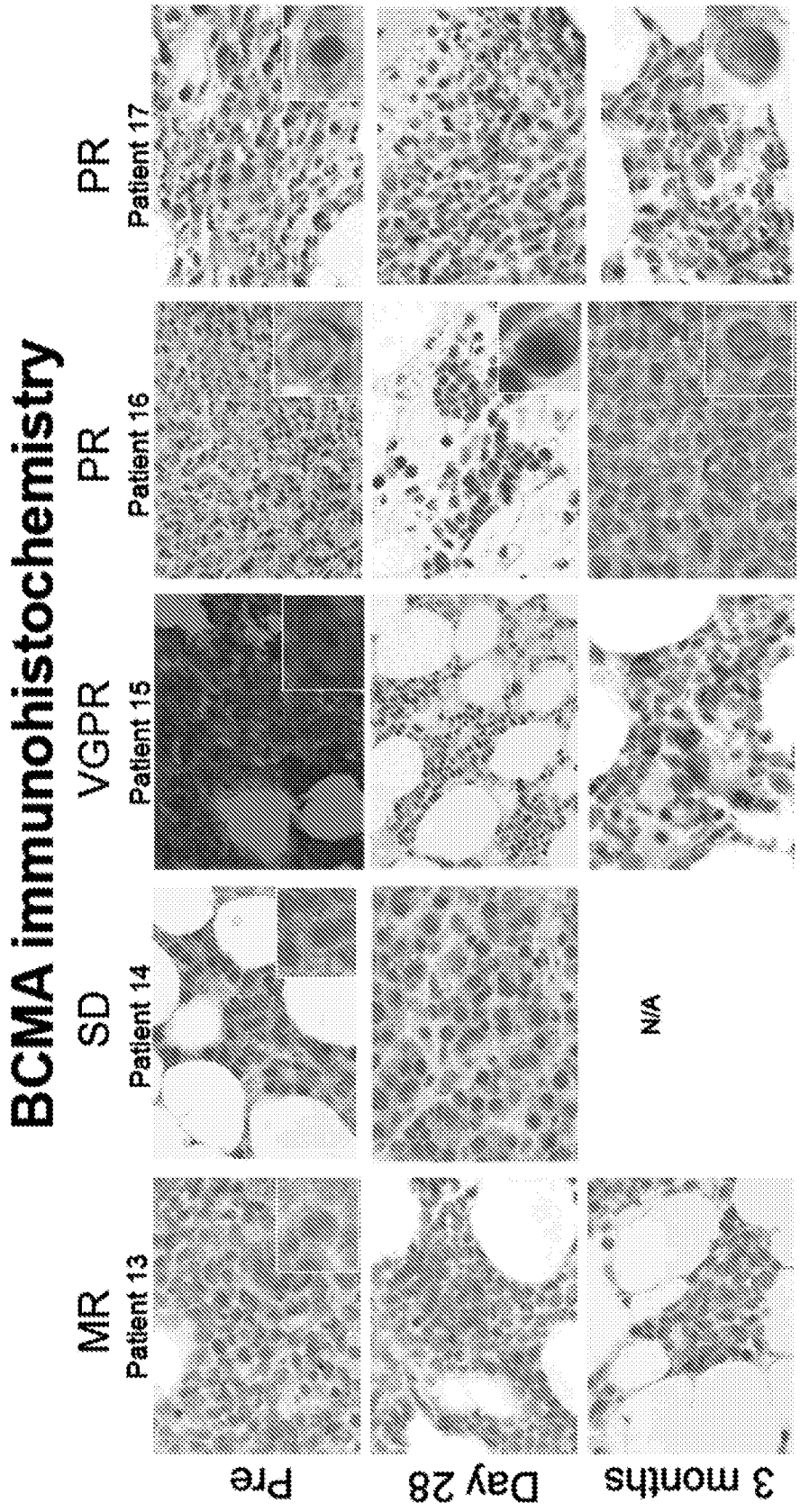

BCMA immunohistochemistry
MR
SD
VGPR
PR
PR
Patient 13
Patient 14
Patient 15
Patient 16
Patient 17
Pre
Day 28
3 months
N/A

FIG. 4

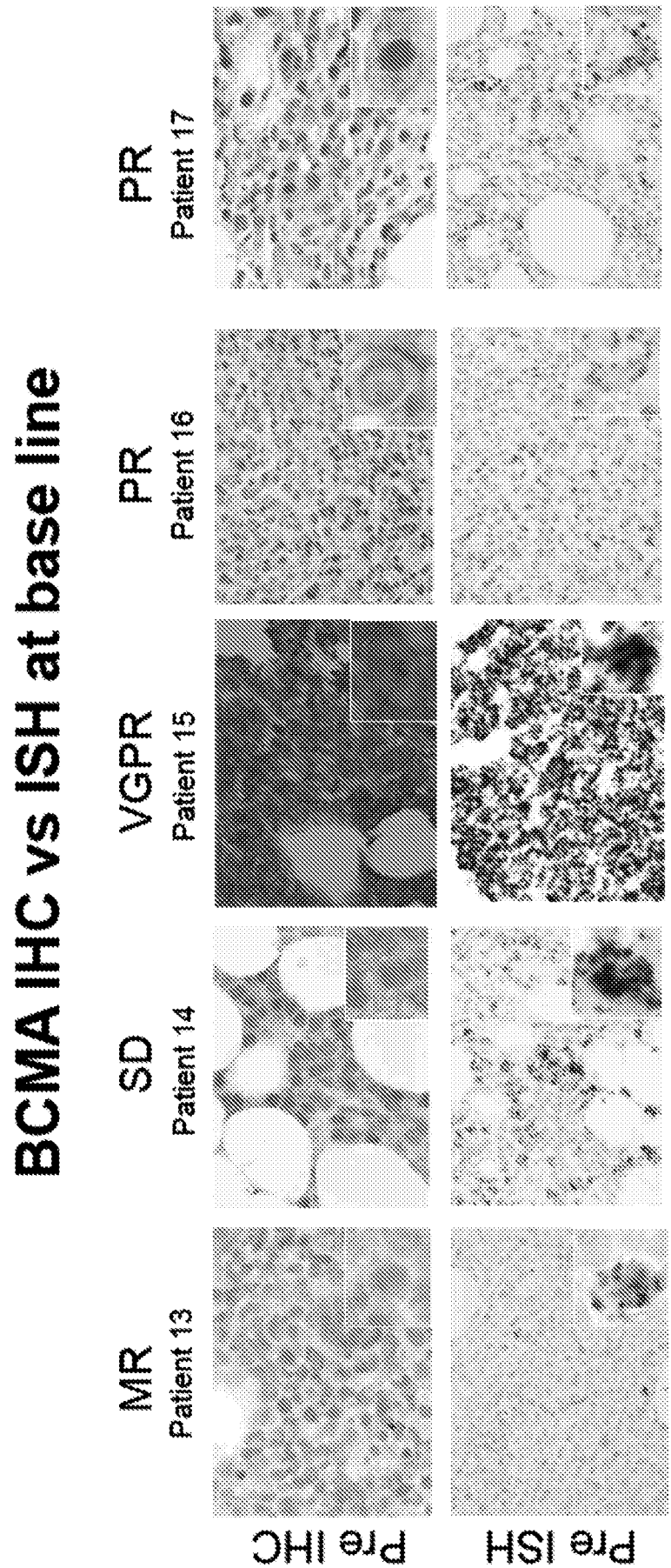

BCMA IHC vs ISH at base line
MR
Patient 13
SD
Patient 14
VGPR
Patient 15
PR
Patient 16
PR
Patient 17
Pre IHC
Pre ISH
• Discordance between BCMA surface protein and mRNA expression observed in patients 13 and 14

FIG. 5

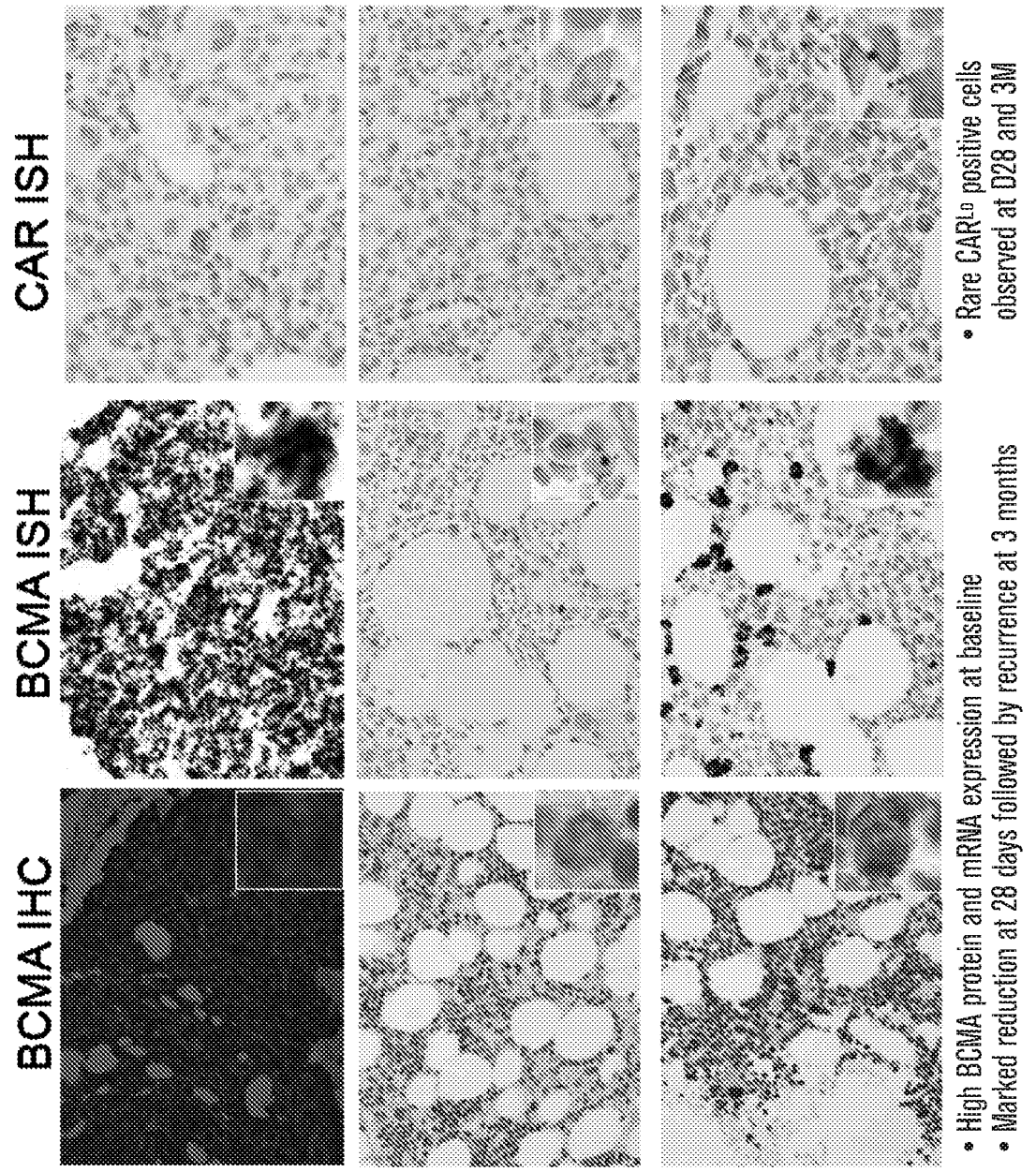

Patient 15
BCMA IHC
BCMA ISH
CAR ISH
Pre
Day 28
3 month
• High BCMA protein and mRNA expression at baseline
• Marked reduction at 28 days followed by recurrence at 3 months
• Rare CARLo positive cells observed at D28 and 3M

FIG. 6A

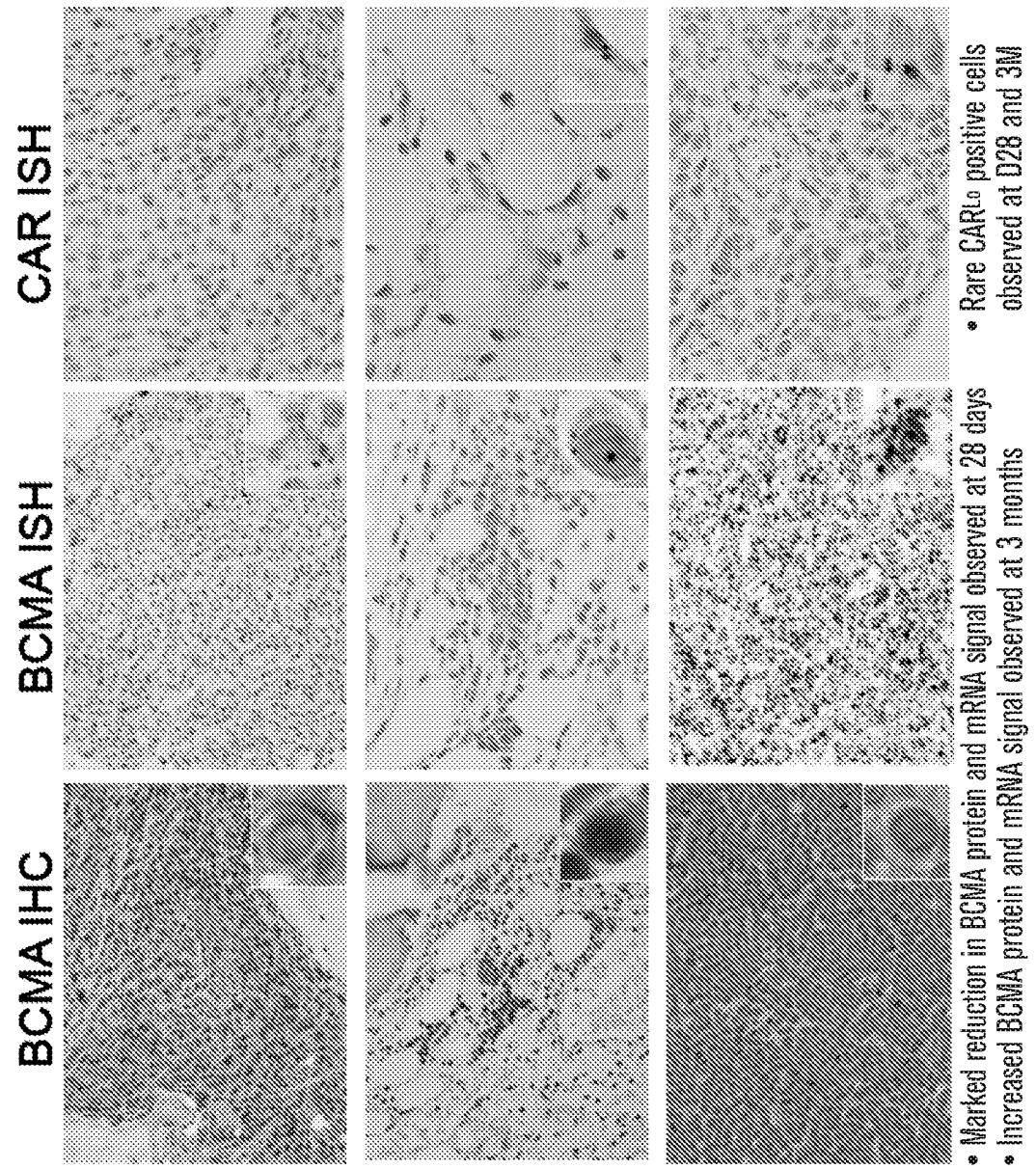

Patient 16
BCMA IHC
BCMA ISH
CAR ISH
Pre
Day 28
3 month
• Marked reduction in BCMA protein and mRNA signal observed at 28 days
• Increased BCMA protein and mRNA signal observed at 3 months
• Rare CARLo positive cells observed at D28 and 3M

FIG. 6B

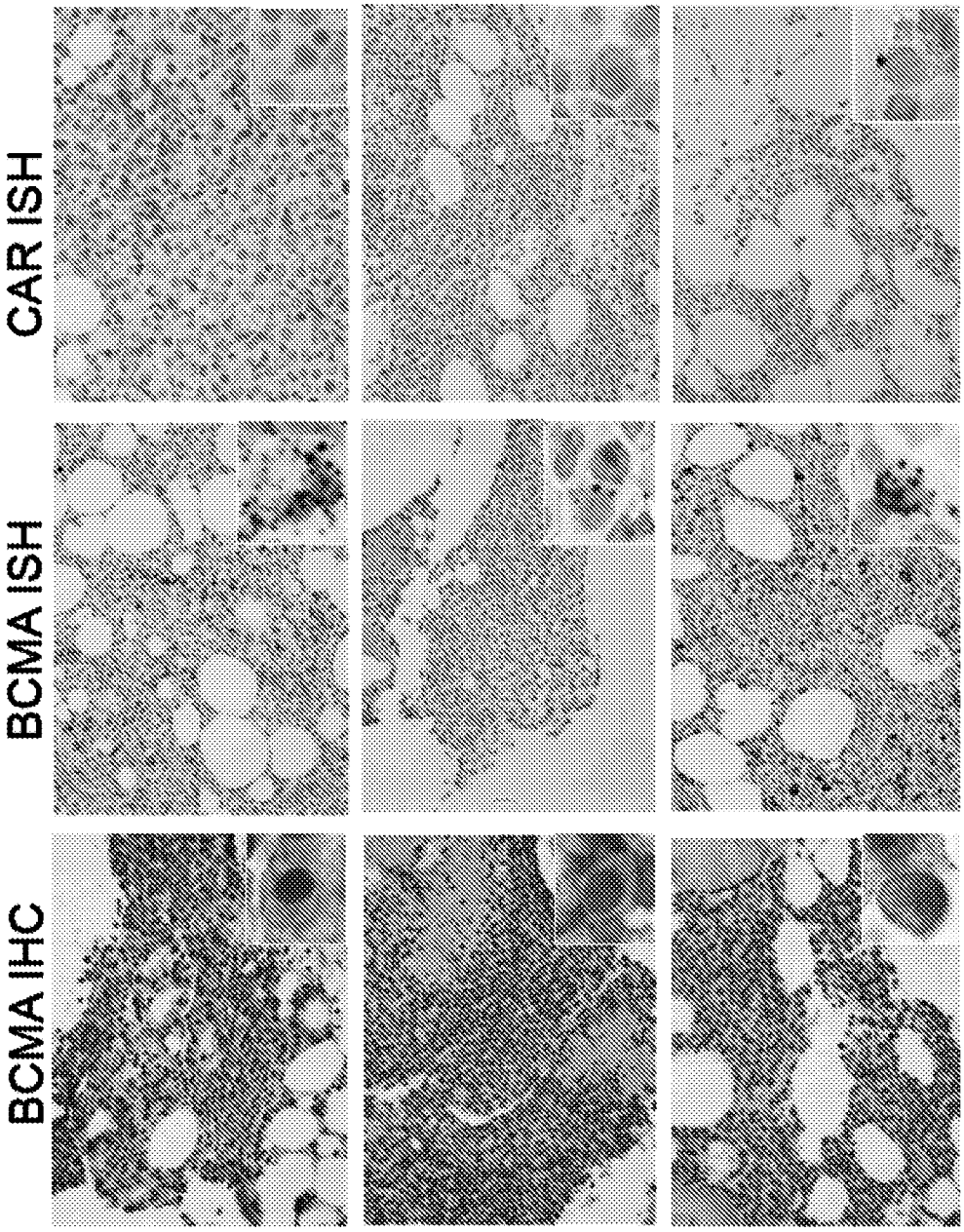

Patient 17
BCMA IHC
BCMA ISH
CAR ISH
Pre
Day 28
3 month
• Reduction in number of BCMA positive cells observed at D28 and reduction in BCMA mRNA signal/cell
• BCMA mRNA signal/cell returns to base line at 3M
• Equivocal CARLo mRNA signal detected at 3M

FIG. 6C

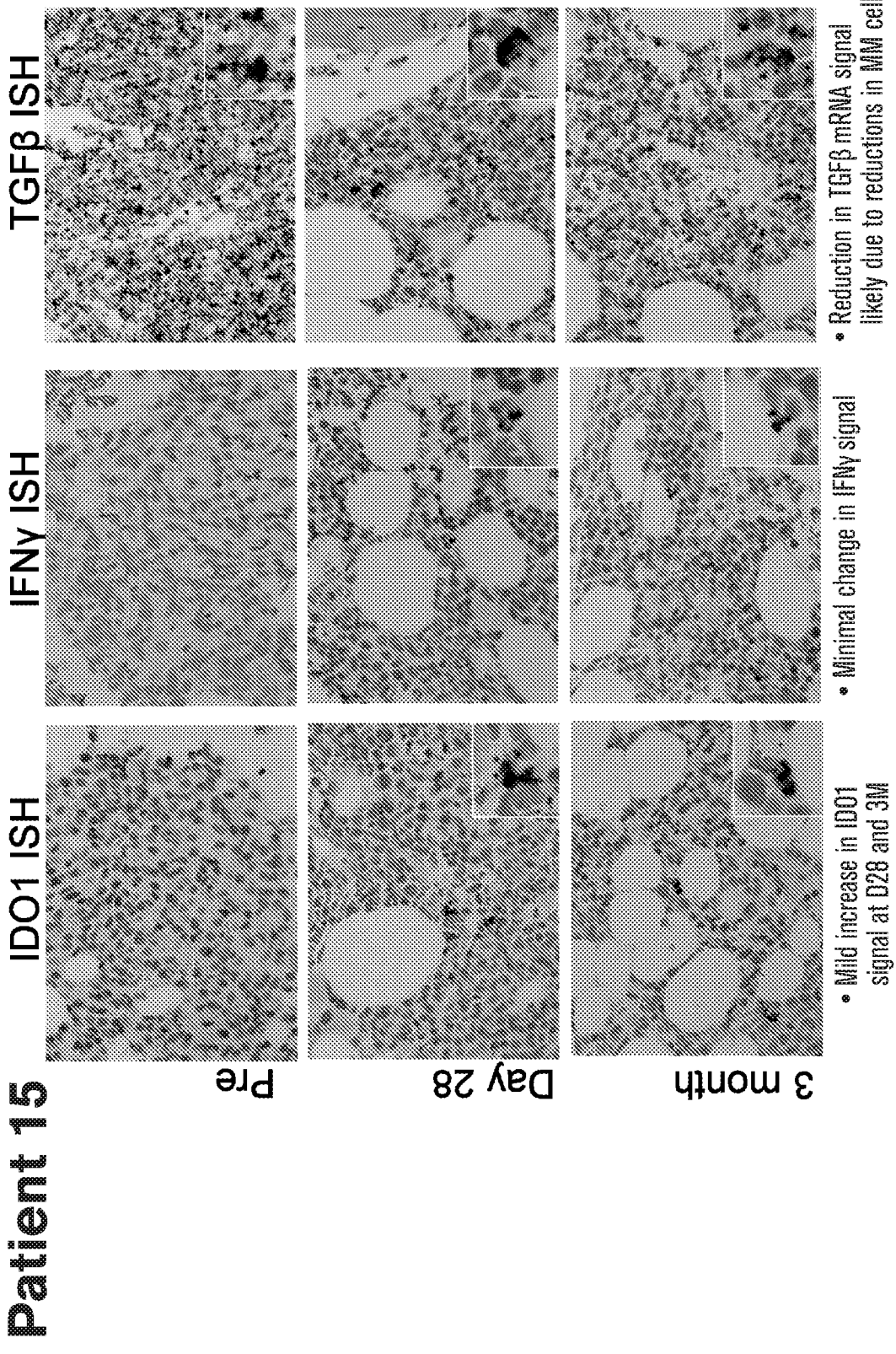

Patient 15
IDO1 ISH
IFNγ ISH
TGFβ ISH
Pre
Day 28
3 month
• Mild increase in IDO1 signal at D28 and 3M
• Minimal change in IFNγ signal
• Reduction in TGFβ mRNA signal likely due to reductions in MM cells

FIG. 7A

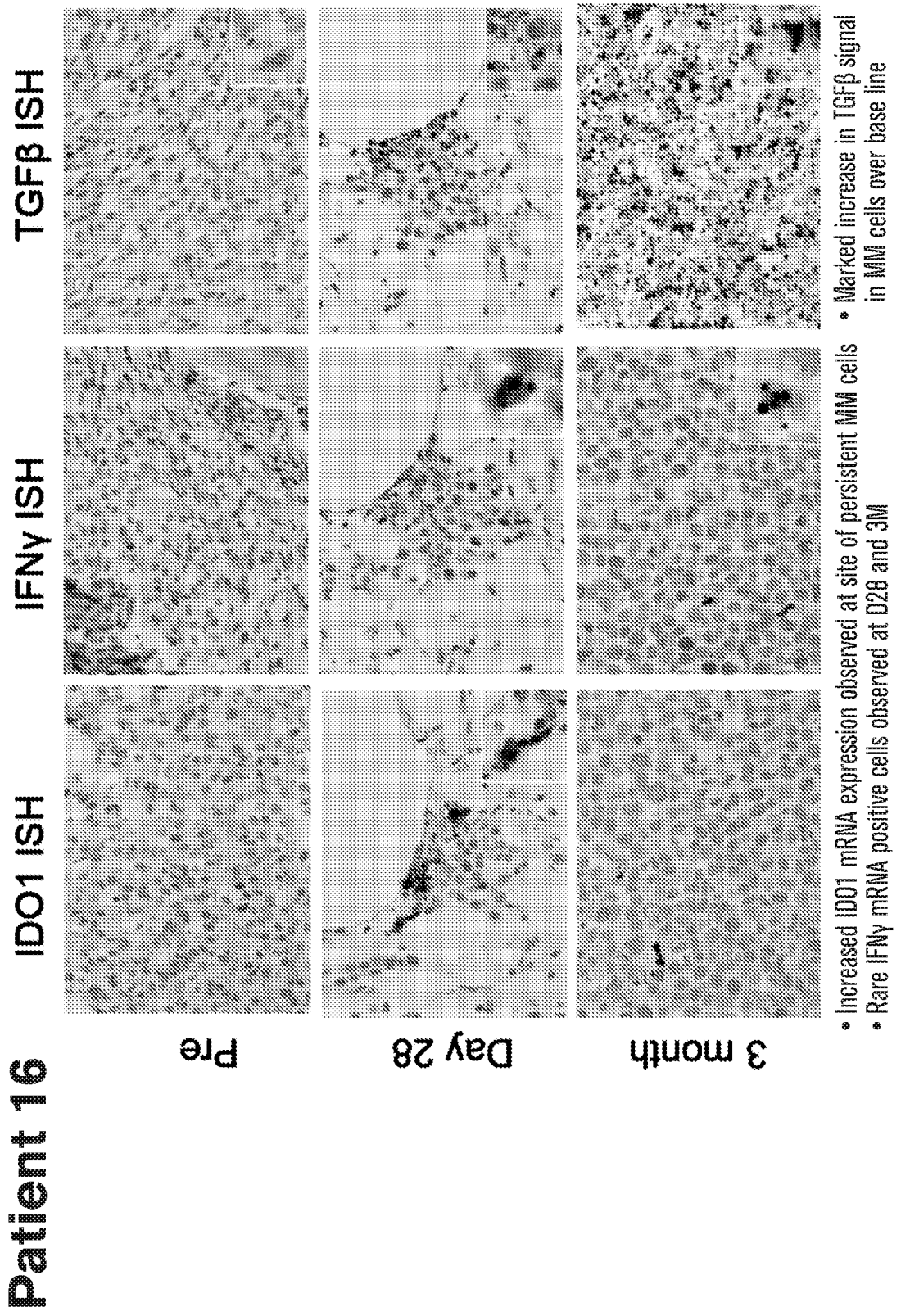

Patient 16
IDO1 ISH
IFNγ ISH
TGFβ ISH
Pre
Day 28
3 month
• Increased IDO1 mRNA expression observed at site of persistent MM cells
• Rare IFNγ mRNA positive cells observed at D28 and 3M
• Marked increase in TGFβ signal in MM cells over base line

FIG. 7B

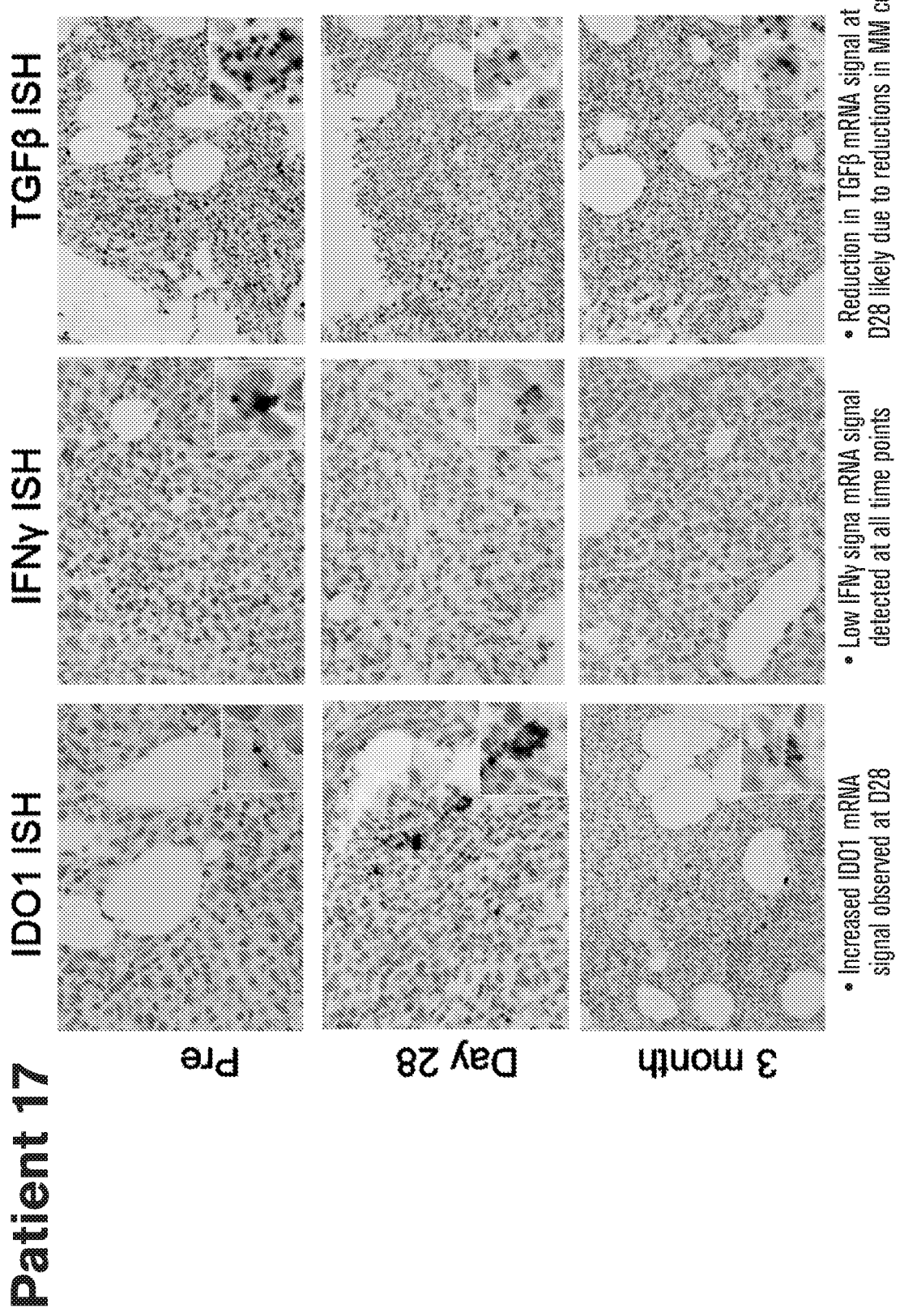

Patient 17
IDO1 ISH
IFNγ ISH
TGFβ ISH
Pre
Day 28
3 month
• Increased IDO1 mRNA signal observed at D28
• Low IFNγ signa mRNA signal detected at all time points
• Reduction in TGFβ mRNA signal at D28 likely due to reductions in MM cells.

FIG. 7C

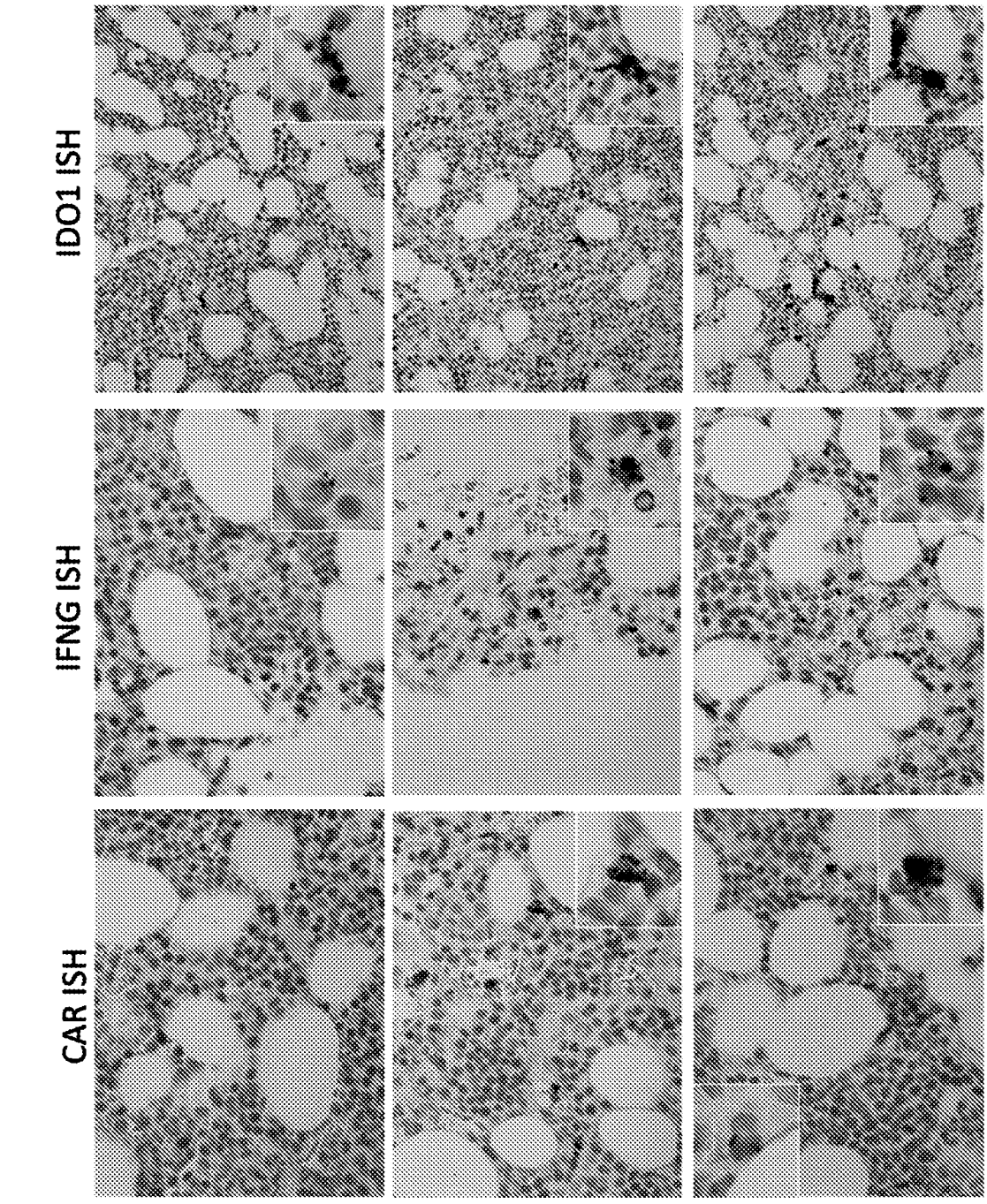


FIG. 7D

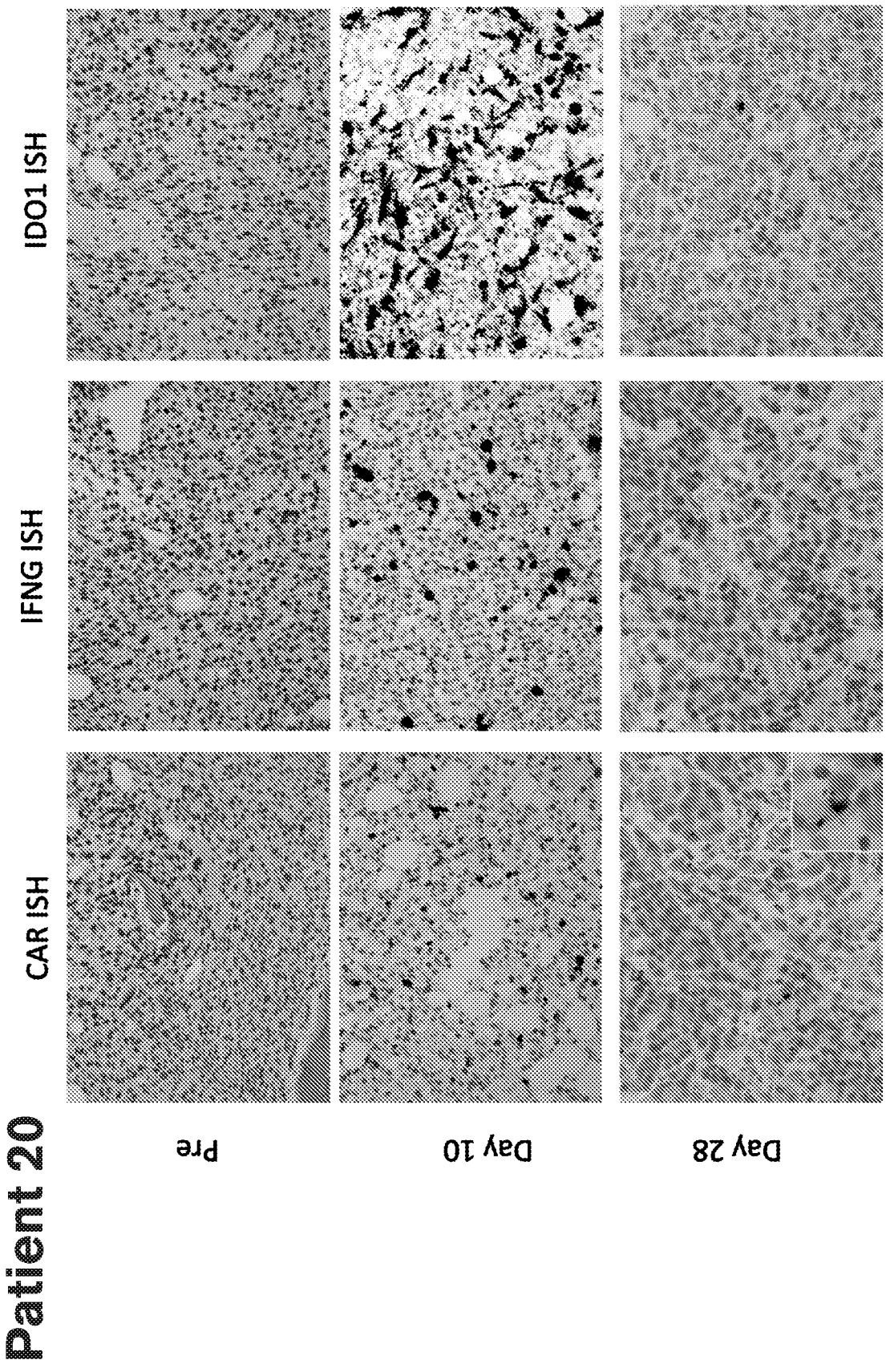


FIG. 7E

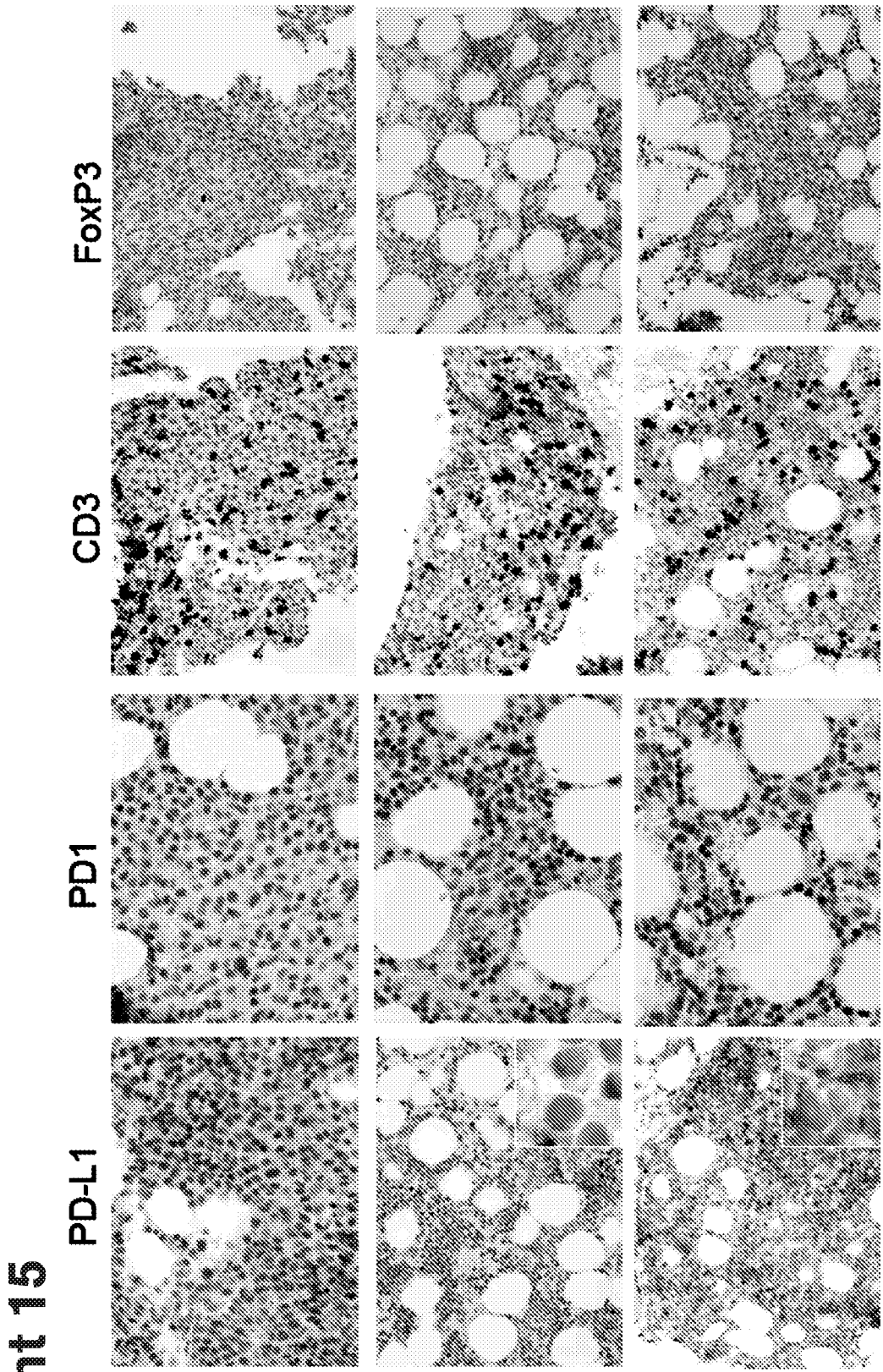

Patient 15
PD-L1
PD1
CD3
FoxP3
Pre
Day 28
3 month
• Increase in PD-L1 stromal cell signal at 3M
• No change in PD1, CD3 or FoxP3 signal observed

FIG. 8A

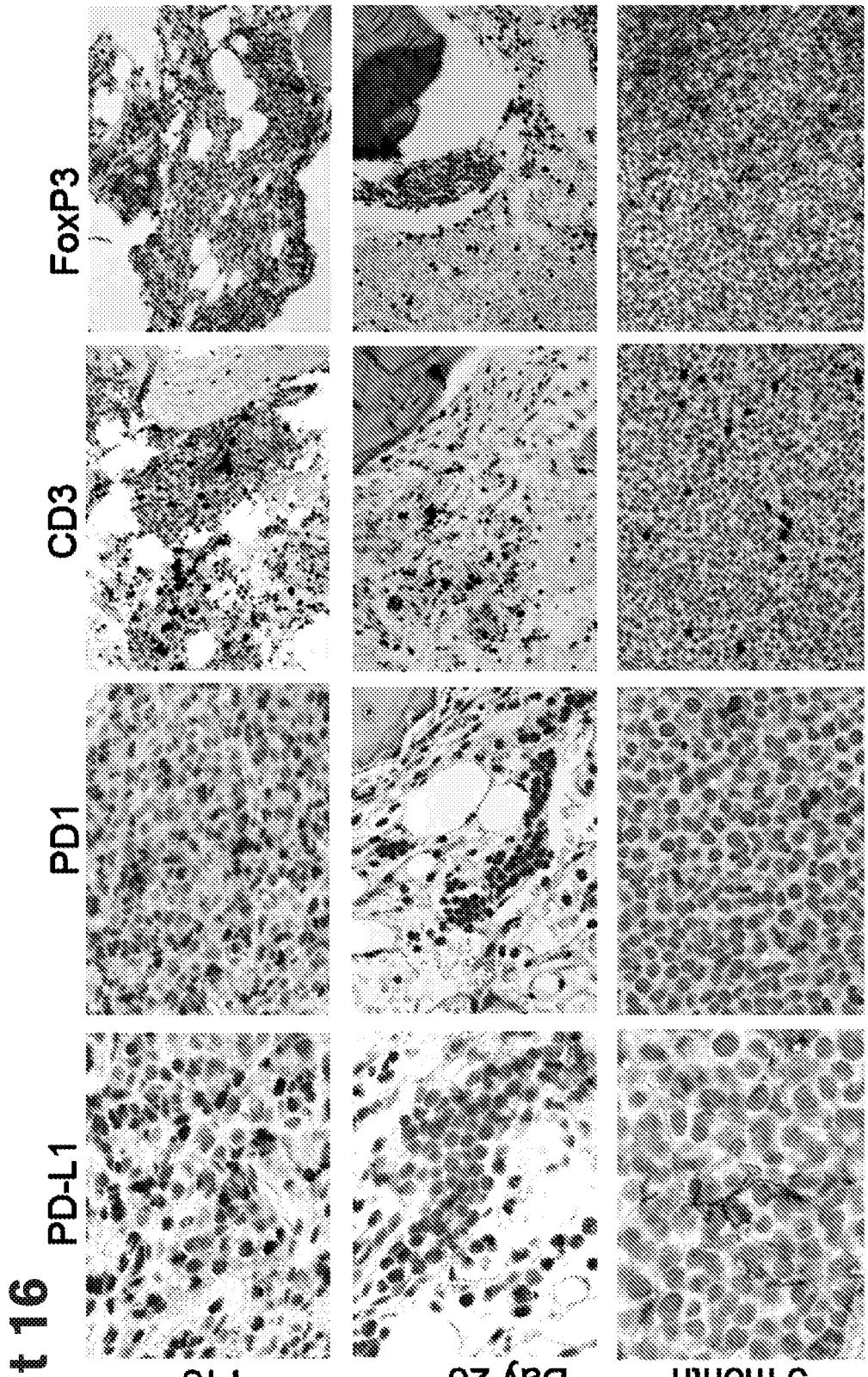

Patient 16
PD-L1
PD1
CD3
FoxP3
Pre
Day 28
3 month
• Increase in PD-L1 expresssion on stromal cells at 3M
• No PD1 infiltration detected
• No change in CD3 or FoxP3 cell number

FIG. 8B

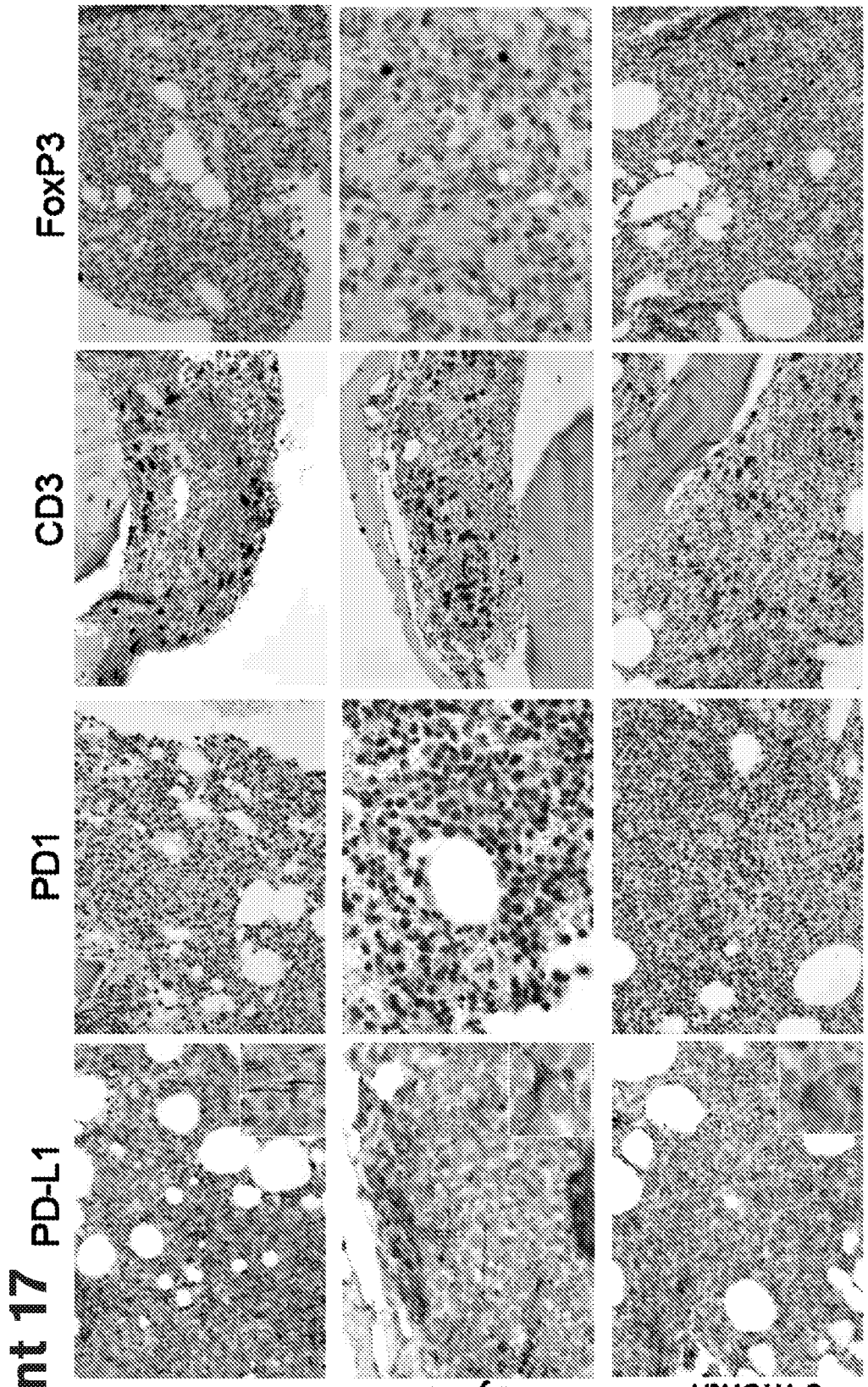

Patient 17
PD-L1
PD1
CD3
FoxP3
Pre
Day 28
3 month
• PD-L1 expresssion detected on stromal cells at all time points
• No PD1 infiltration detected at any time point
• No change in CD3 or FoxP3 infiltration

FIG. 8C

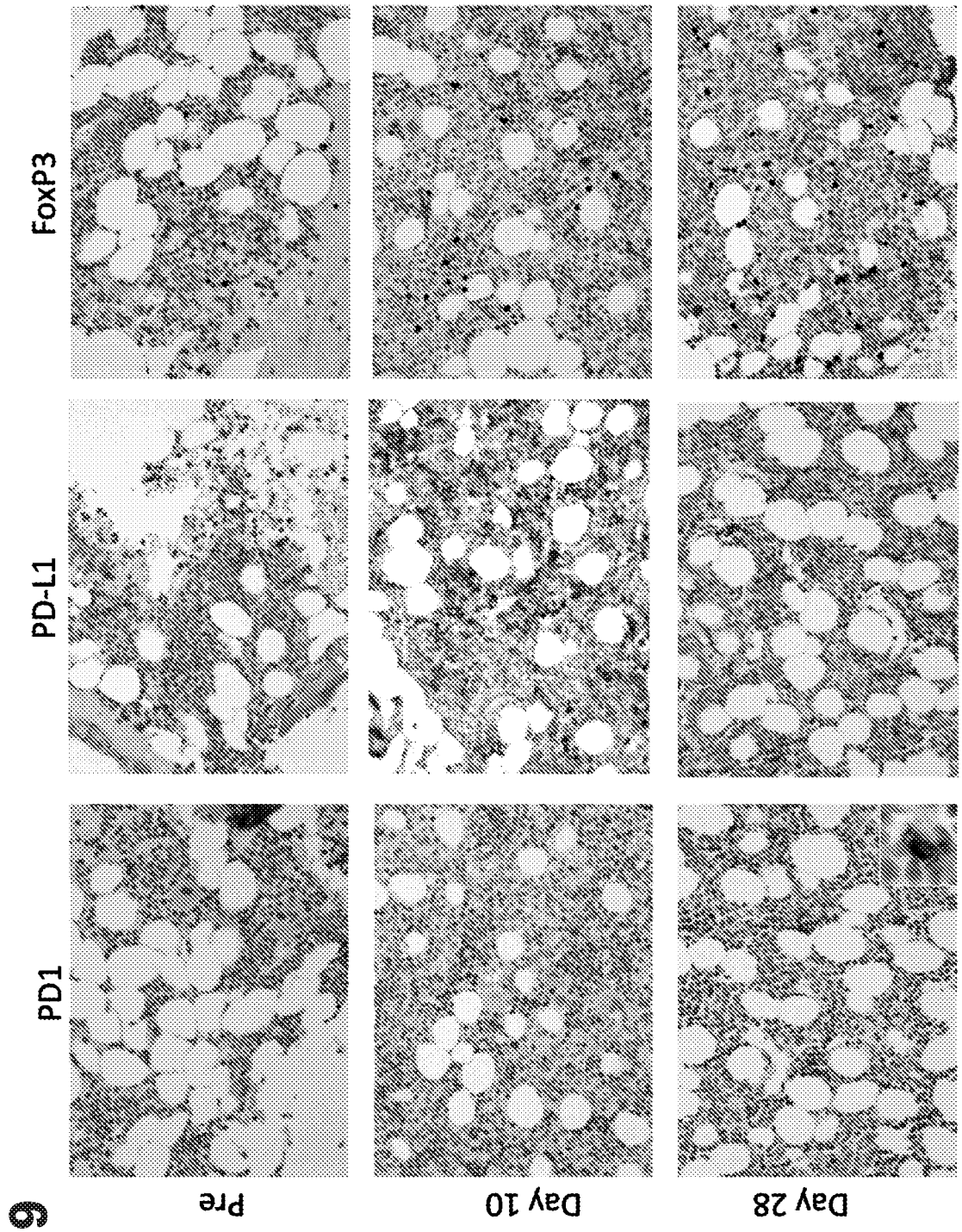


FIG. 8D

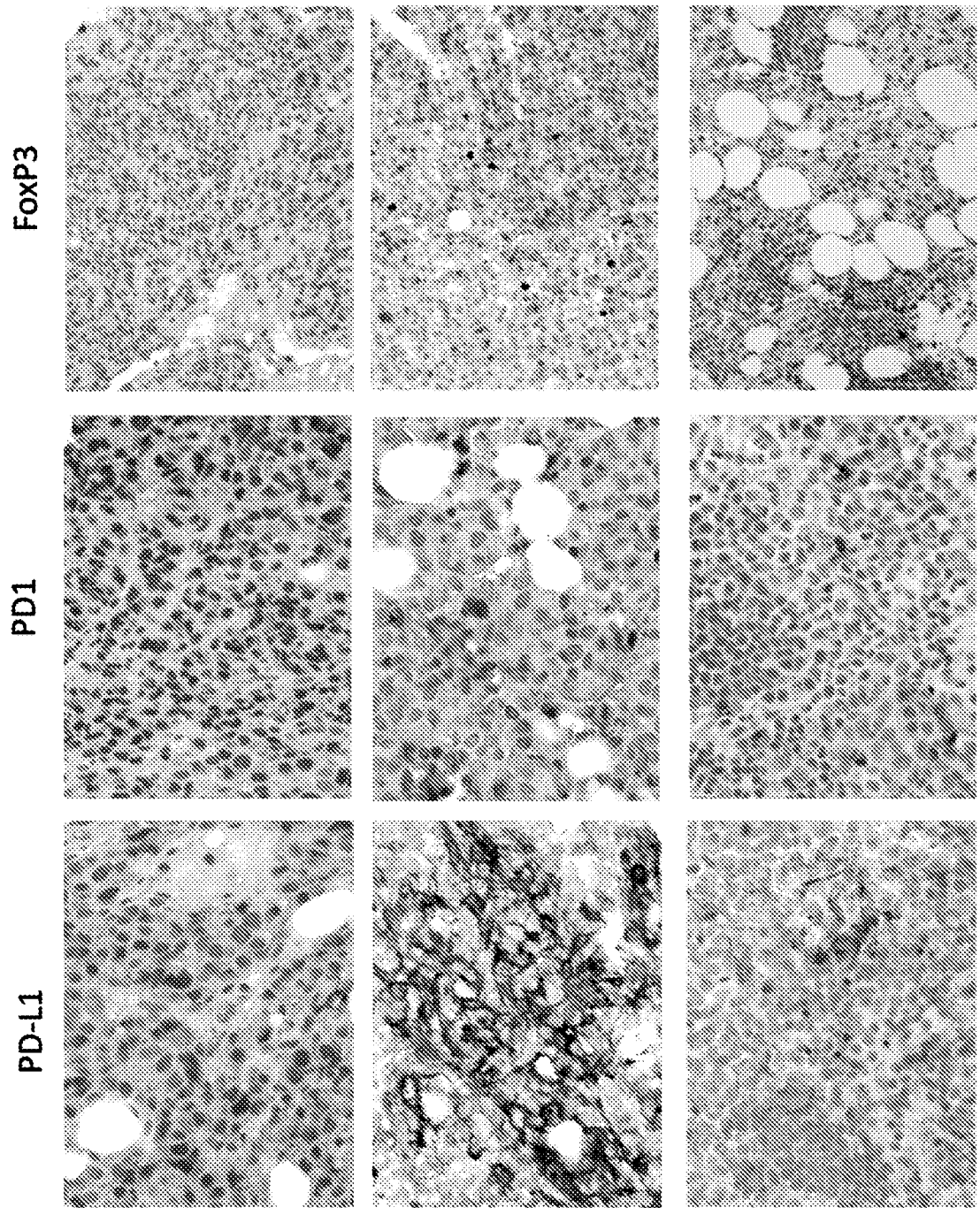


FIG. 8E

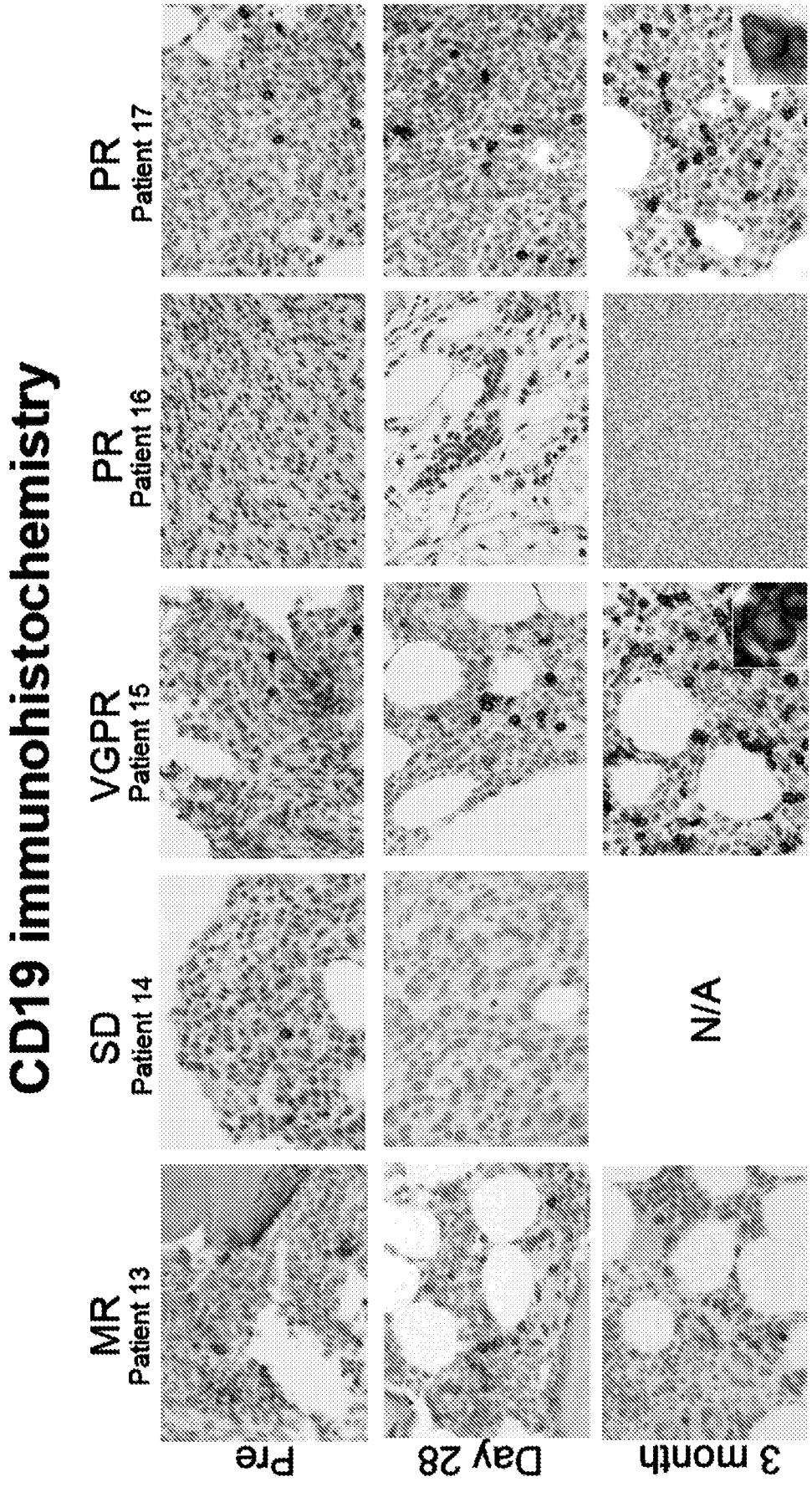

CD19 immunohistochemistry
MR
Patient 13
SD
Patient 14
VGPR
Patient 15
PR
Patient 16
PR
Patient 17
Pre
Day 28
3 month
N/A

FIG. 9

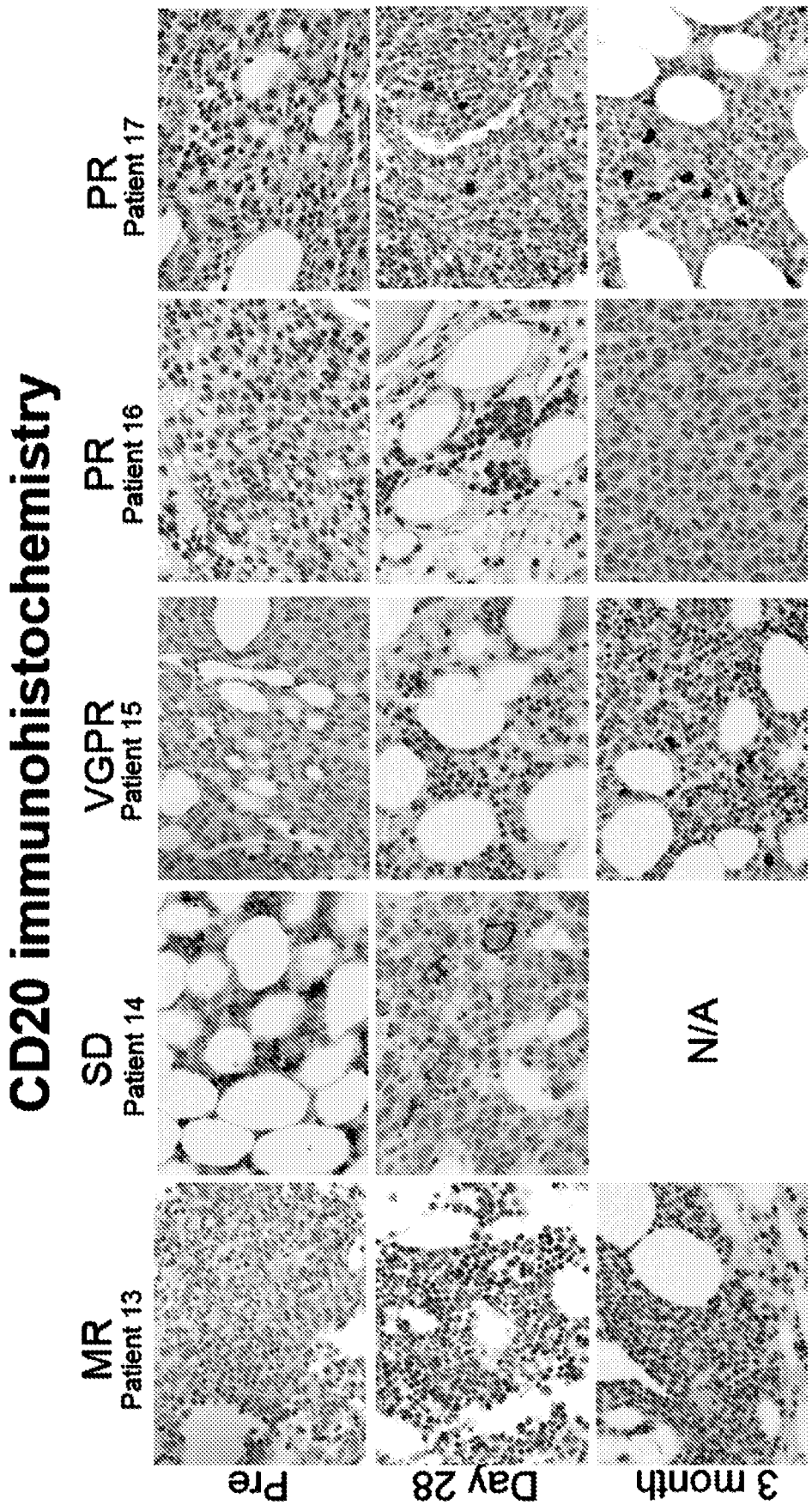

CD20 immunohistochemistry
MR
Patient 13
SD
Patient 14
VGPR
Patient 15
PR
Patient 16
PR
Patient 17
Pre
Day 28
3 month
N/A

FIG. 10

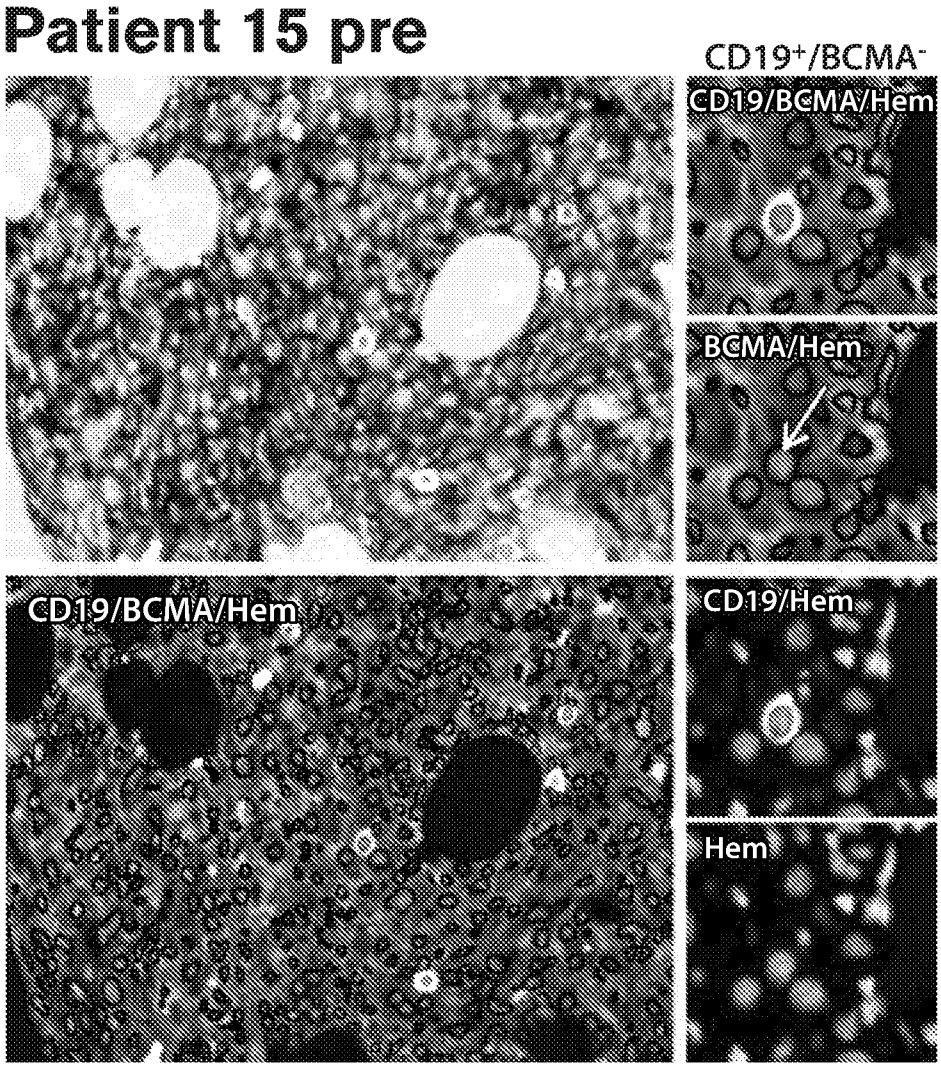

Patient 15 pre
CD19+/BCMA-
CD19/BCMA/Hem
BCMA/Hem
CD19/BCMA/Hem
CD19/Hem
Hem

FIG. 11A

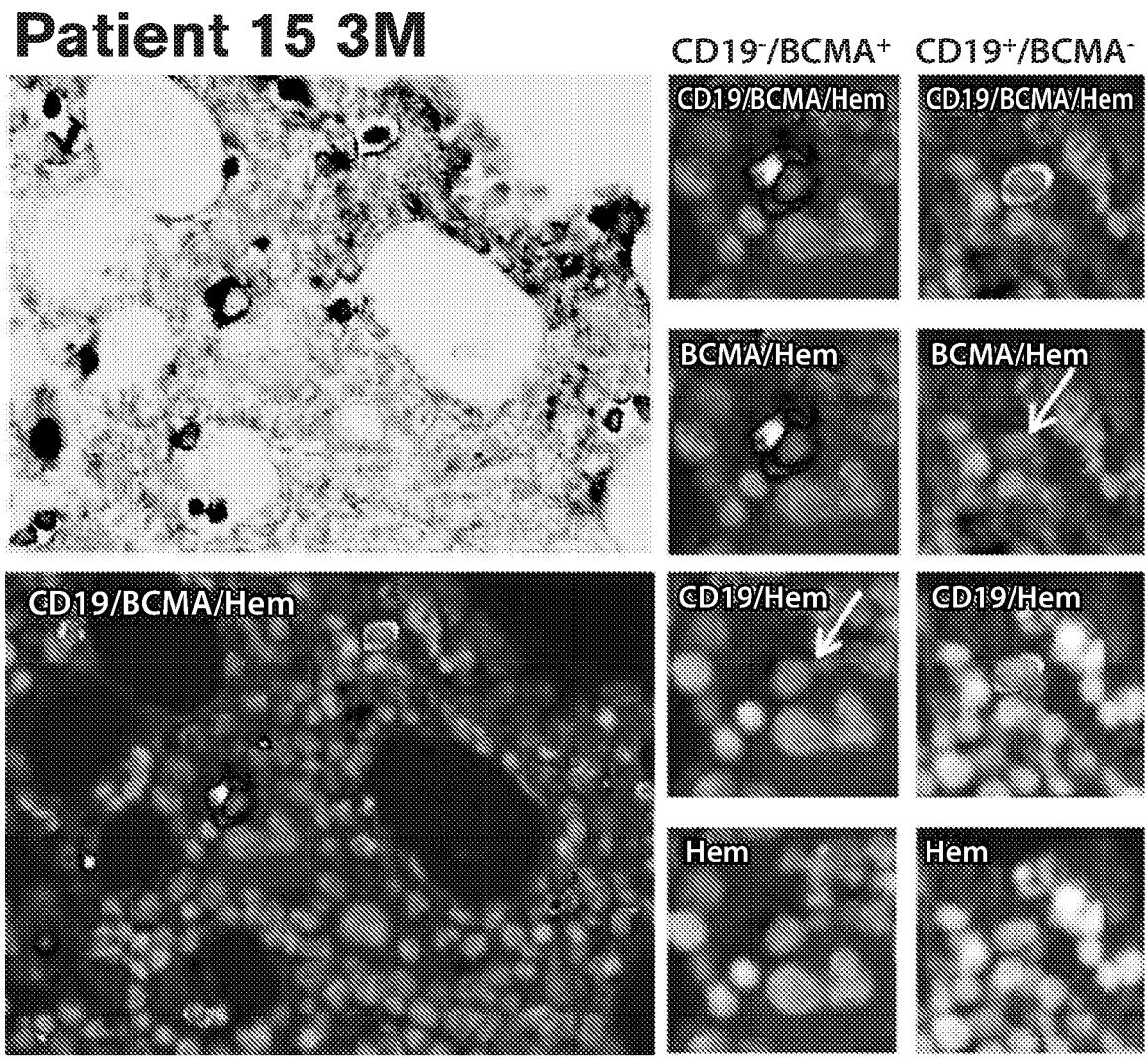

Patient 15 3M
CD19-/BCMA+
CD19+/BCMA-
CD19/BCMA/Hem
CD19/BCMA/Hem
CD19/BCMA/Hem
BCMA/Hem
BCMA/Hem
CD19/Hem
CD19/Hem
Hem
Hem

FIG. 11B

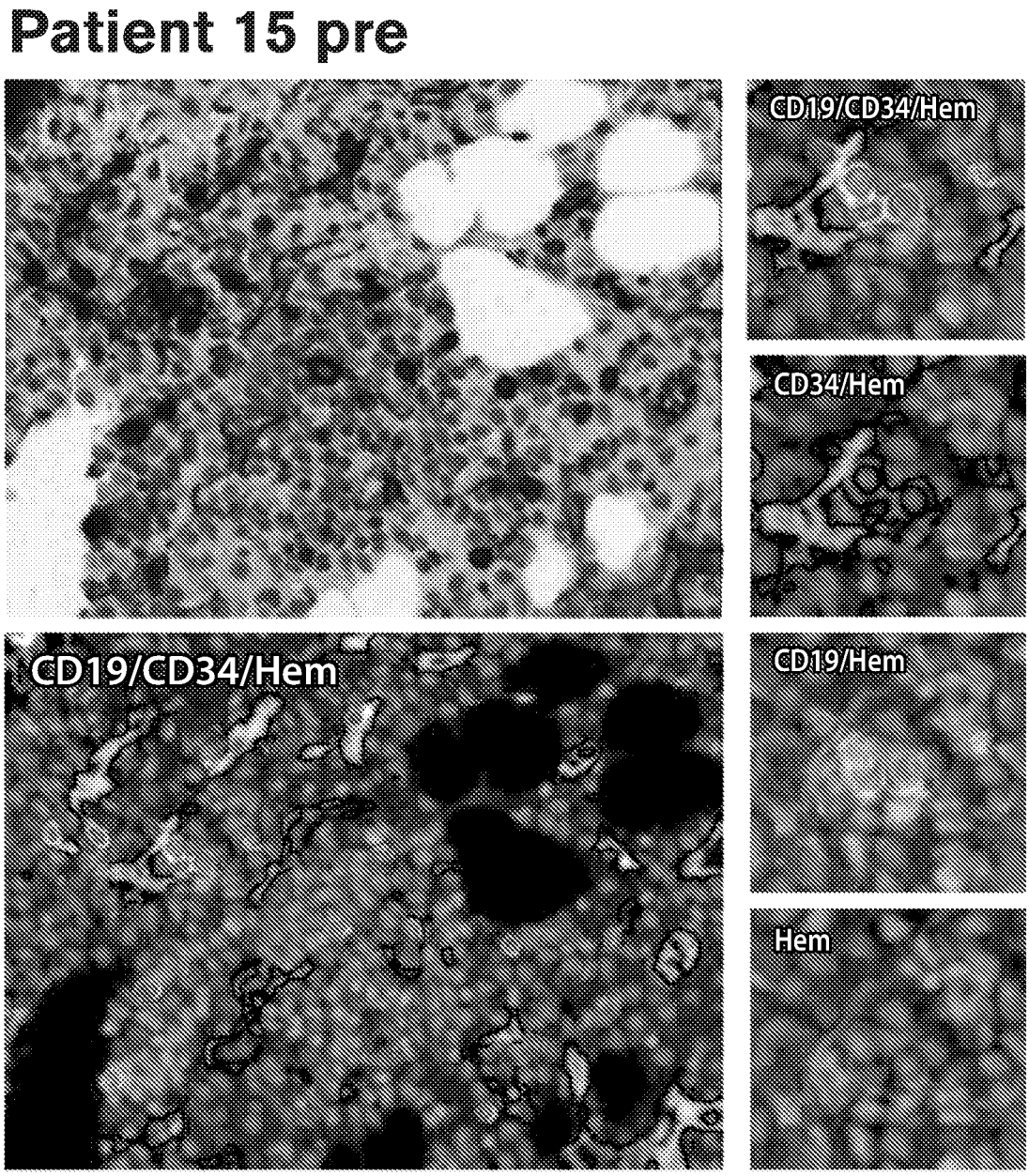

Patient 15 pre
CD19/CD34/Hem
CD34/Hem
CD19/CD34/Hem
CD19/Hem
Hem

FIG. 12A

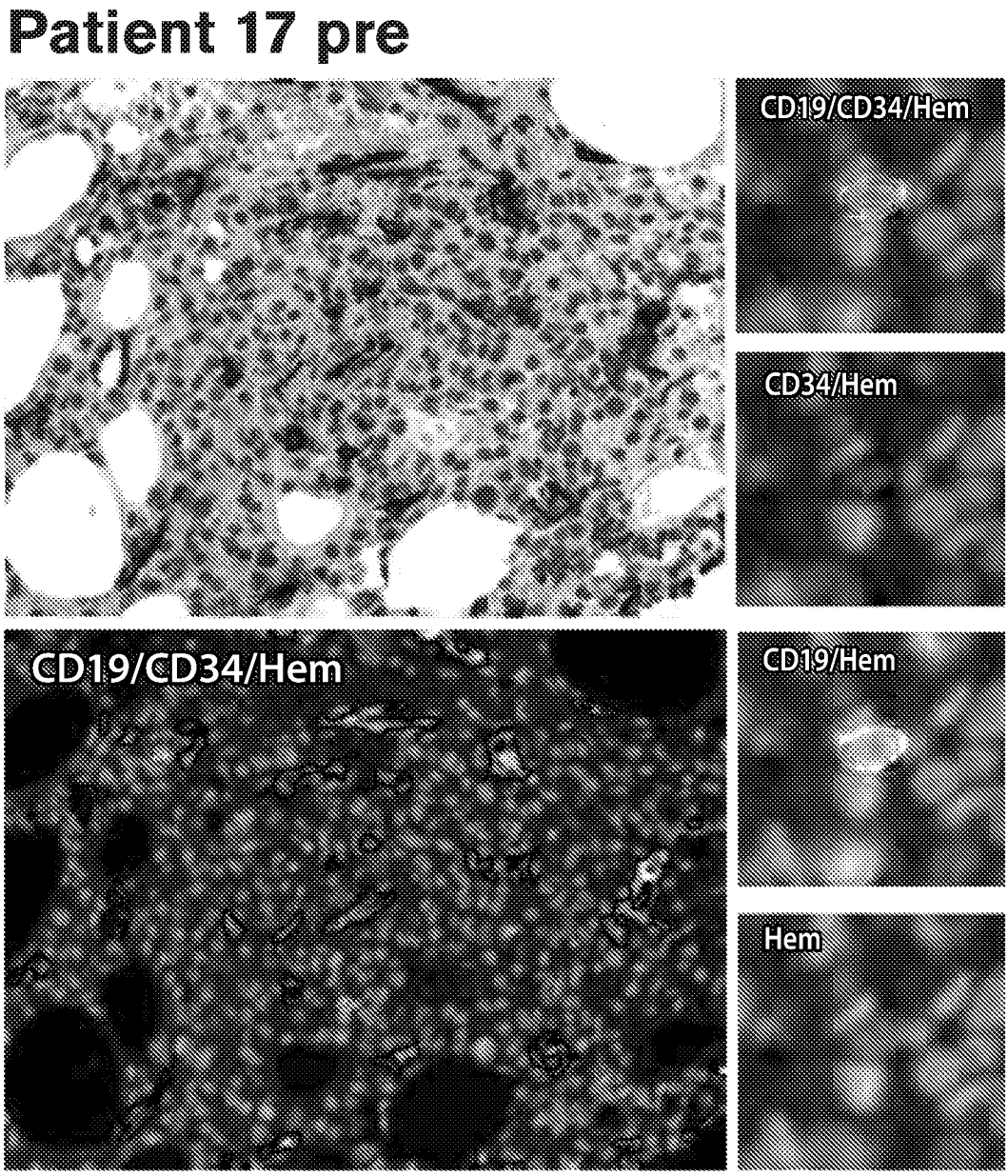

Patient 17 pre
CD19/CD34/Hem
CD34/Hem
CD19/CD34/Hem
CD19/Hem
Hem

FIG. 12B

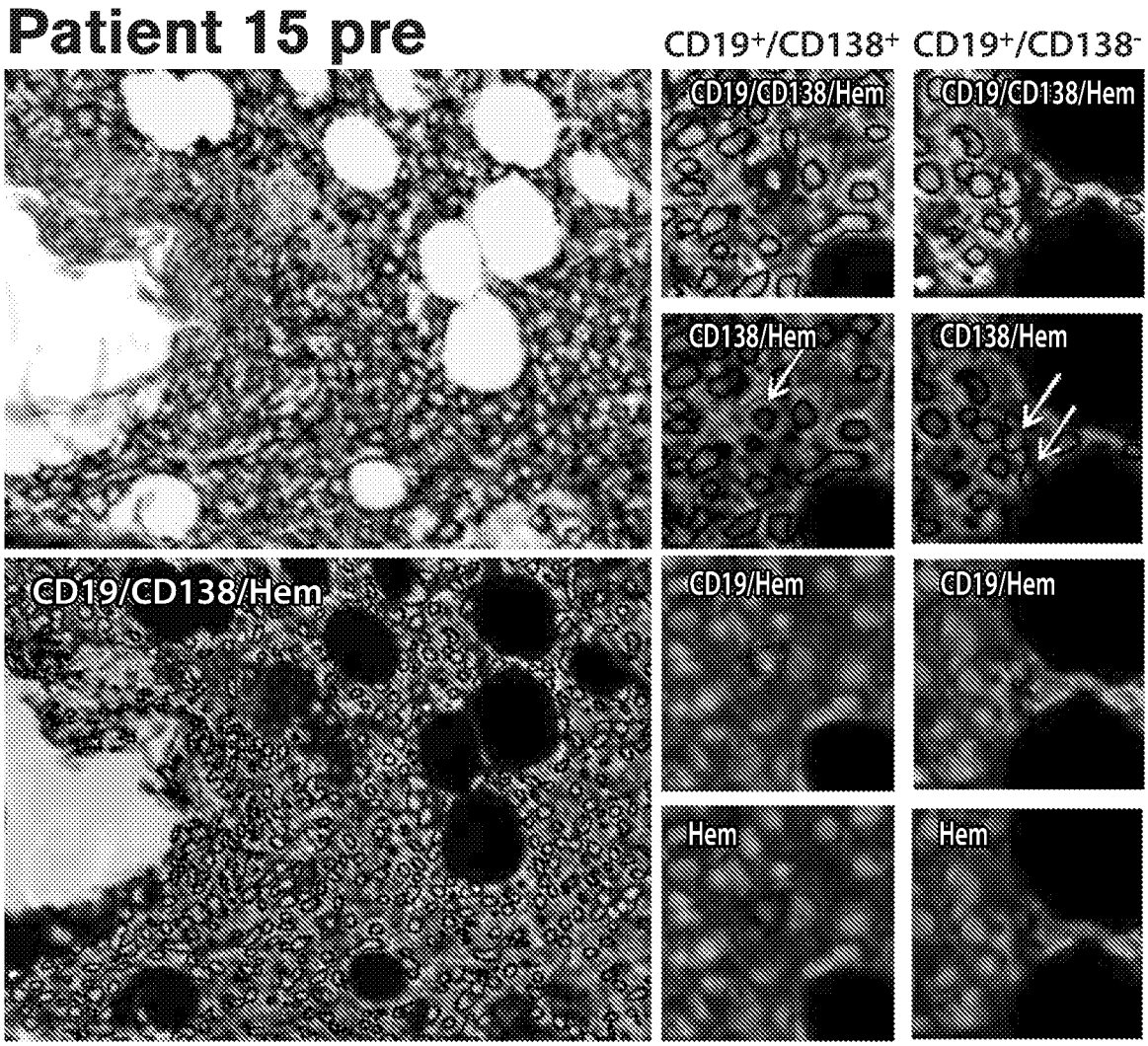

Patient 15 pre
CD19+/CD138+
CD19+/CD138-
CD19/CD138/Hem
CD19/CD138/Hem
CD138/Hem
CD138/Hem
CD19/CD138/Hem
CD19/Hem
CD19/Hem
Hem
Hem

FIG. 13

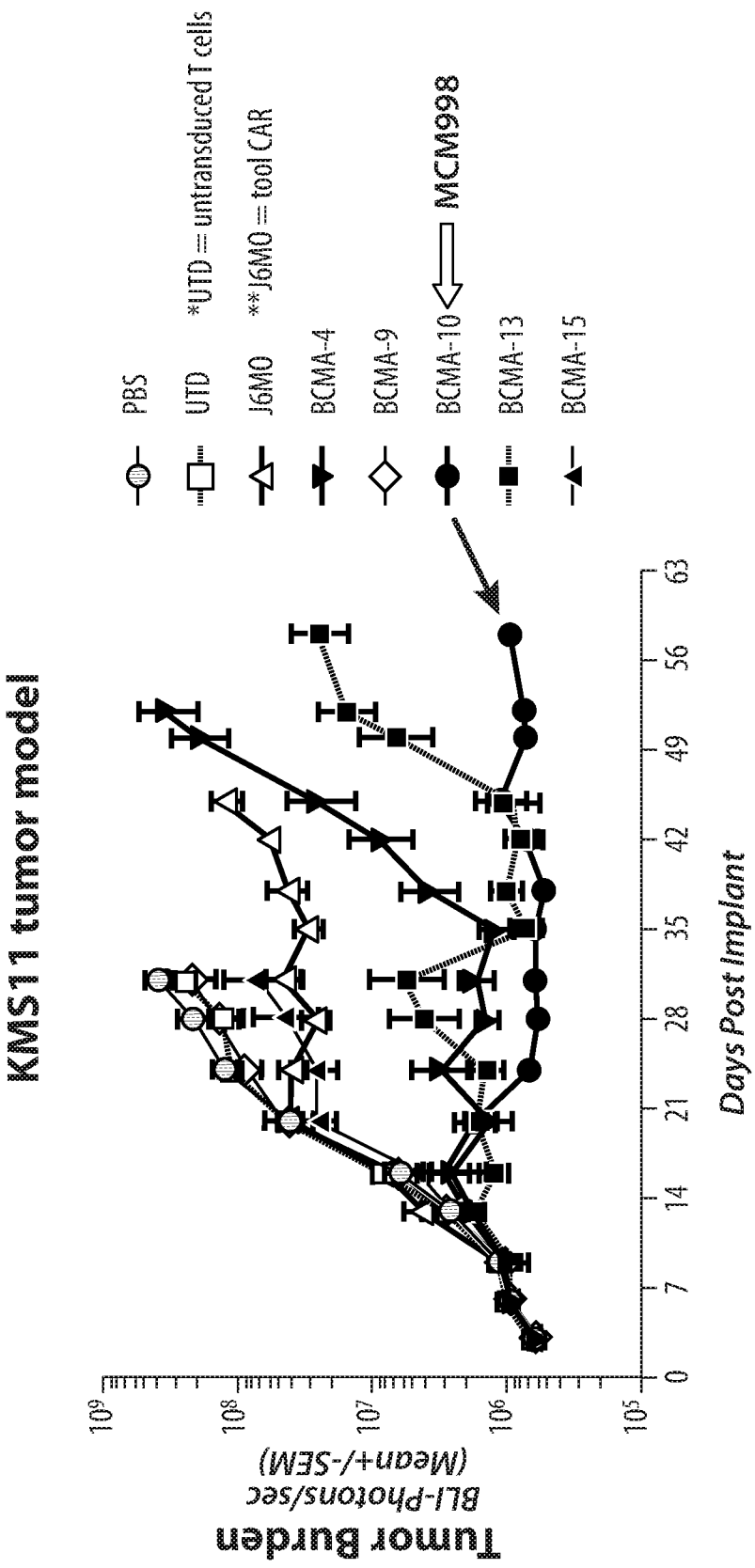

KMS11 tumor model
PBS
UTD
*UTD = untransduced T cells
J6MO
**J6MO = tool CAR
BCMA-4
BCMA-9
BCMA-10
MCM998
BCMA-13
BCMA-15
Tumor Burden
BLI-Photons/sec
(Mean+/-SEM)
Days Post Implant
0
7
14
21
28
35
42
49
56
63

FIG. 14

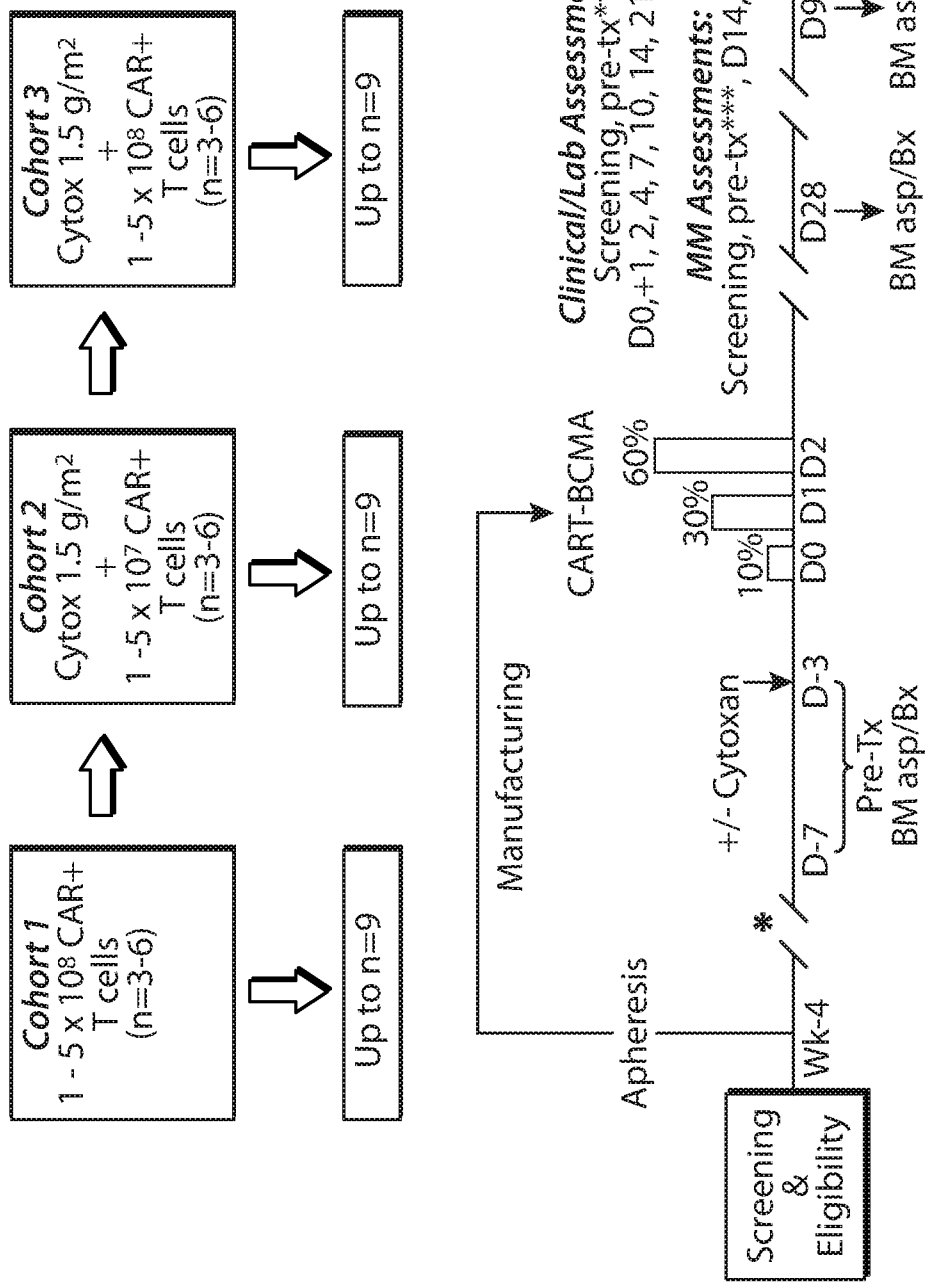

Cohort 1
1 - 5 x 10⁸ CAR+ T cells (n=3-6)
Cohort 2
Cytox 1.5 g/m²
+
1 -5 x 10⁷ CAR+ T cells (n=3-6)
Cohort 3
Cytox 1.5 g/m²
+
1 -5 x 10⁸ CAR+ T cells (n=3-6)
Up to n=9
Up to n=9
Up to n=9
Screening & Eligibility
Wk-4
Apheresis
Manufacturing
CART-BCMA
*
D-7
D-3
Pre-Tx
BM asp/Bx
+/- Cytoxan
10%
30%
60%
D0 D1D2
Clinical/Lab Assessments:
Screening, pre-tx***
D0,+1, 2, 4, 7, 10, 14, 21, 28**
MM Assessments:
Screening, pre-tx***, D14, D28**
D28
BM asp/Bx
D90
BM asp/Bx

FIG. 15

	All patients (n=14)	Cohort 1 (n=9)	Cohort 2/3 (n=5)
Age	55.5 (44-70)	57 (44-70)	54 (51-64)
Gender	57% M; 43% F	67% male; 33% female	40% M; 60% F
Years from diagnosis	4.9 (1.8-9.6)	4.9 (1.8-9.6)	4.9 (2.9-9.4)
Isotype	IgG (42%), IgA (42%) LC (14%)	IgG (33%), IgA (44%) LC (22%)	IgG (60%), IgA (40%)
Prior lines of therapy	7 (4-11)	9 (4-11)	7 (5-10)
Lenalidomide	100% (ref 86%)	100% (refractory: 78%)	100% (ref 80%)
Bortezomib	100% (ref 86%)	100% (refr: 89%)	100% (ref 80%)
Pomalidomide	100% (ref 93%)	100% (refr: 89%)	100% (ref 100%)
Carfilzomib	93%* (ref 92%)	100%* (refr: 89%)	80%* (ref 80%)
Autologous SCT	86%	78%	100%
Cyclophosphamide	100% (ref 71%)	100% (refr: 67%)	100% (ref 80%)
Daratumumab	57% (ref 57%)	44% (refr: 44%)	80% (ref 80%)
Anti-PD1	29% (ref 29%)	33% (refr: 33%)	20% (ref 20%)
High-risk genetics -17P or *TP53* mutation	100% 64%	100% 67%	100% 60%
Extramededullary dz	35%	33%	40%
% BM plasma cells	65% (0-95)	80 (15-95)	45% (0-95%)

FIG. 16A

Median peripheral T cell counts (cells/μL)

	Cohort 1 (n=9)	Cohort 2/3 (n=5)
Pre-pheresis	CD3: 325 (171 - 1134) CD4: 182 (42 - 519) CD8: 149 (80 - 600)	CD3: 633 (295 - 1231) CD4: 371 (129 - 518) CD8: 395 (168 - 706)
Pre-Cytoxan		CD3: 423 (237 - 646) CD4: 158 (95 - 296) CD8: 277 (140 - 343)
Day 0	CD3: 258 (117 - 1354) CD4: 169 (36 - 497) CD8: 126 (66 - 832)	CD3: 138 (79 - 261) CD4: 62 (42 - 131) CD8: 84 (37 - 161)

FIG. 16B

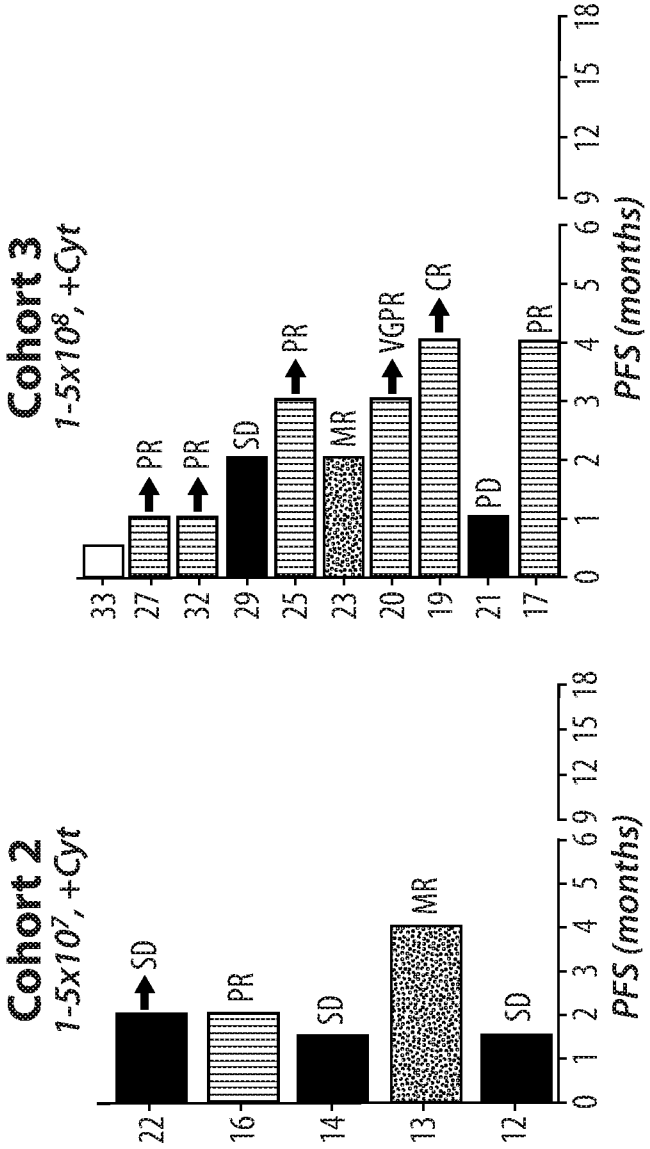


FIG. 17C

FIG. 17B

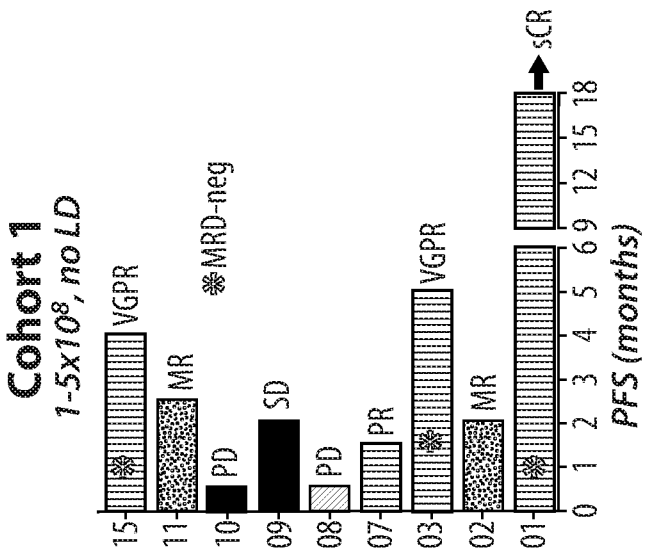


FIG. 17A

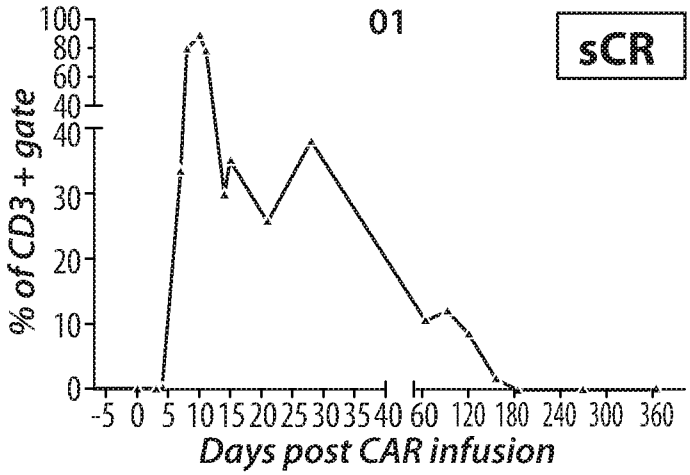


FIG. 18A-1

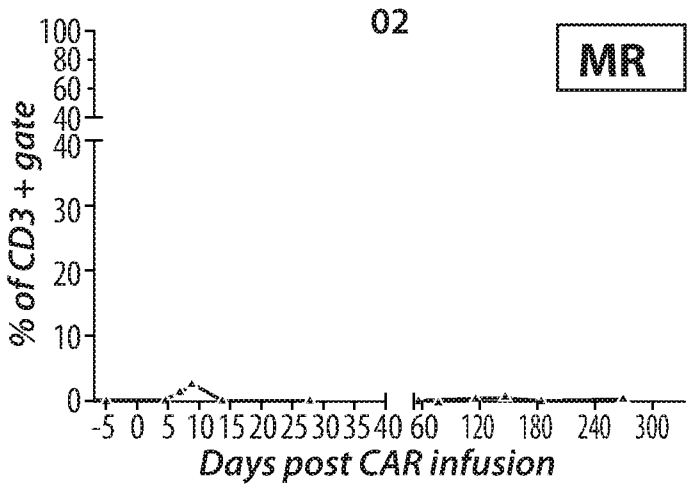


FIG. 18A-2

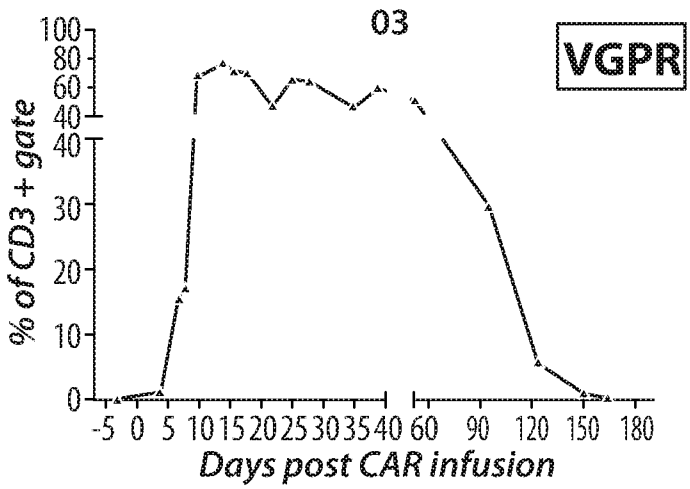


FIG. 18A-3

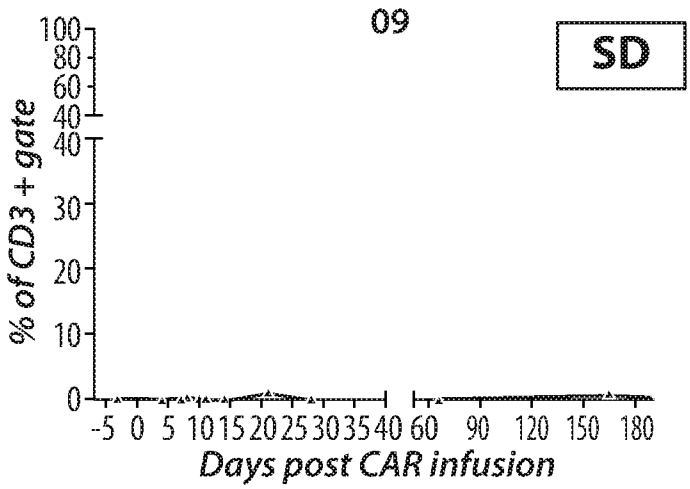


FIG. 18A-4

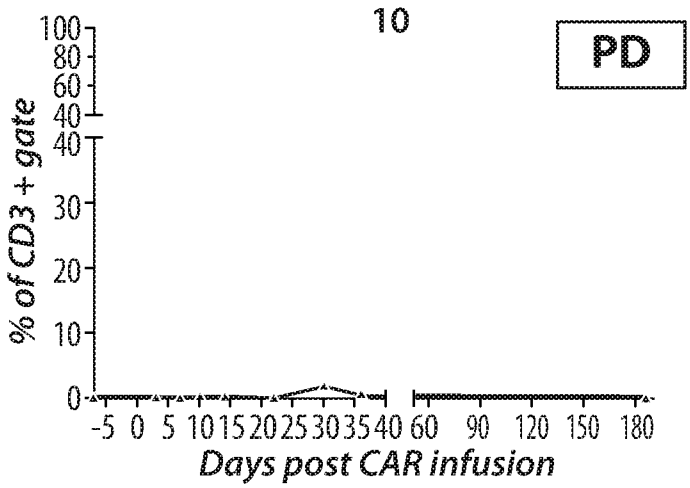


FIG. 18A-5

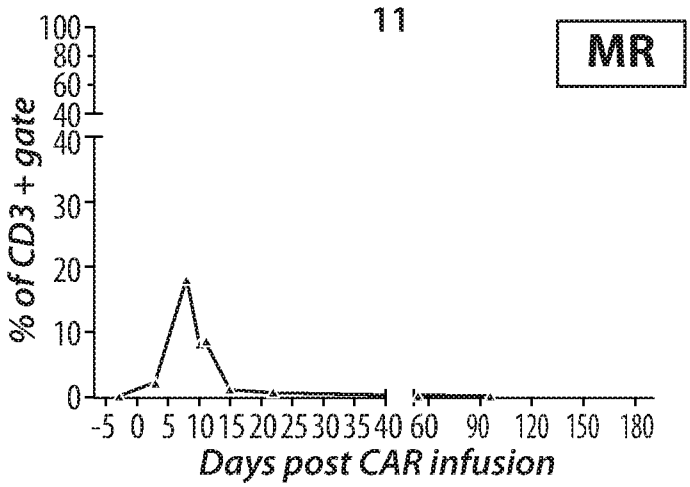


FIG. 18A-6

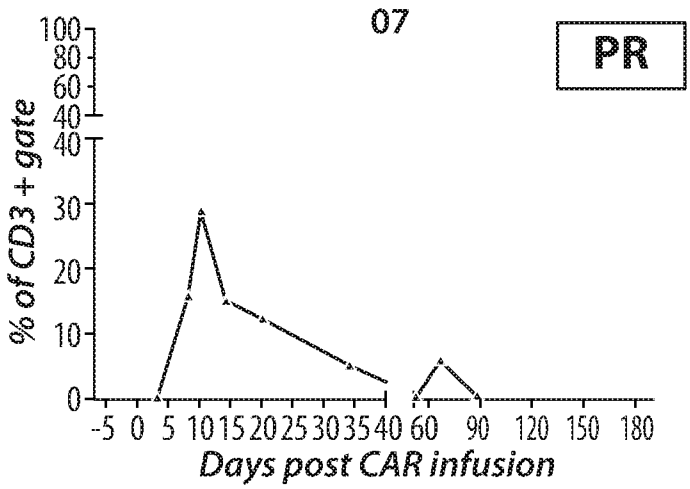


FIG. 18A-7

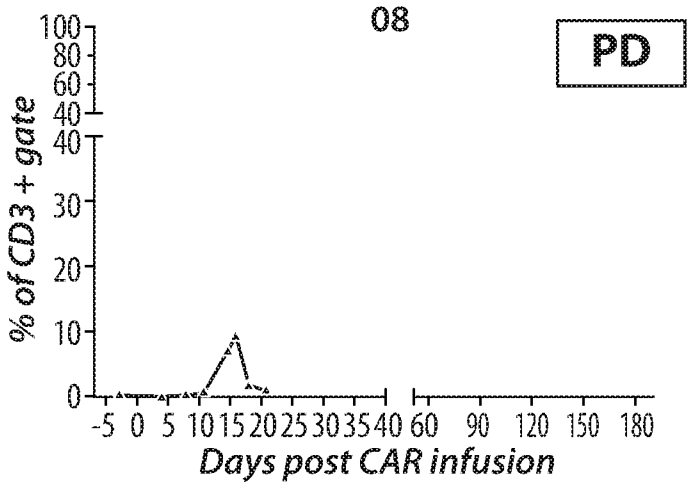


FIG. 18A-8

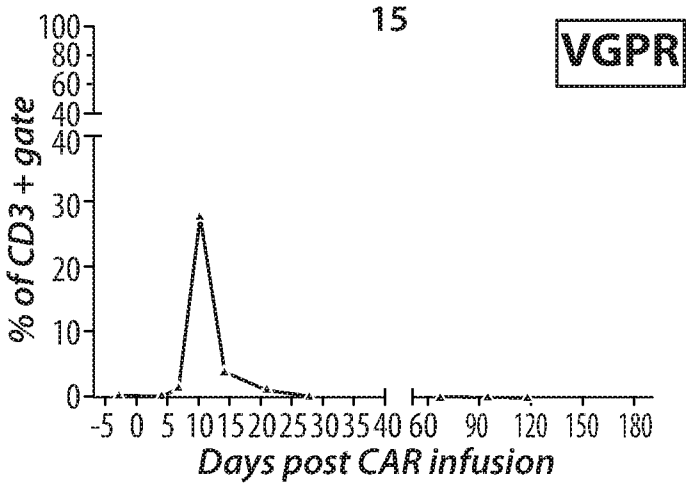


FIG. 18A-9

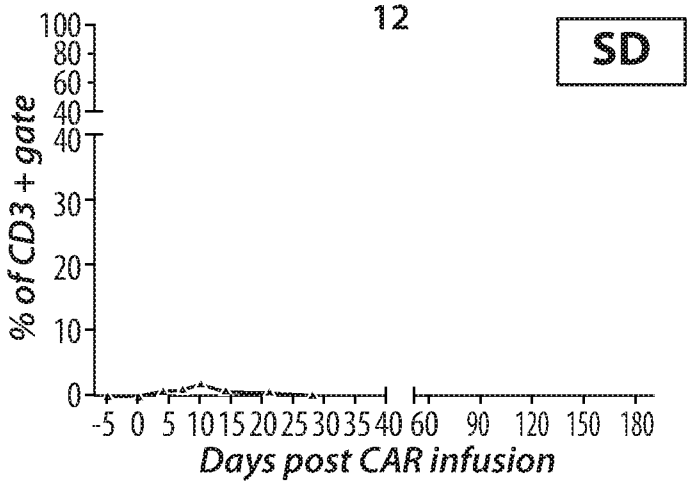


FIG. 18B-1

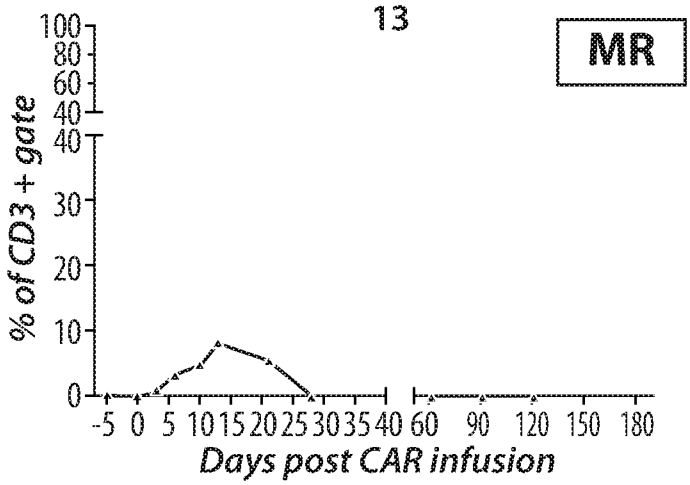


FIG. 18B-2

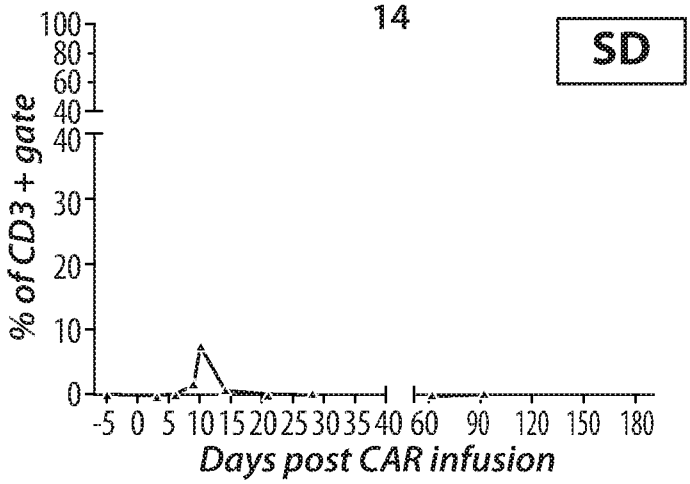


FIG. 18B-3

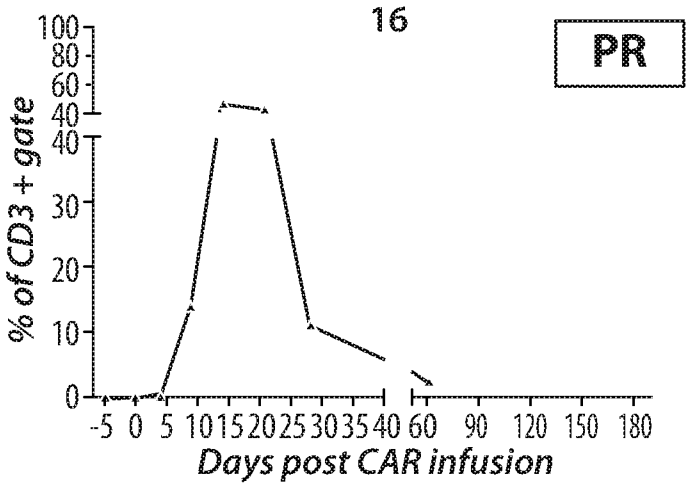


FIG. 18B-4

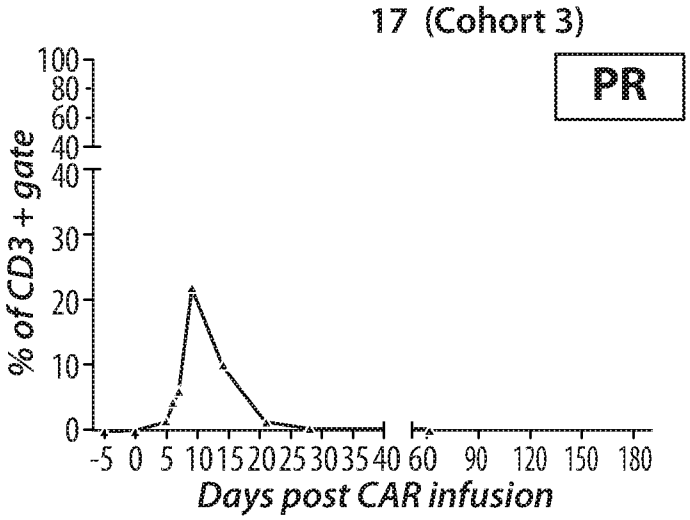


FIG. 18B-5

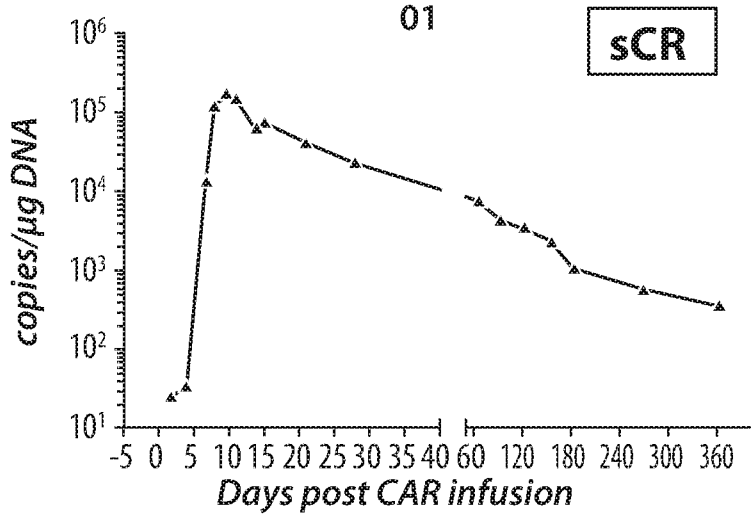


FIG. 19A-1

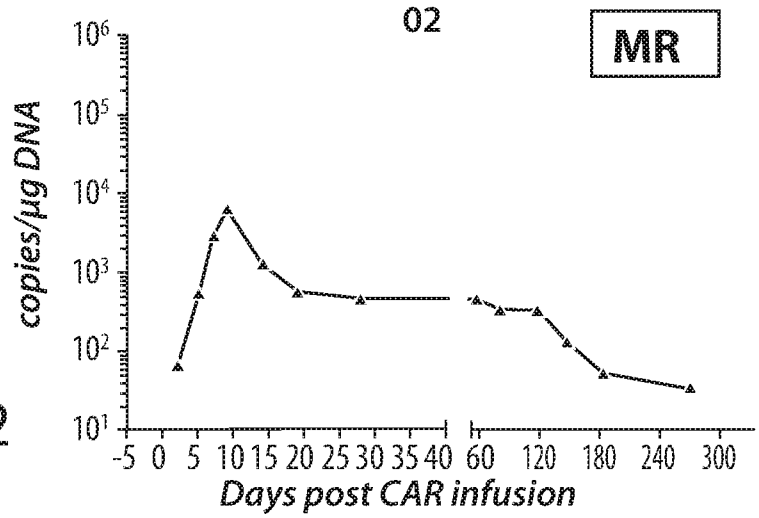


FIG. 19A-2

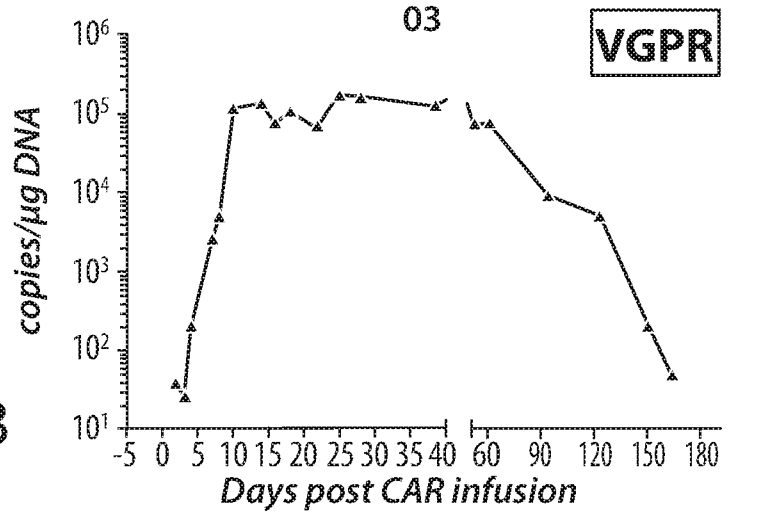


FIG. 19A-3

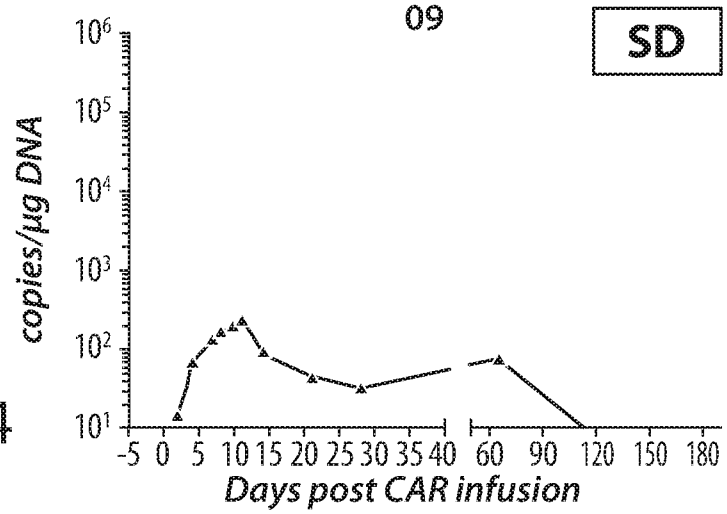


FIG. 19A-4

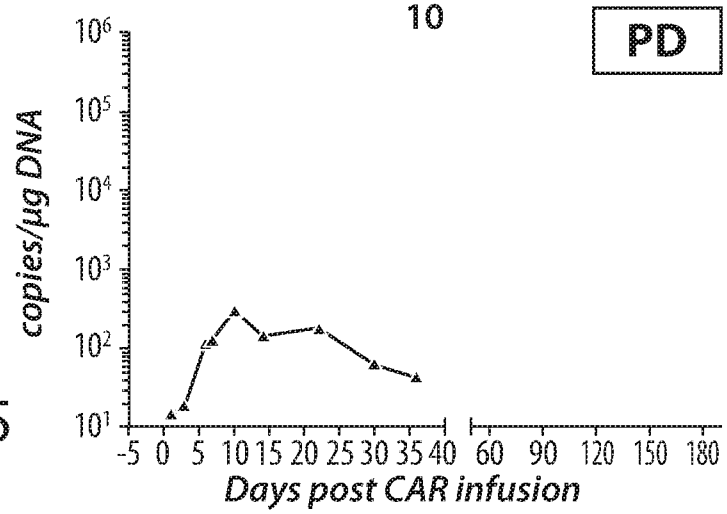


FIG. 19A-5

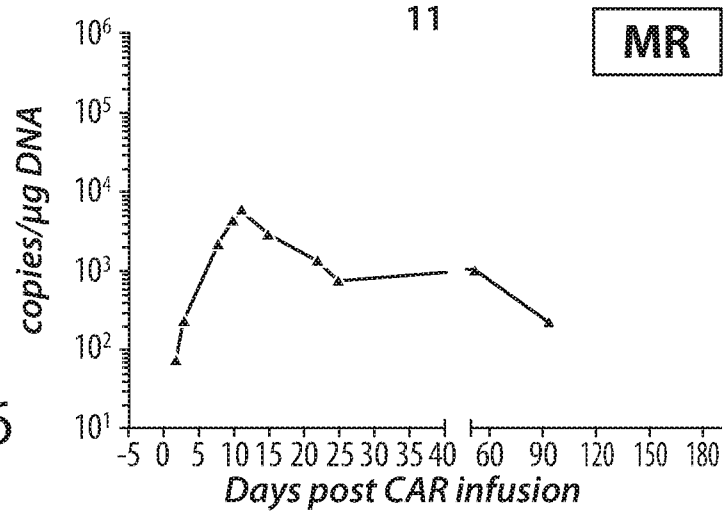


FIG. 19A-6

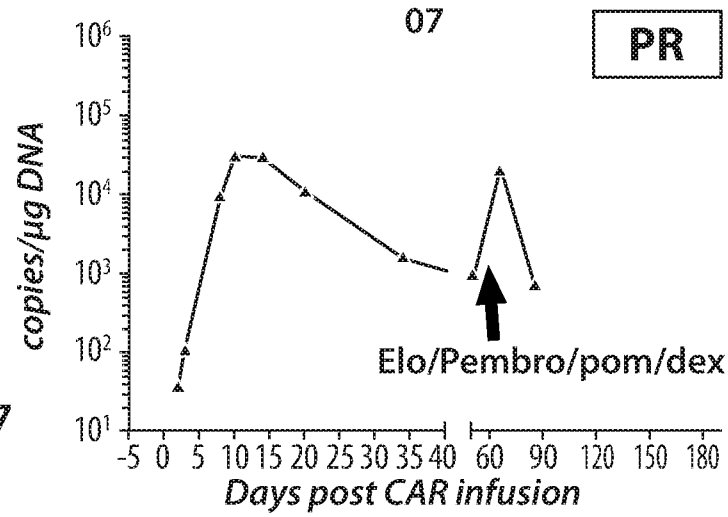


FIG. 19A-7

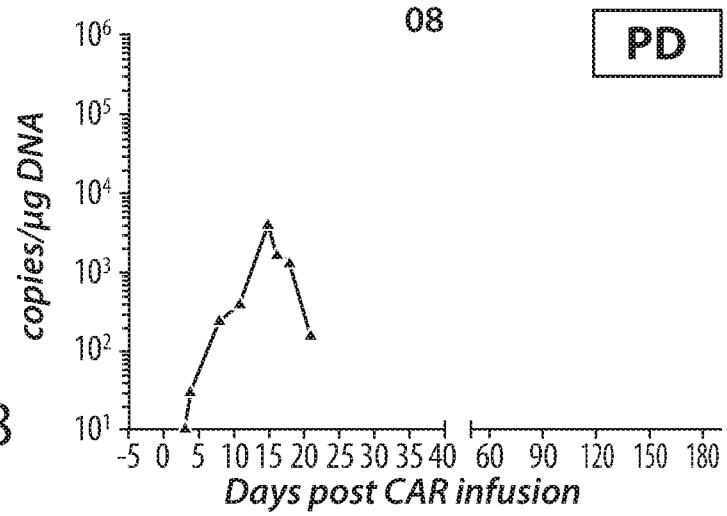


FIG. 19A-8

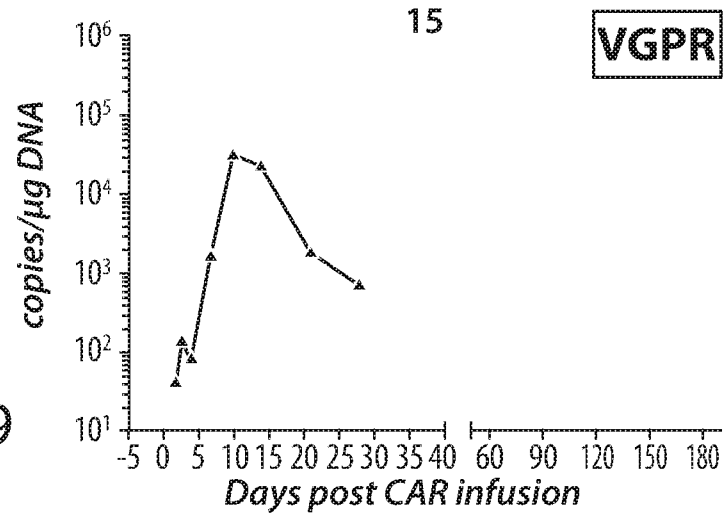


FIG. 19A-9

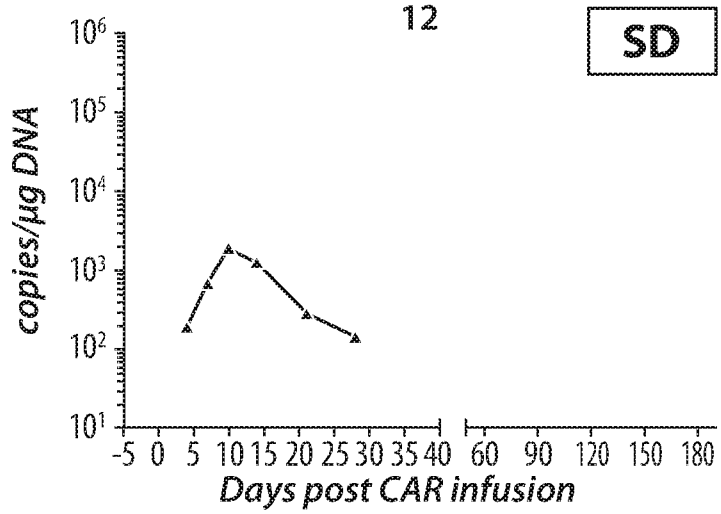


FIG. 19B-1

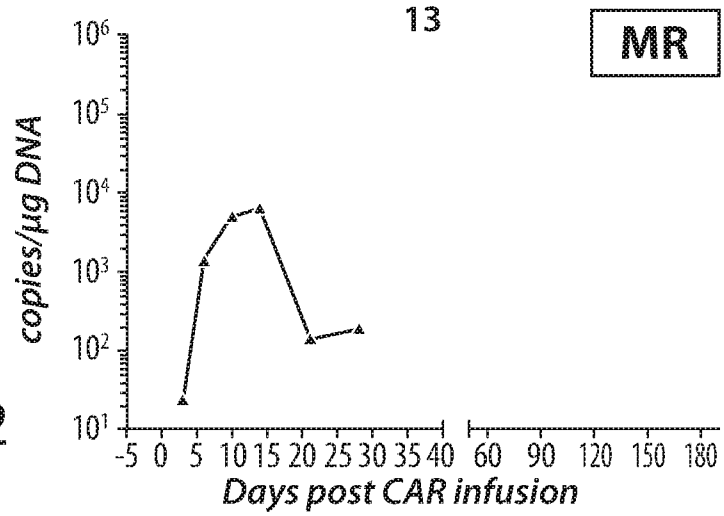


FIG. 19B-2

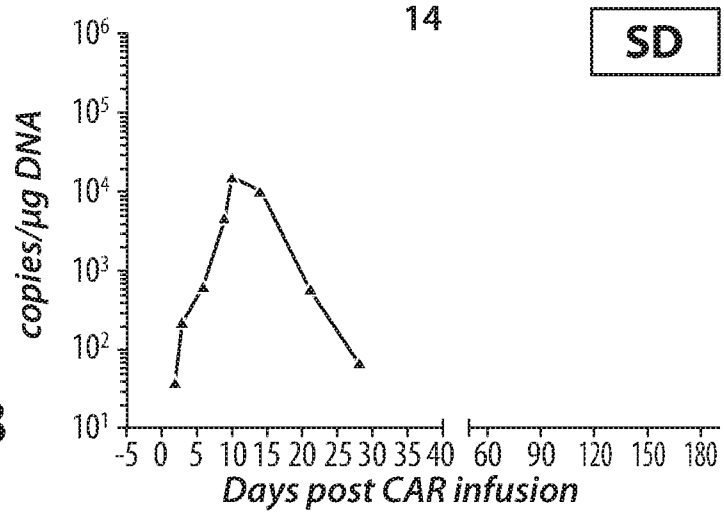


FIG. 19B-3

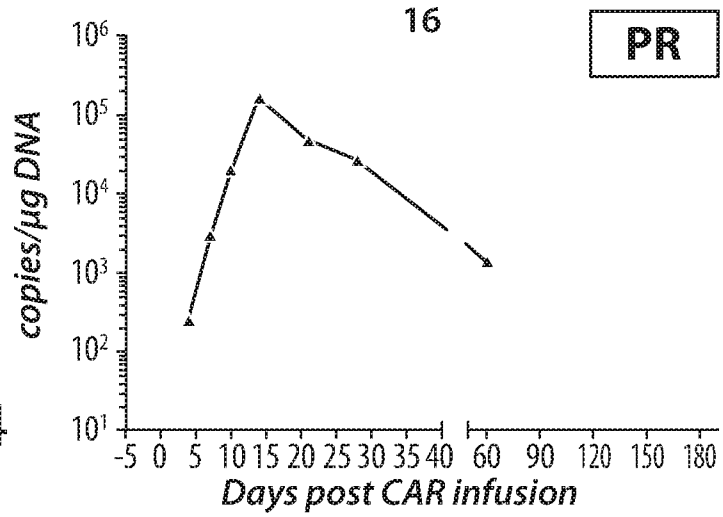


FIG. 19B-4

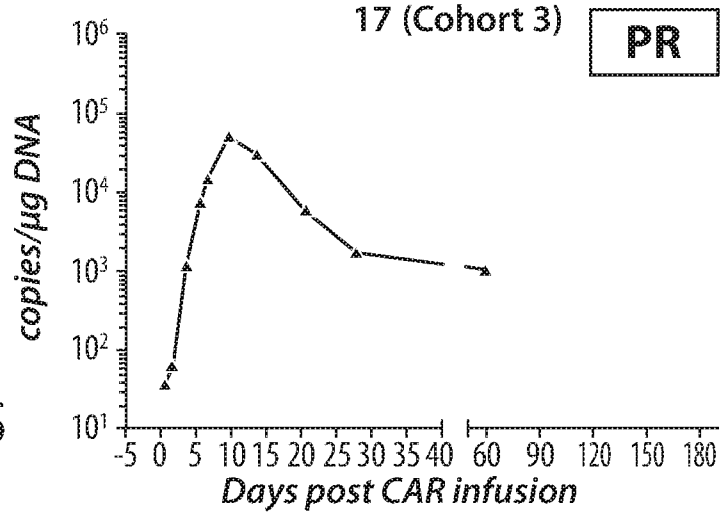


FIG. 19B-5

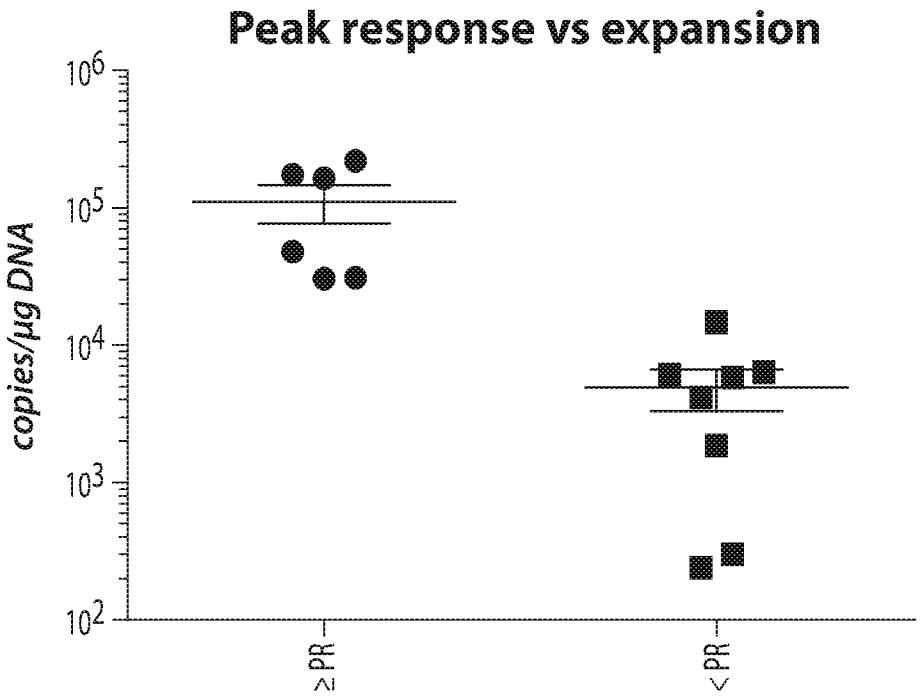


FIG. 20A

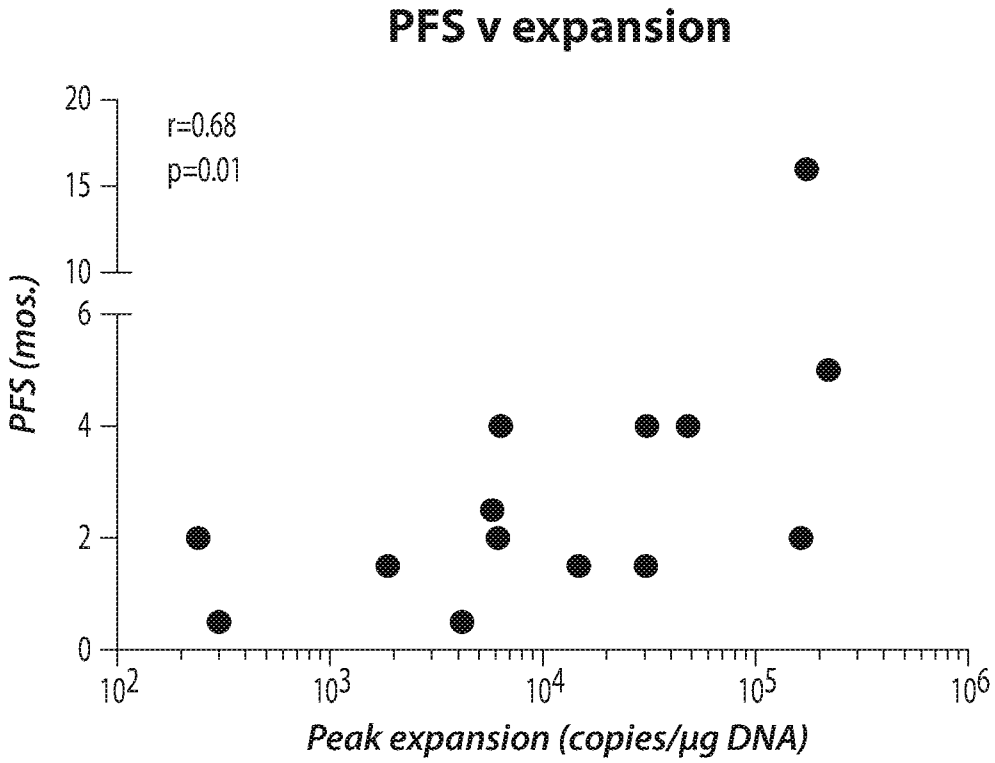


FIG. 20B

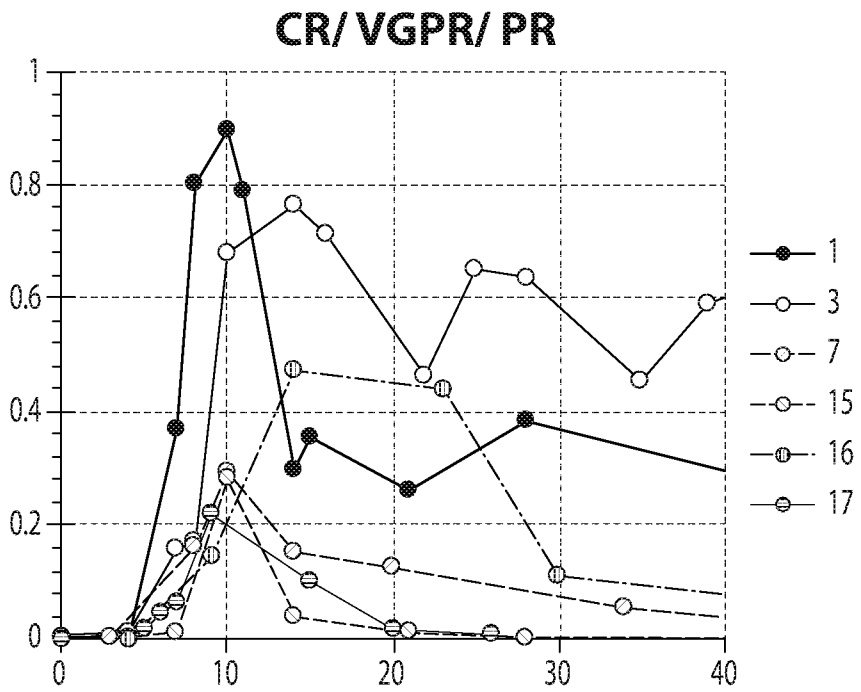
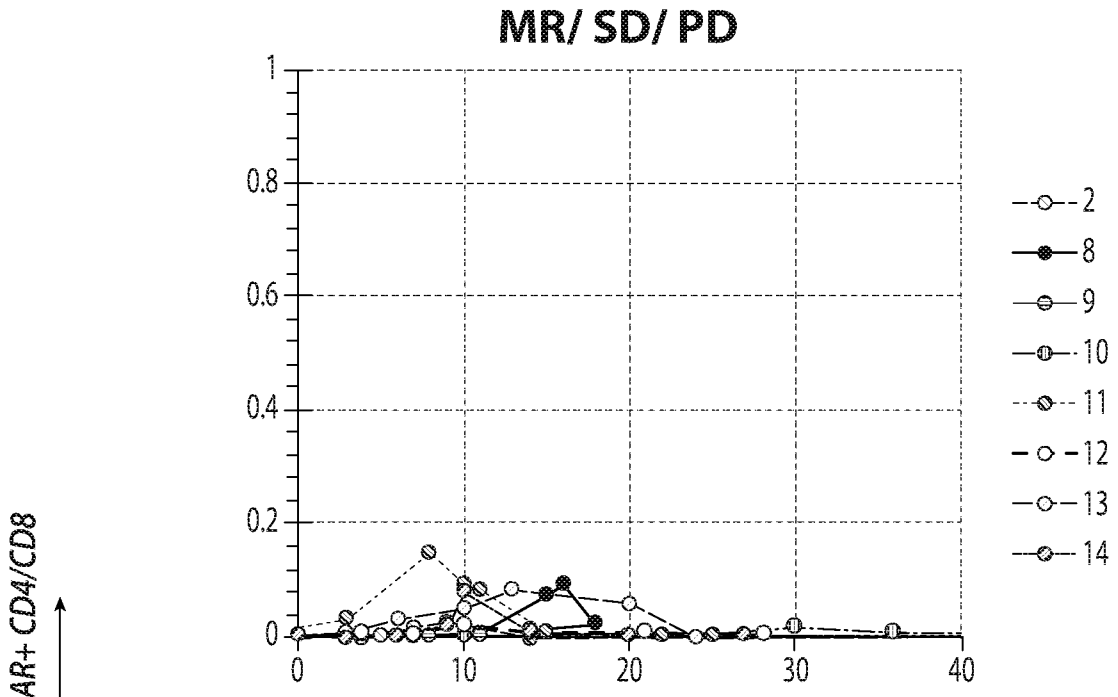


FIG. 21A



CR	VGPR	PR	MR	SD	PD
1	3, 15	7	2, 11, 13	9, 12, 14	8, 10
Unknown: 16, 17					

FIG. 21B

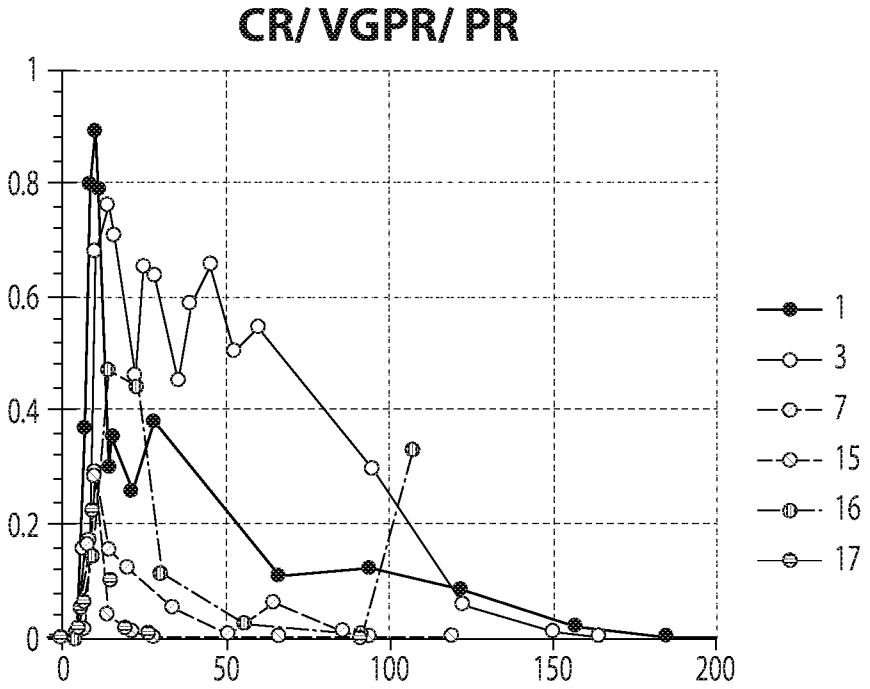
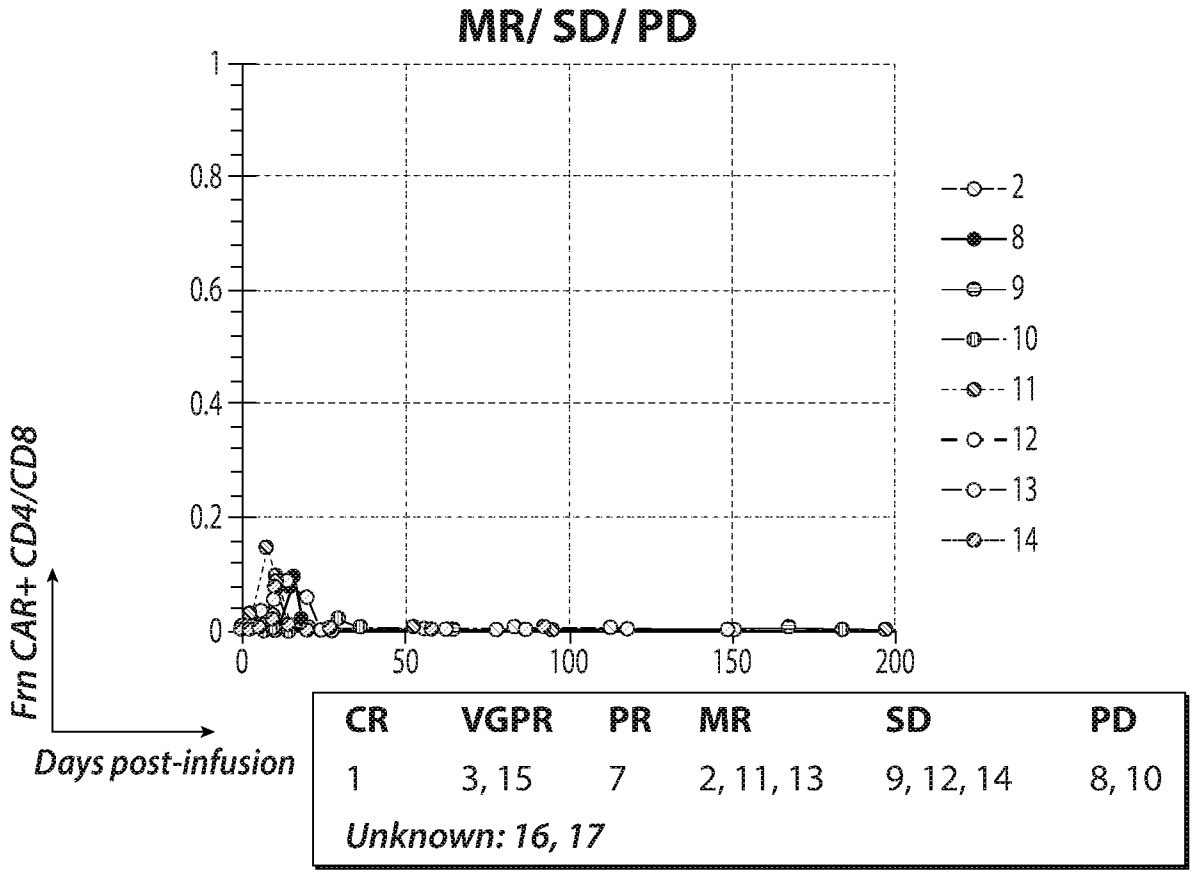


FIG. 21C



CR	VGPR	PR	MR	SD	PD
1	3, 15	7	2, 11, 13	9, 12, 14	8, 10
Unknown: 16, 17					

FIG. 21D

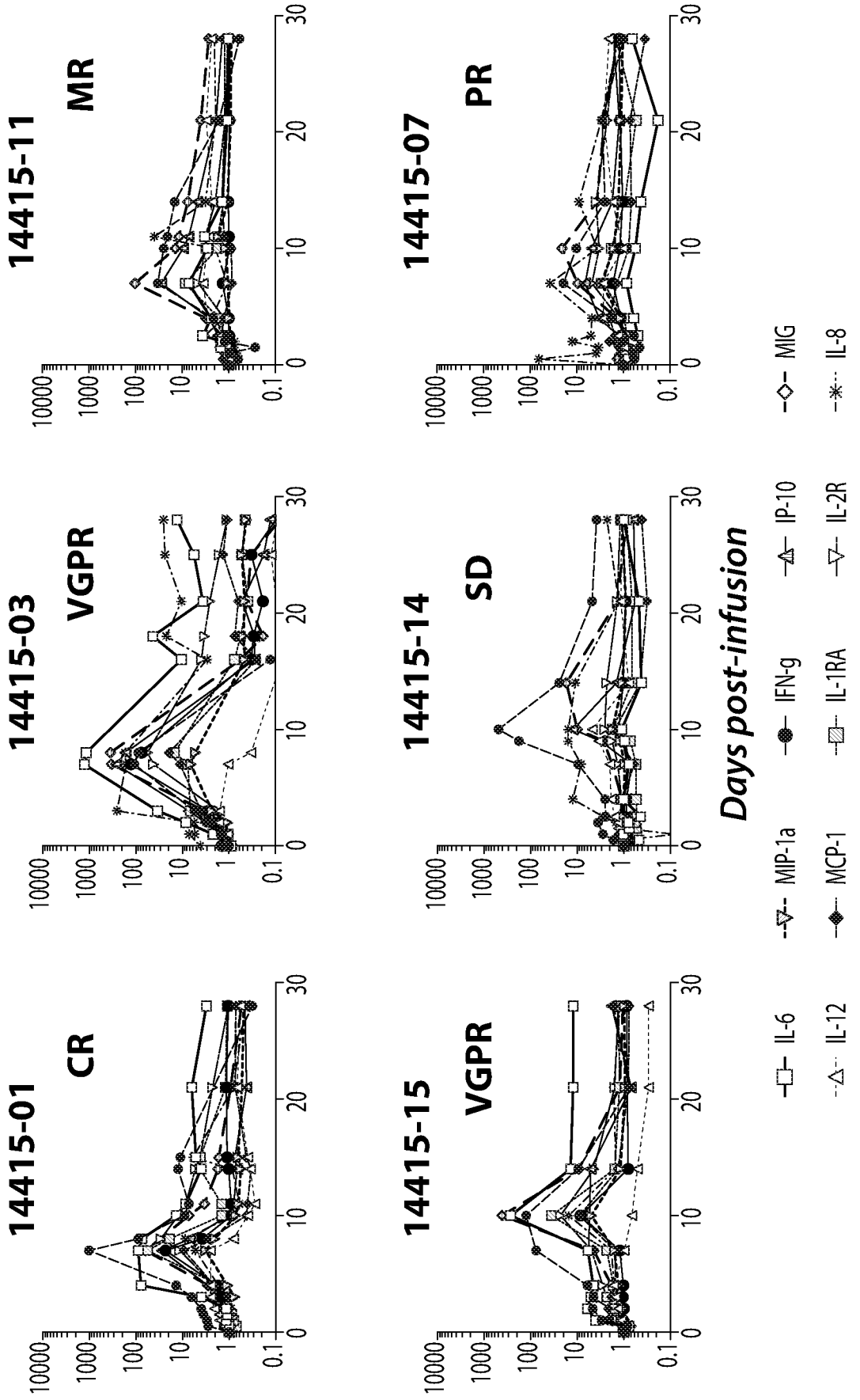

14415-01
CR
14415-03
VGPR
14415-11
MR
14415-15
VGPR
14415-14
SD
14415-07
PR
Cytokines, change from day 0
Days post-infusion
IL-6
MIP-1a
IFN-g
IP-10
MIG
IL-12
MCP-1
IL-1RA
IL-2R
IL-8

Fig. 22-1

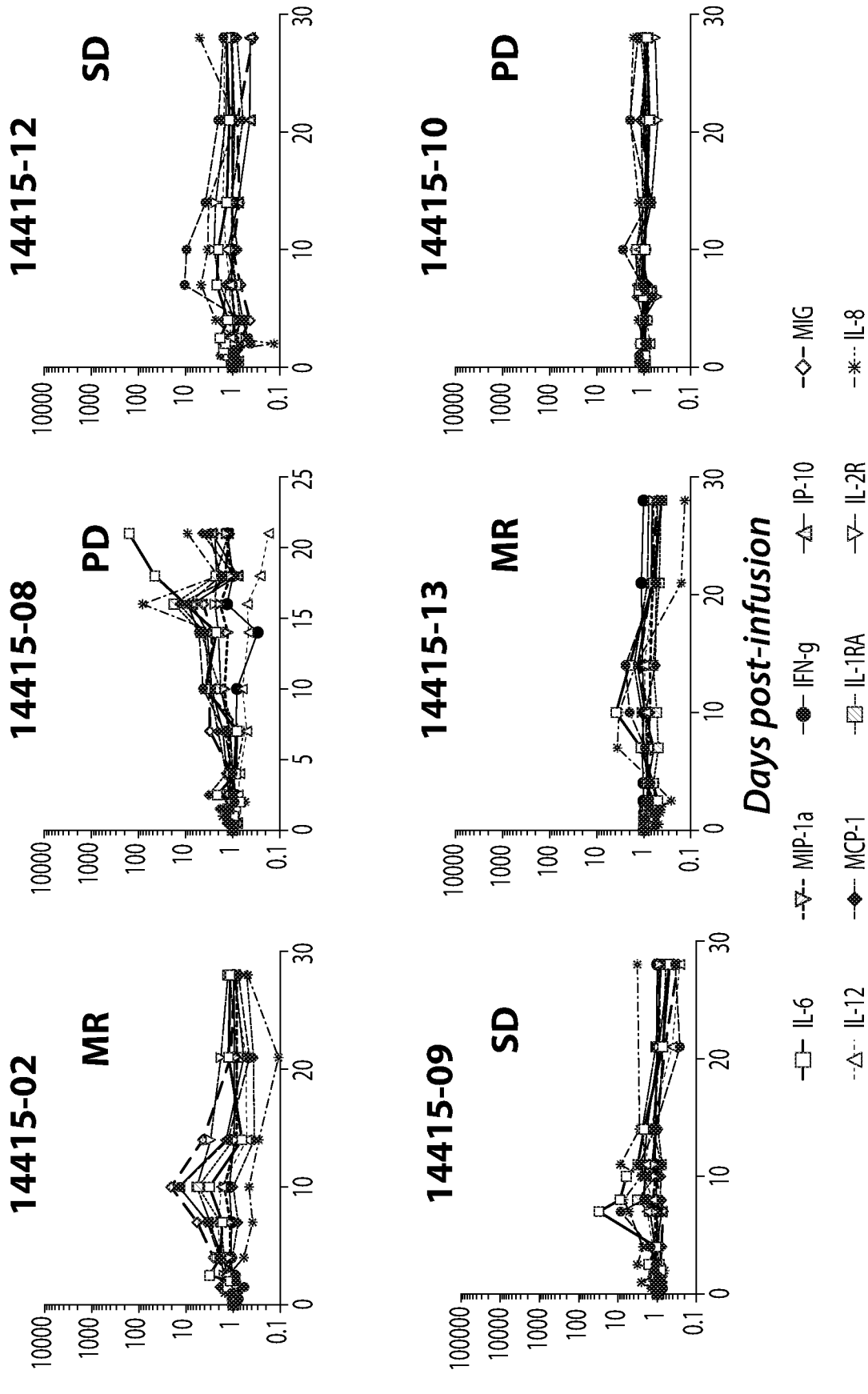

14415-02
MR
14415-08
PD
14415-12
SD
14415-09
SD
14415-13
MR
14415-10
PD
Cytokines, change from day 0
Days post-infusion
IL-6
MIP-1a
IFN-g
IP-10
MIG
IL-12
MCP-1
IL-1RA
IL-2R
IL-8

Fig. 22-2

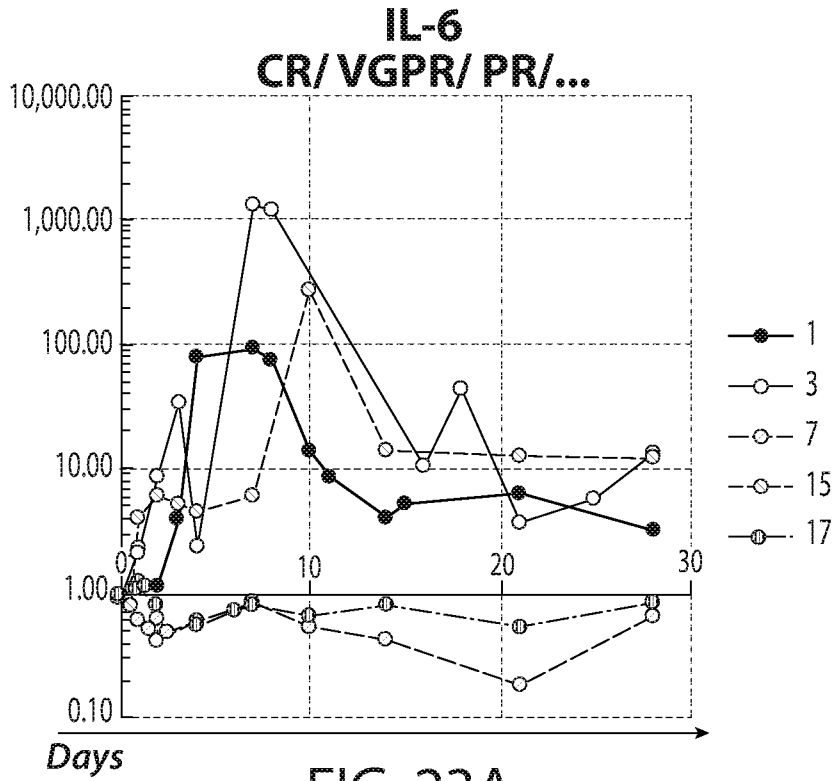
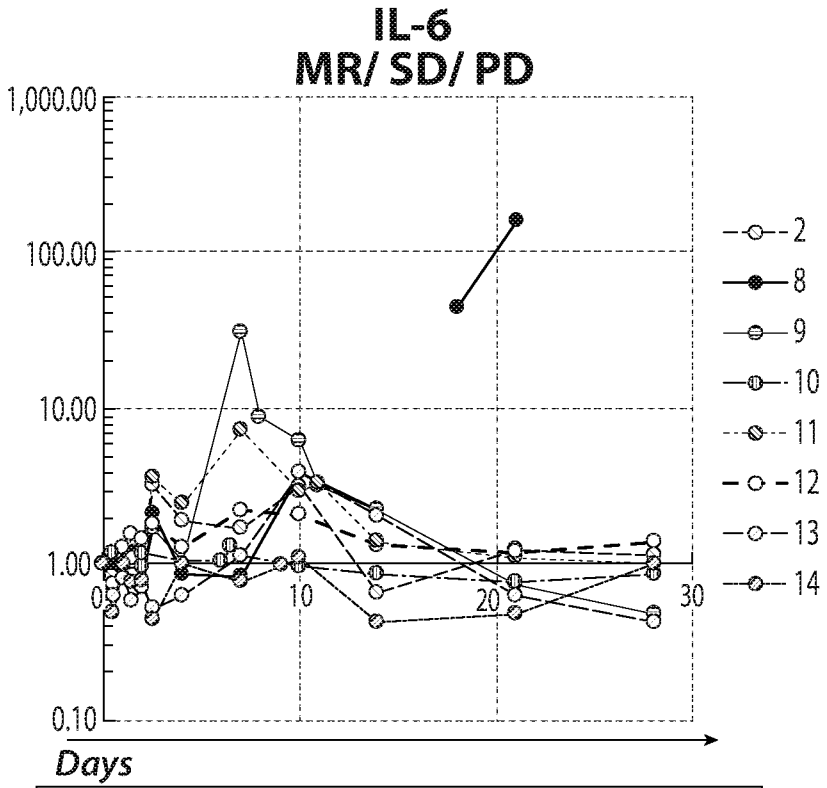


FIG. 23A



CR	VGPR	PR	MR	SD	PD
1	3, 15	7	2, 11, 13	9, 12, 14	8, 10
Unknown: 16, 17					

FIG. 23B

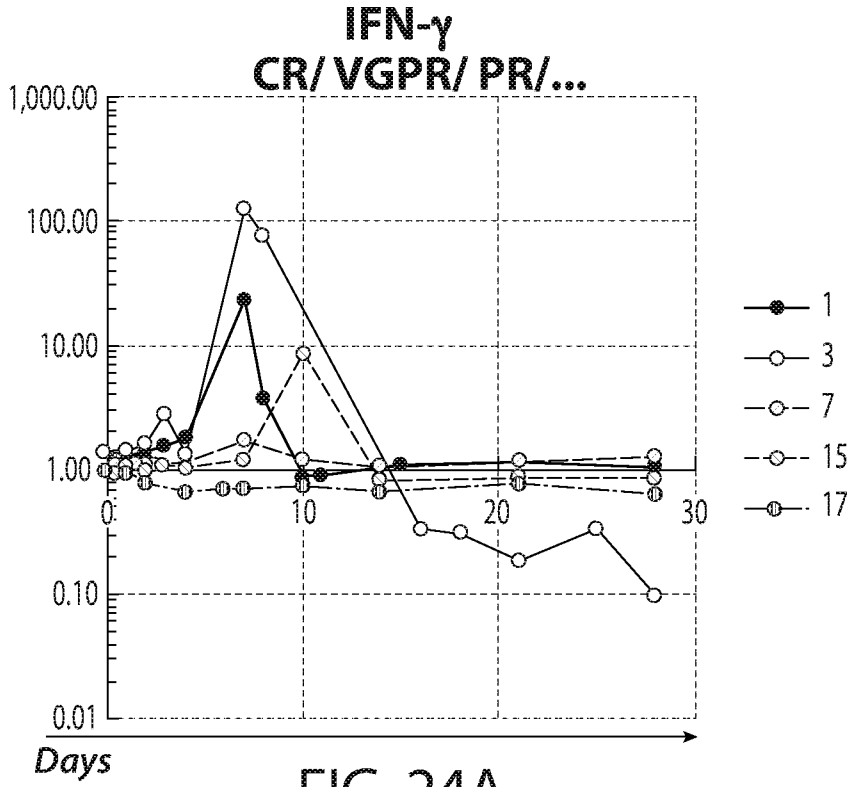
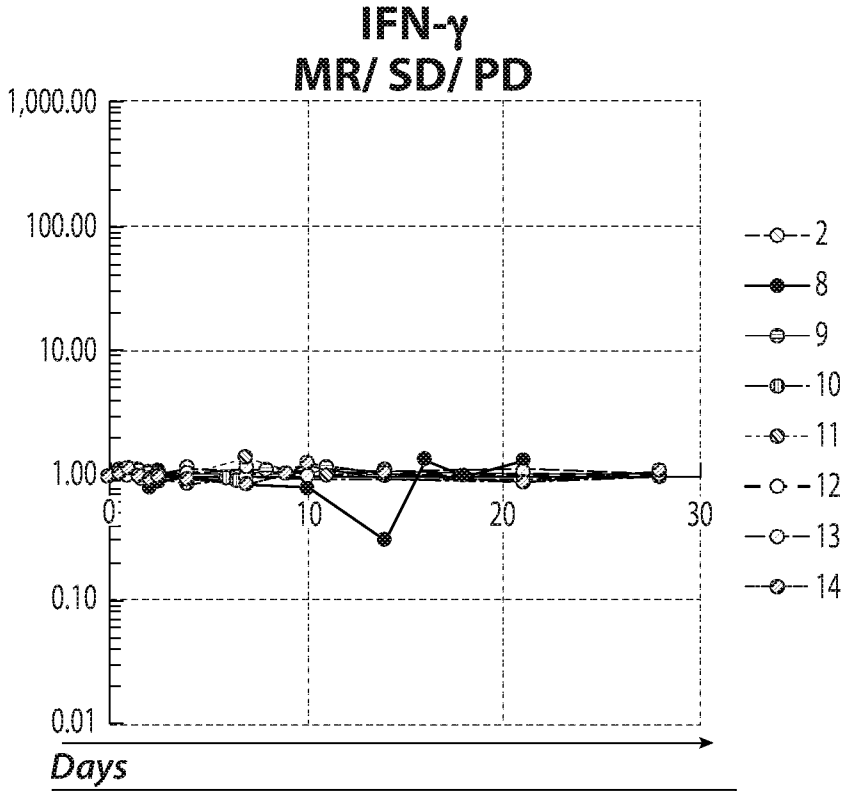


FIG. 24A



CR	VGPR	PR	MR	SD	PD
1	3, 15	7	2, 11, 13	9, 12, 14	8, 10

Unknown: 16, 17

FIG. 24B

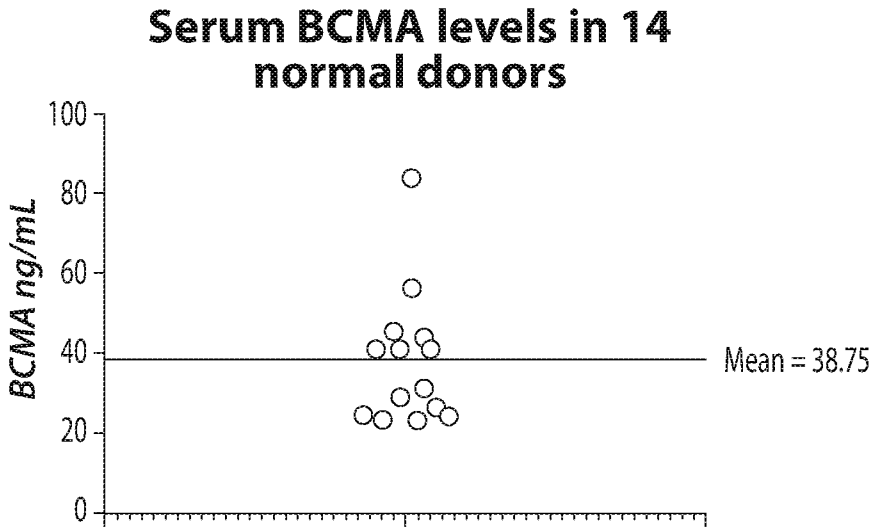


FIG. 25A

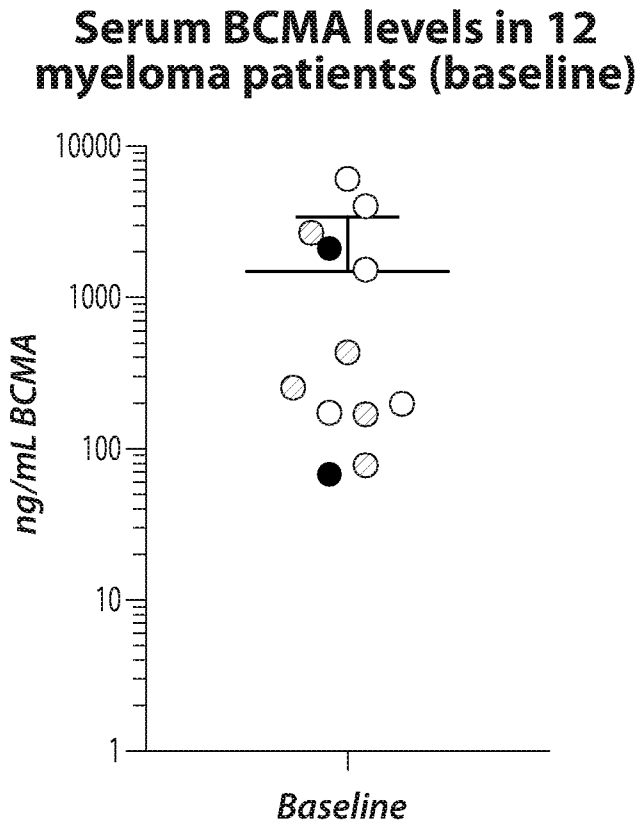


FIG. 25B

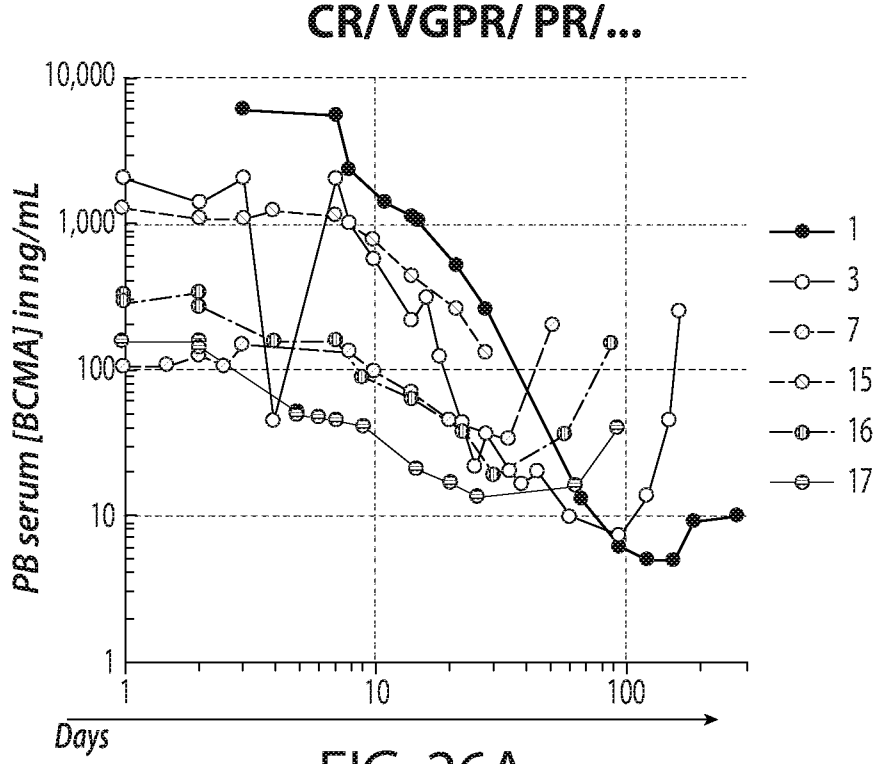
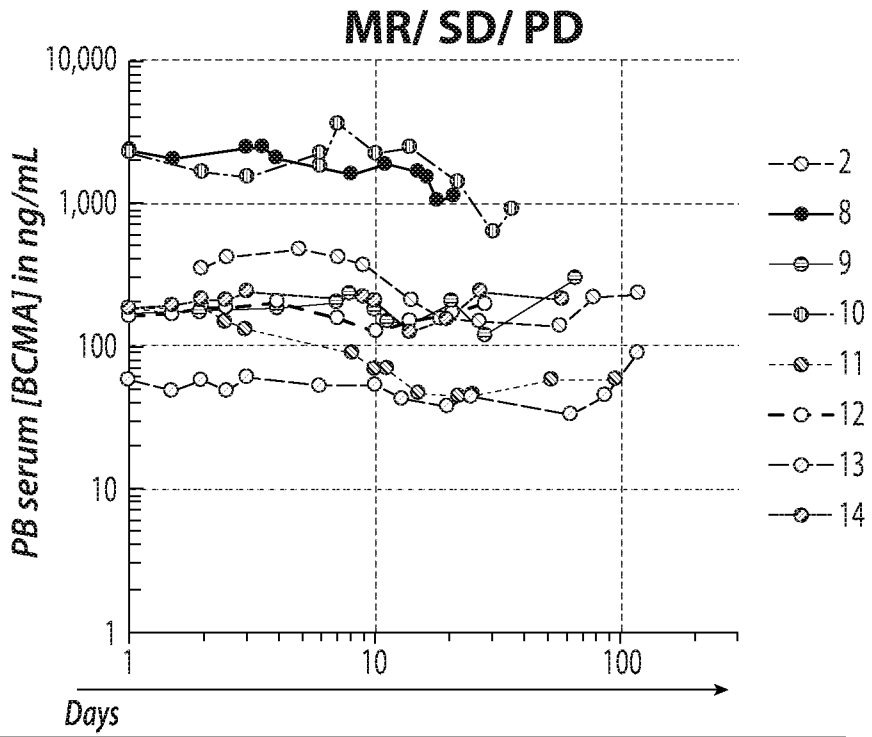


FIG. 26A



CR	VGPR	PR	MR	SD	PD
1	3, 15	7	2, 11, 13	9, 12, 14	8, 10
Unknown: 16, 17					

FIG. 26B

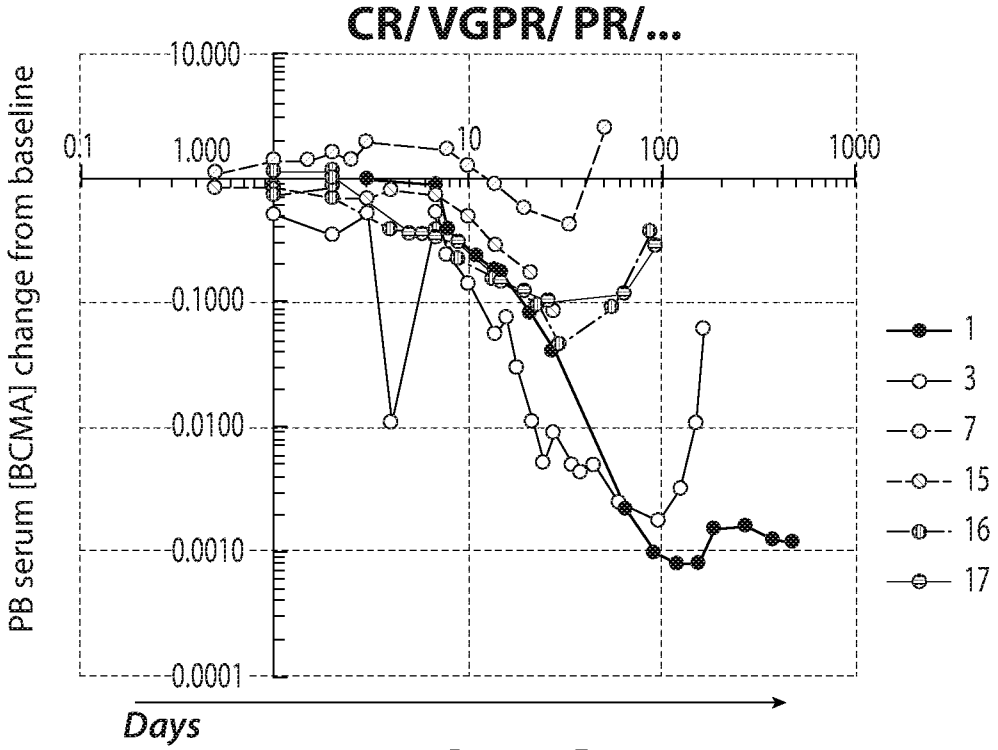
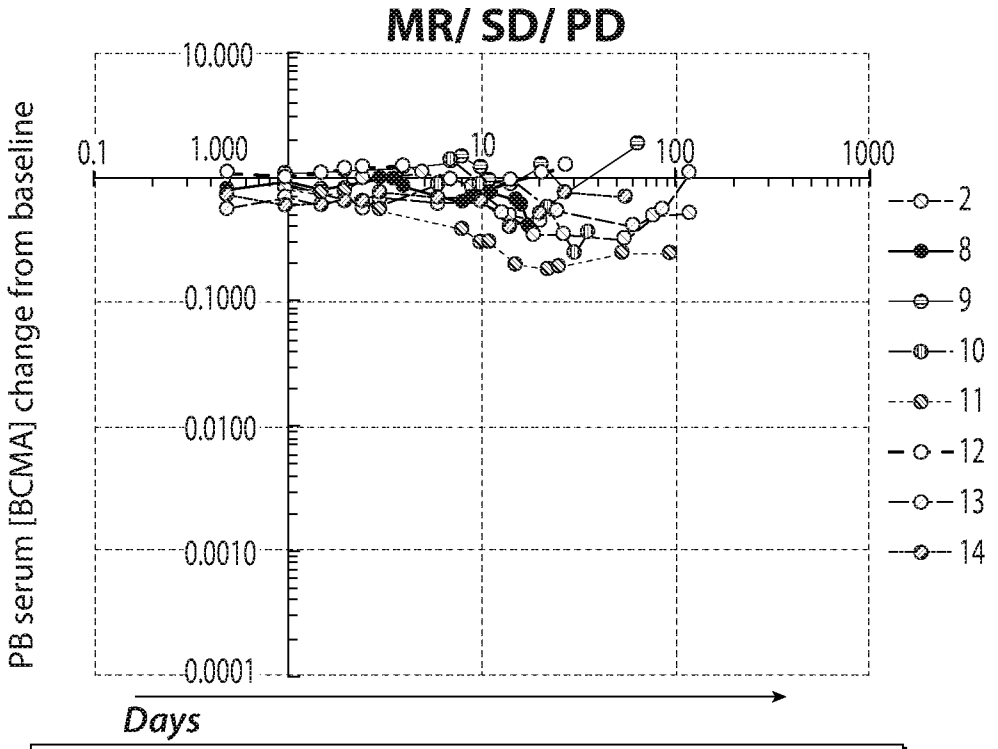


FIG. 26C



CR	VGPR	PR	MR	SD	PD
1	3, 15	7	2, 11, 13	9, 12, 14	8, 10

Unknown: 16, 17

FIG. 26D

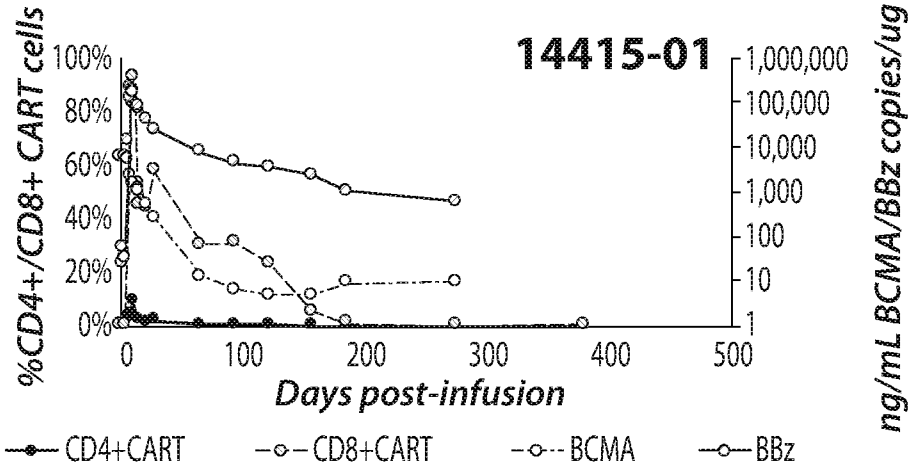


FIG. 27A

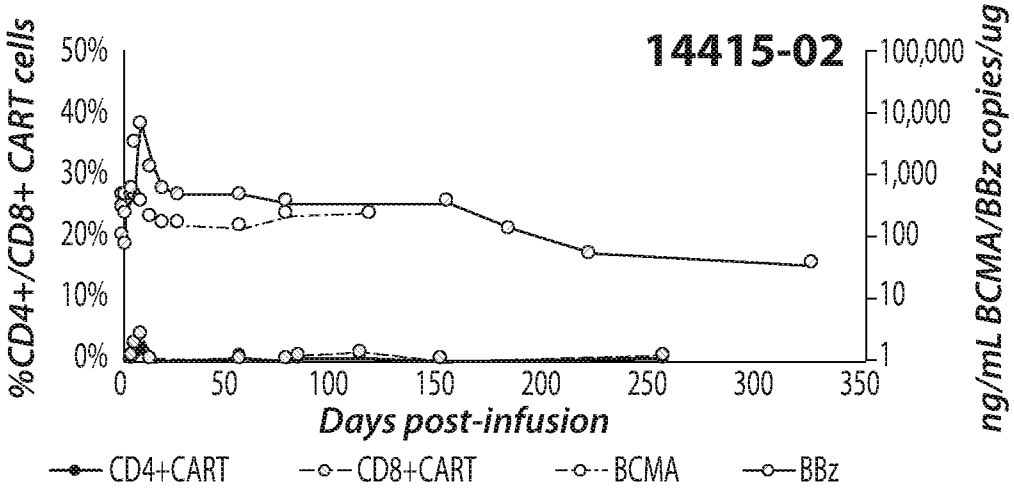


FIG. 27B

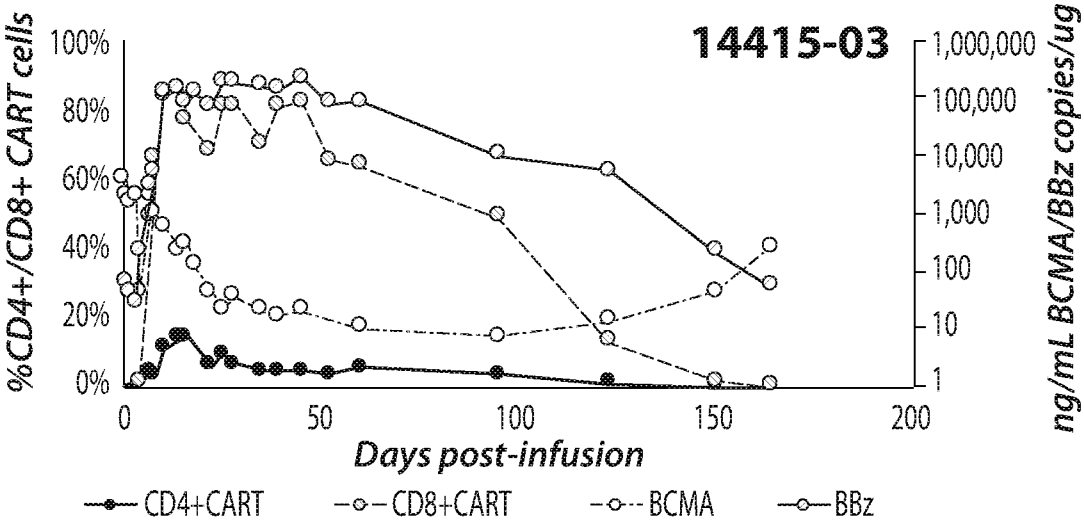


FIG. 27C

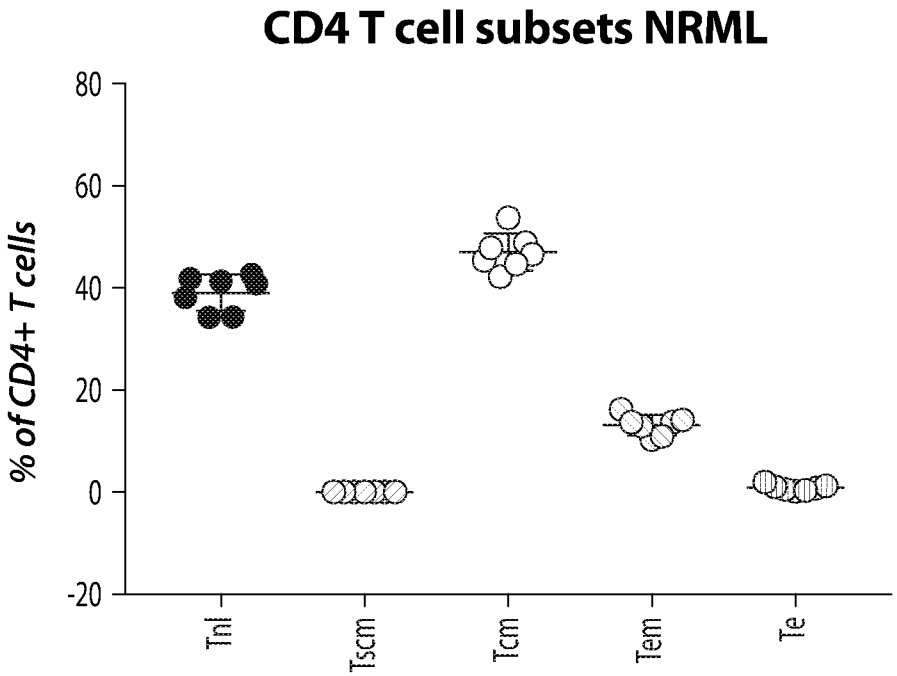


FIG. 28A

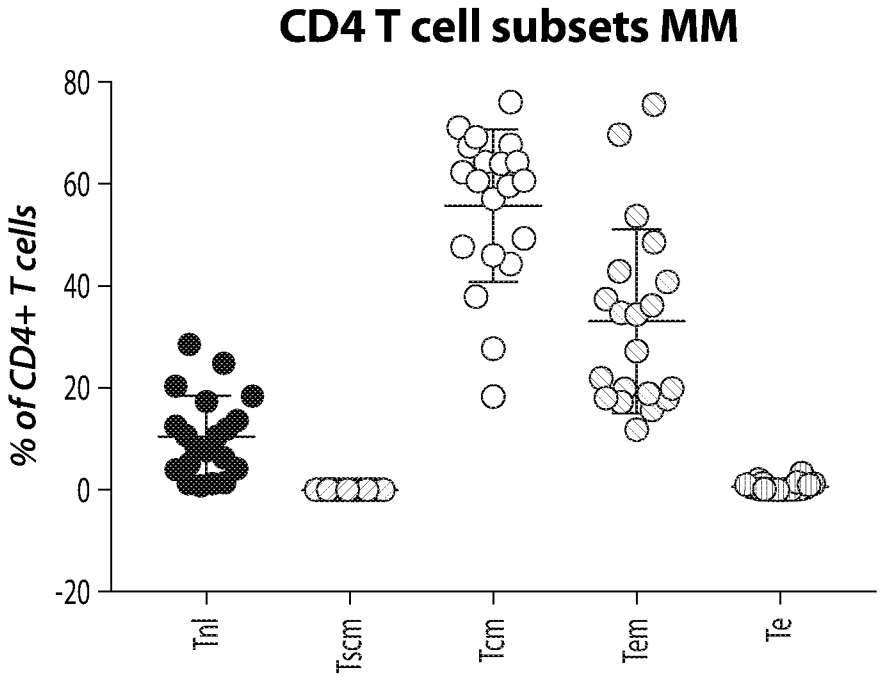


FIG. 28B

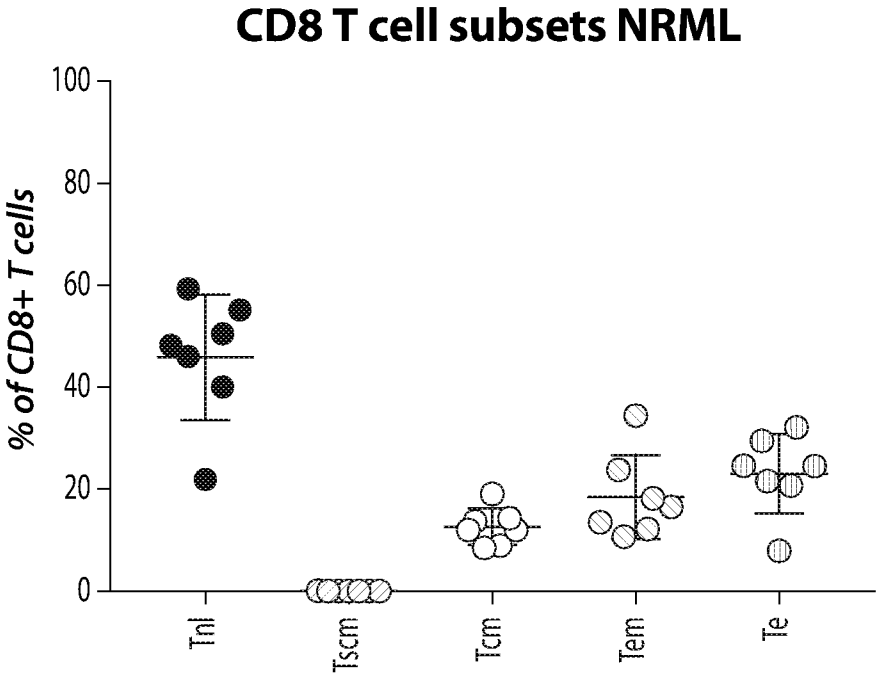


FIG. 28C

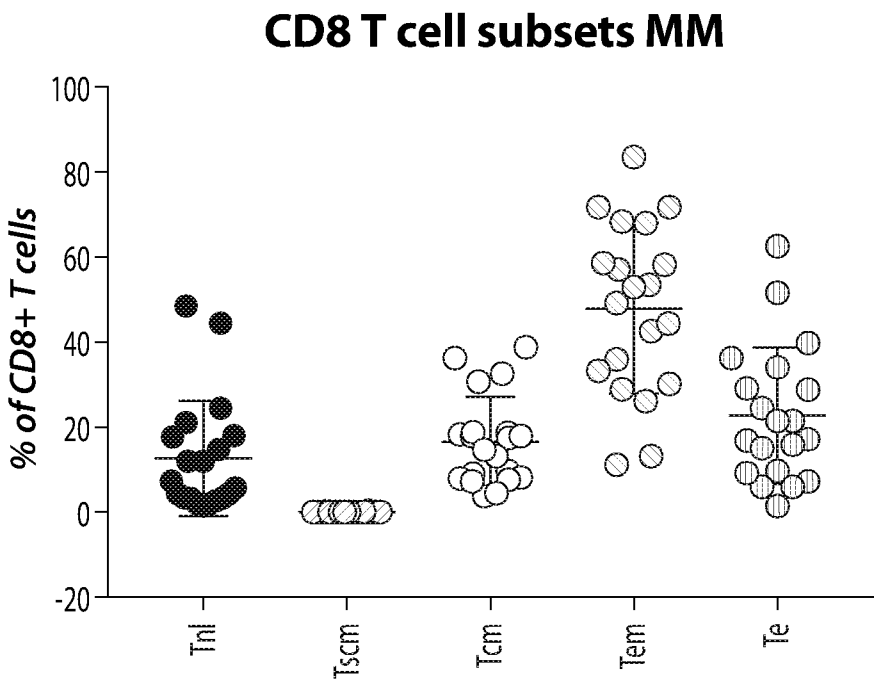


FIG. 28D

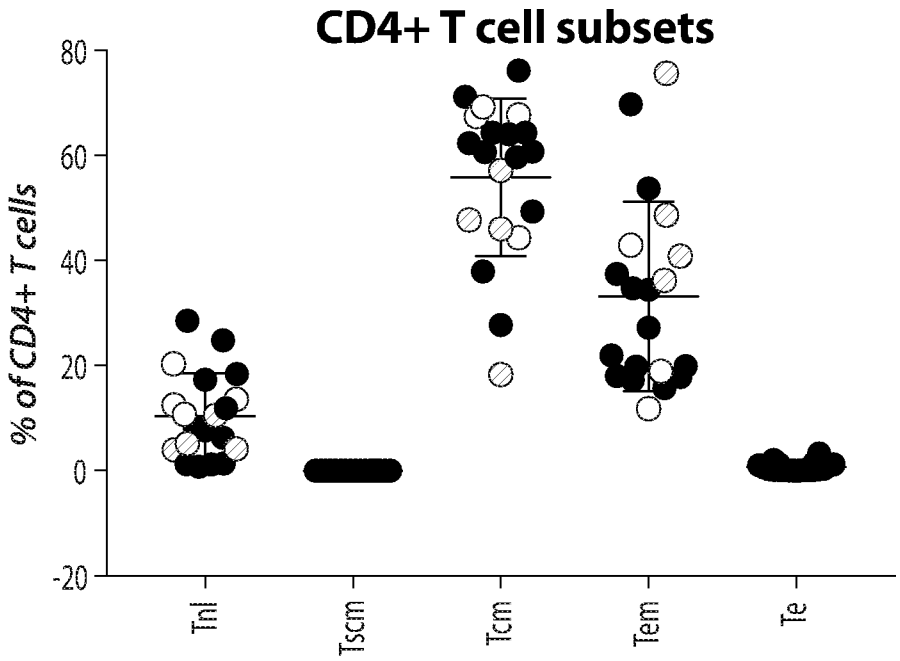


FIG. 28E

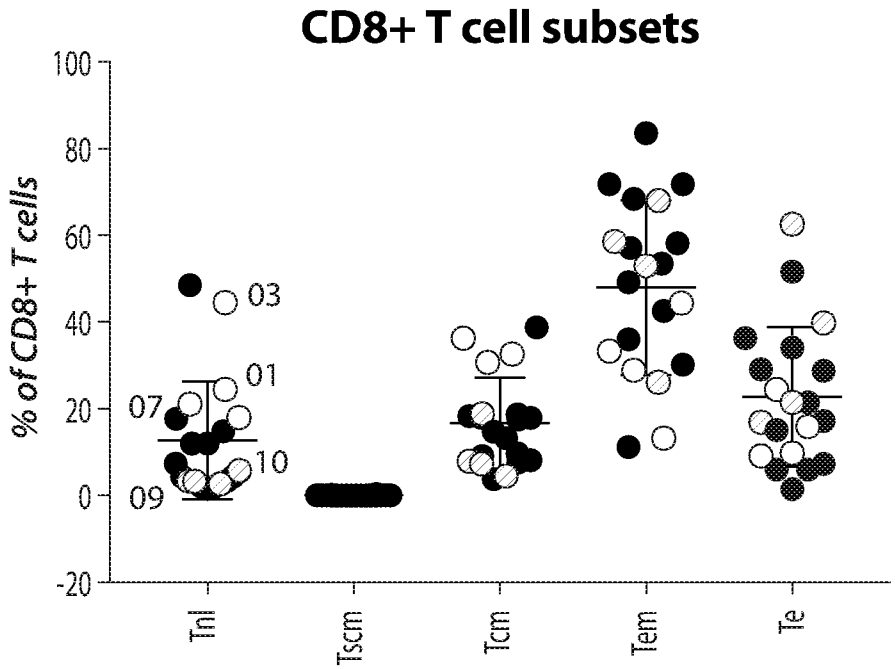


FIG. 28F

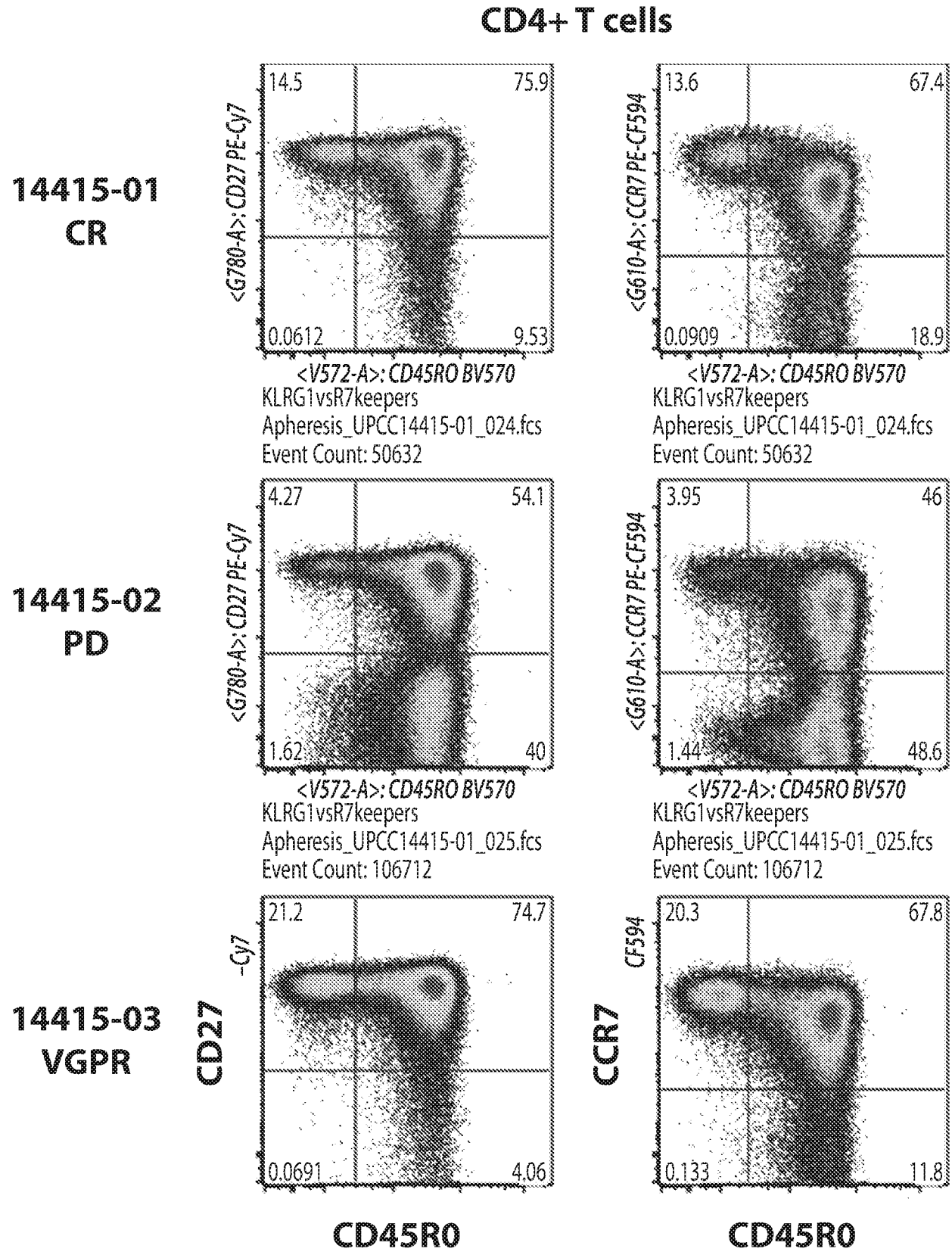

CD4+ T cells
14415-01
CR
14415-02
PD
14415-03
VGPR
CD27
CCR7
CD45R0
CD45R0
<G780-A>: CD27 PE-Cy7
<G610-A>: CCR7 PE-CF594
<V572-A>: CD45RO BV570
14.5
75.9
0.0612
9.53
13.6
67.4
0.0909
18.9
KLRG1vsR7keepers
Apheresis_UPCC14415-01_024.fcs
Event Count: 50632
4.27
54.1
1.62
40
3.95
46
1.44
48.6
KLRG1vsR7keepers
Apheresis_UPCC14415-01_025.fcs
Event Count: 106712
21.2
74.7
0.0691
4.06
20.3
67.8
0.133
11.8

FIG. 29-1

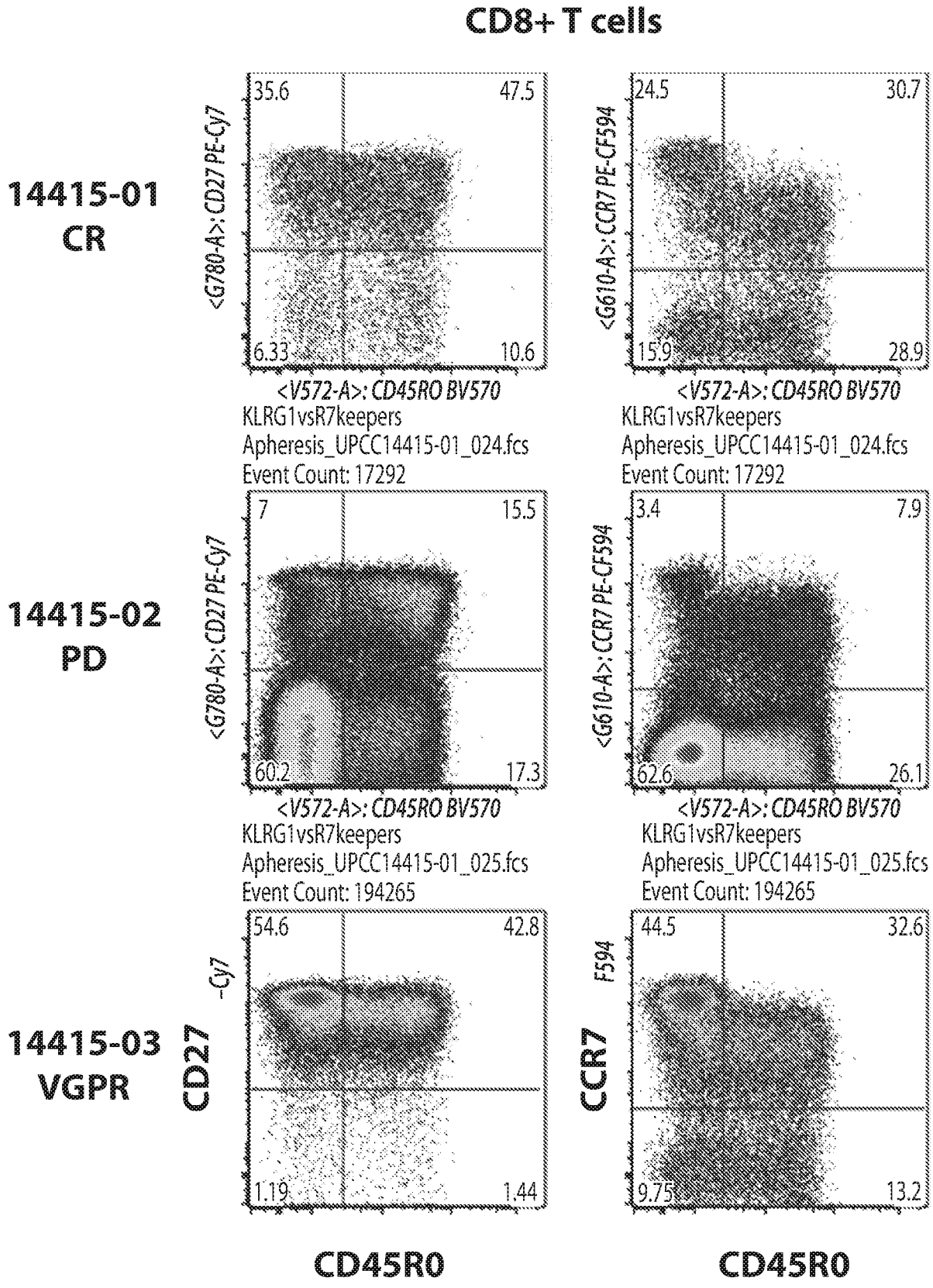

CD8+ T cells
14415-01
CR
14415-02
PD
14415-03
VGPR
<G780-A>: CD27 PE-Cy7
<G610-A>: CCR7 PE-CF594
35.6
47.5
6.33
10.6
24.5
30.7
15.9
28.9
<V572-A>: CD45RO BV570
KLRG1vsR7keepers
Apheresis_UPCC14415-01_024.fcs
Event Count: 17292
7
15.5
60.2
17.3
3.4
7.9
62.6
26.1
KLRG1vsR7keepers
Apheresis_UPCC14415-01_025.fcs
Event Count: 194265
CD27
-Cy7
CCR7
F594
54.6
42.8
1.19
1.44
44.5
32.6
9.75
13.2
CD45R0
CD45R0

FIG. 29-2

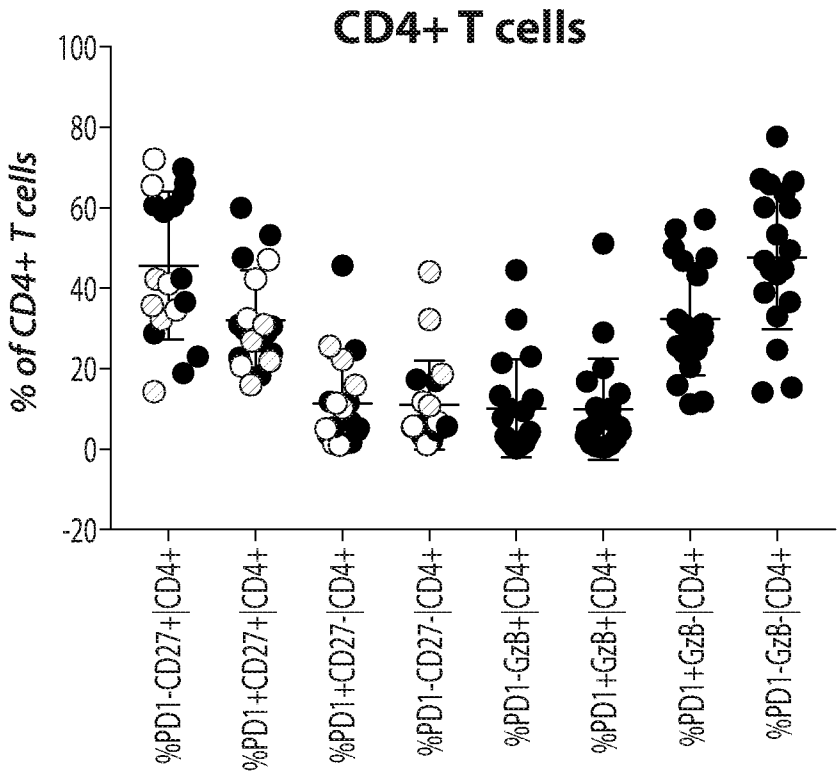


FIG. 30A

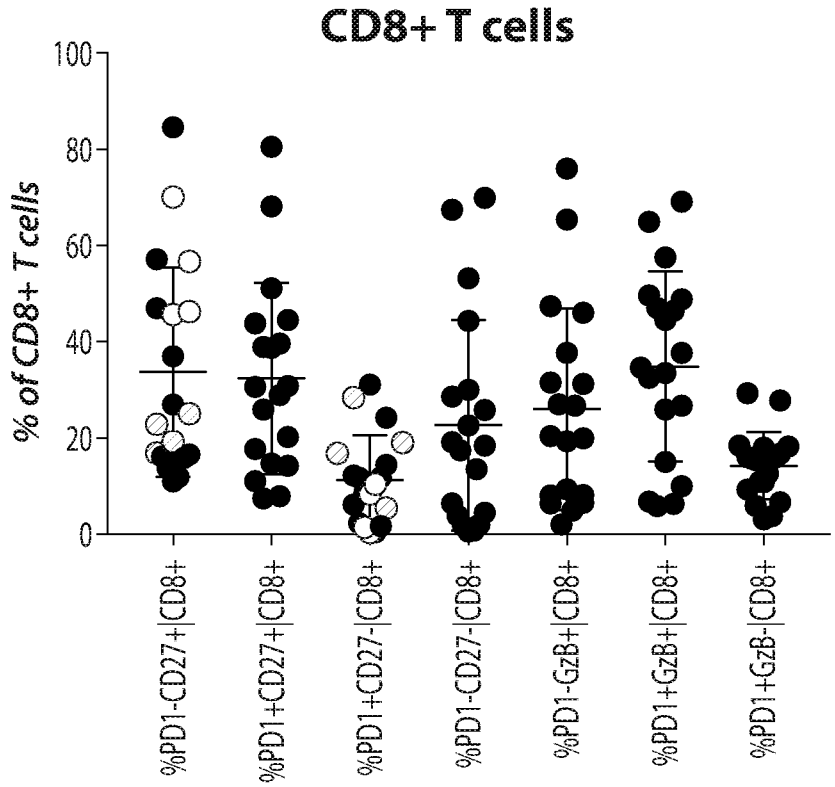


FIG. 30B

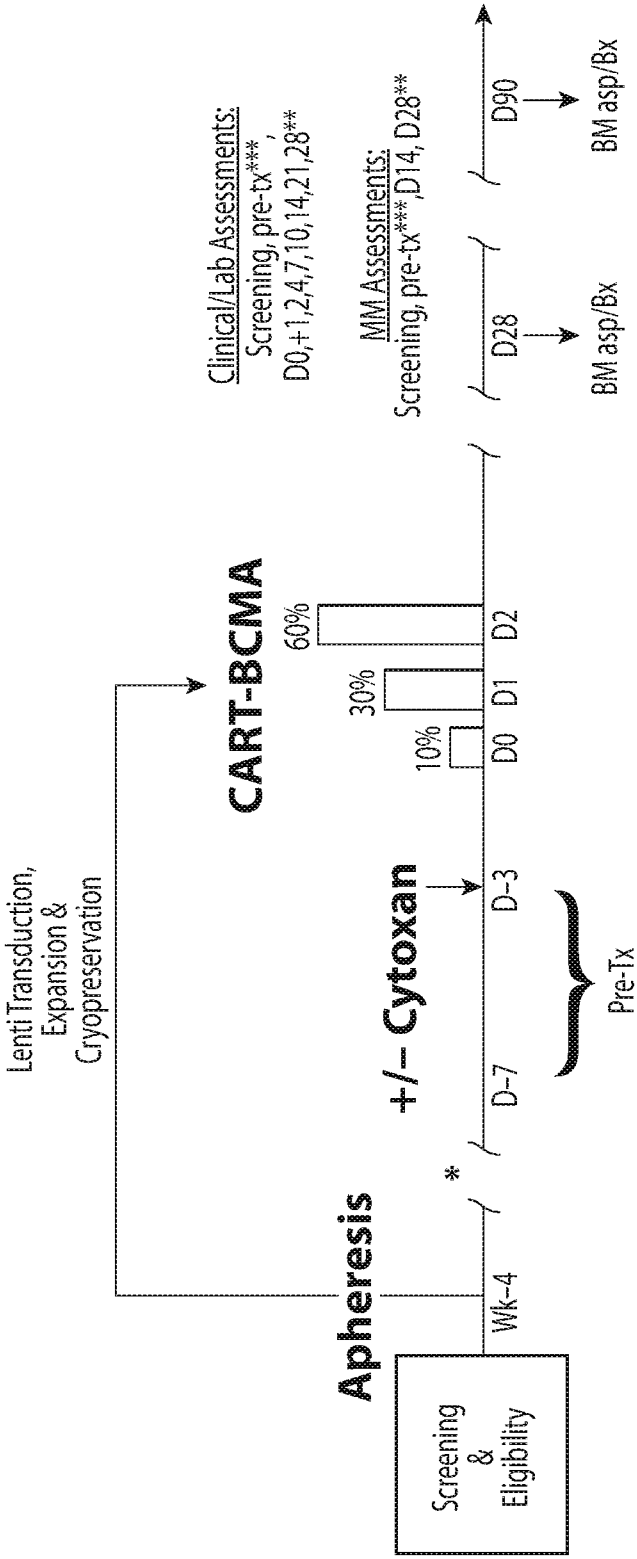

Screening & Eligibility
Wk-4
Apheresis
Lenti Transduction, Expansion & Cryopreservation
*
D-7
D-3
+/– Cytoxan
Pre-Tx BM asp/Bx
D0
D1
D2
10%
30%
60%
CART-BCMA
D28
BM asp/Bx
D90
BM asp/Bx
Clinical/Lab Assessments:
Screening, pre-tx***,
D0,+1,2,4,7,10,14,21,28**
MM Assessments:
Screening, pre-tx***,D14, D28**
* Patients may receive therapy during manufacturing to maintain disease control
** After first 28 days, follow-up is q4 awks up to 6 mos., then q3 mos. up to 2 years
*** Pre-tx = pre-treatment, 3 to 7 days before CAR T cell infusion

FIG. 31

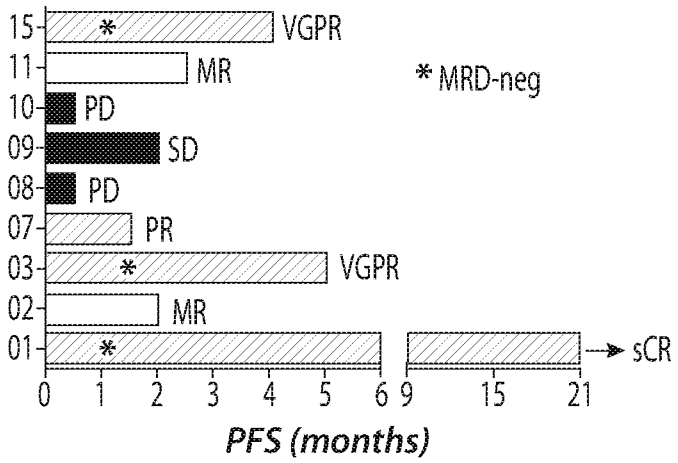


FIG. 32A

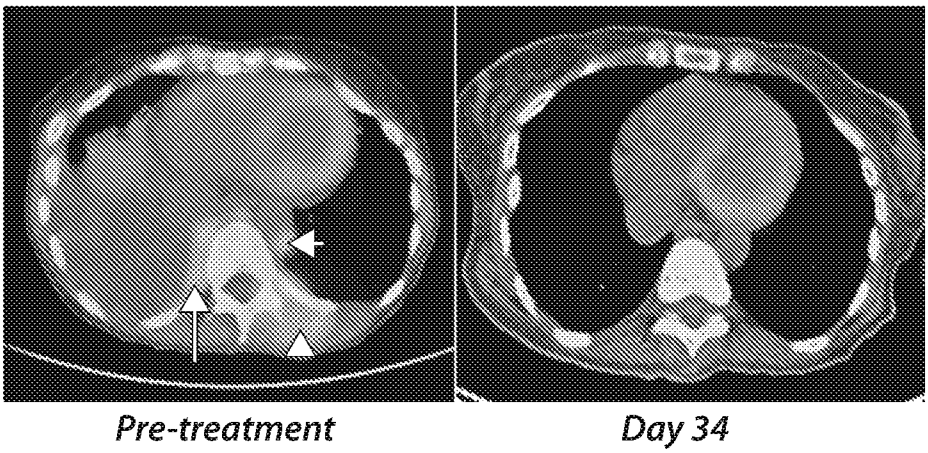


FIG. 32B

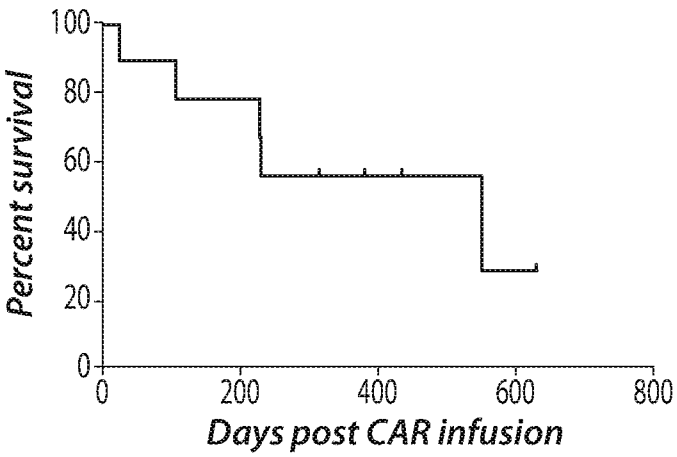


FIG. 32C

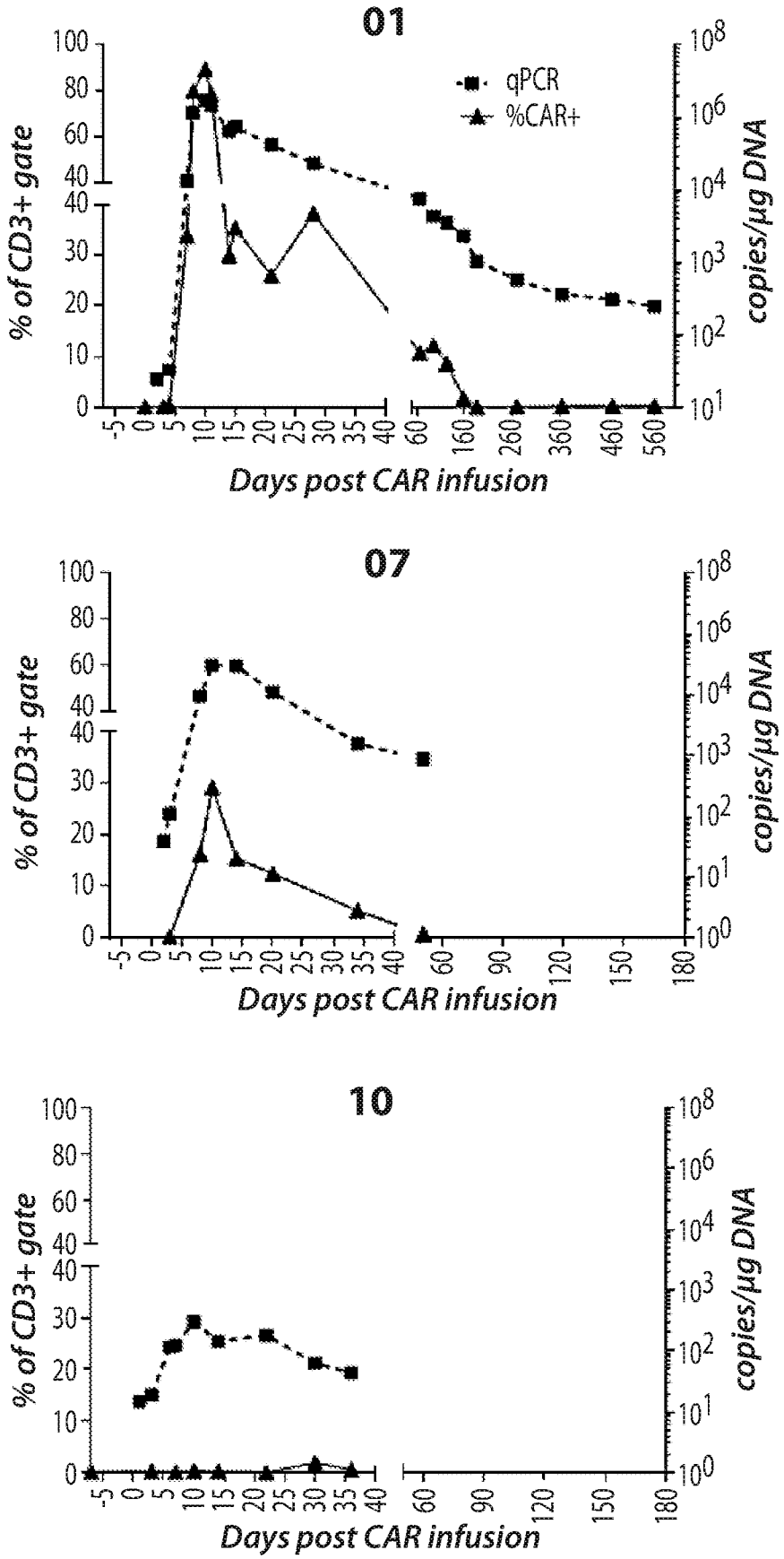

01
qPCR
%CAR+
% of CD3+ gate
copies/µg DNA
Days post CAR infusion
07
% of CD3+ gate
copies/µg DNA
Days post CAR infusion
10
% of CD3+ gate
copies/µg DNA
Days post CAR infusion

FIG. 33A-1

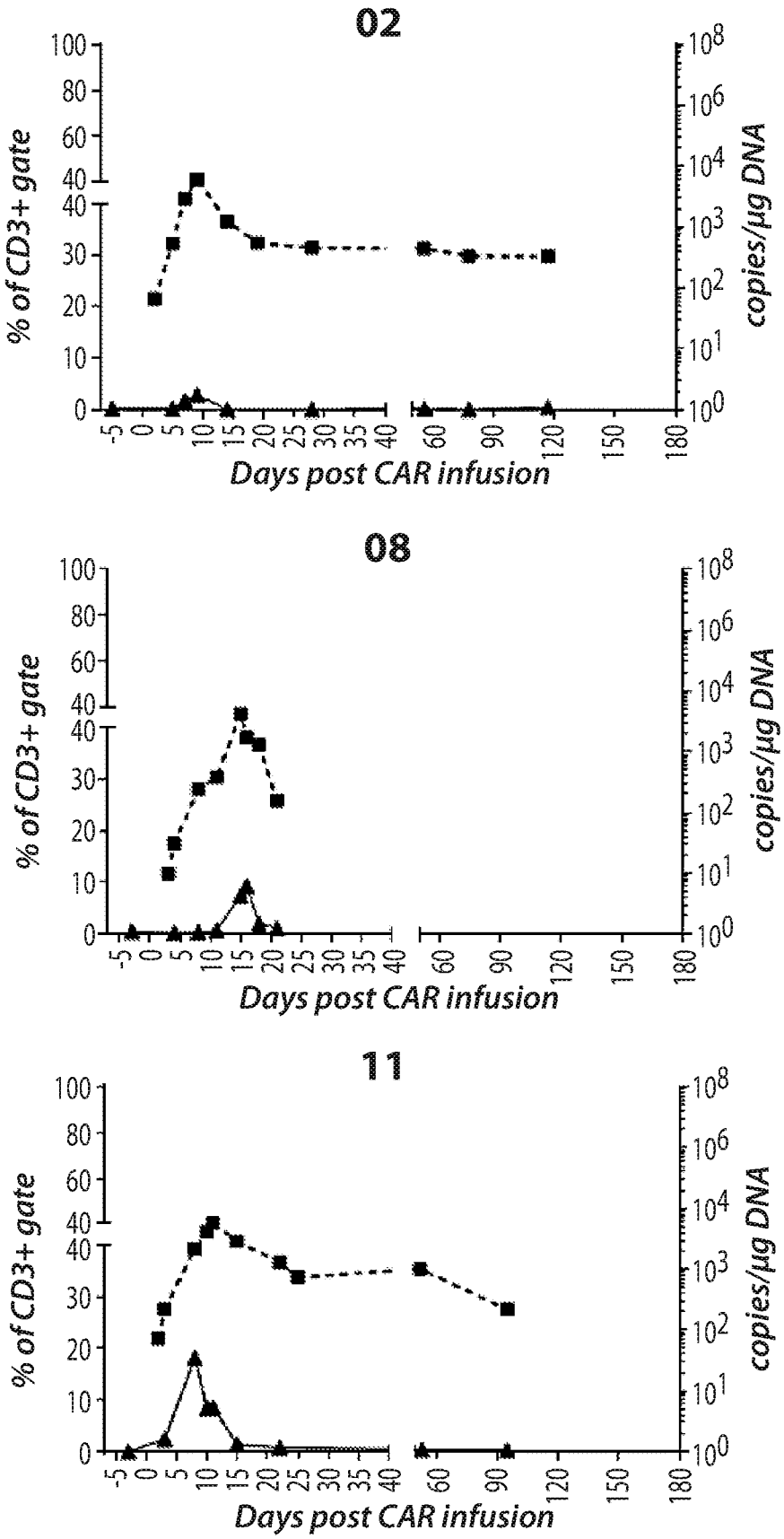

02
% of CD3+ gate
copies/µg DNA
Days post CAR infusion
08
% of CD3+ gate
copies/µg DNA
Days post CAR infusion
11
% of CD3+ gate
copies/µg DNA
Days post CAR infusion

FIG. 33A-2

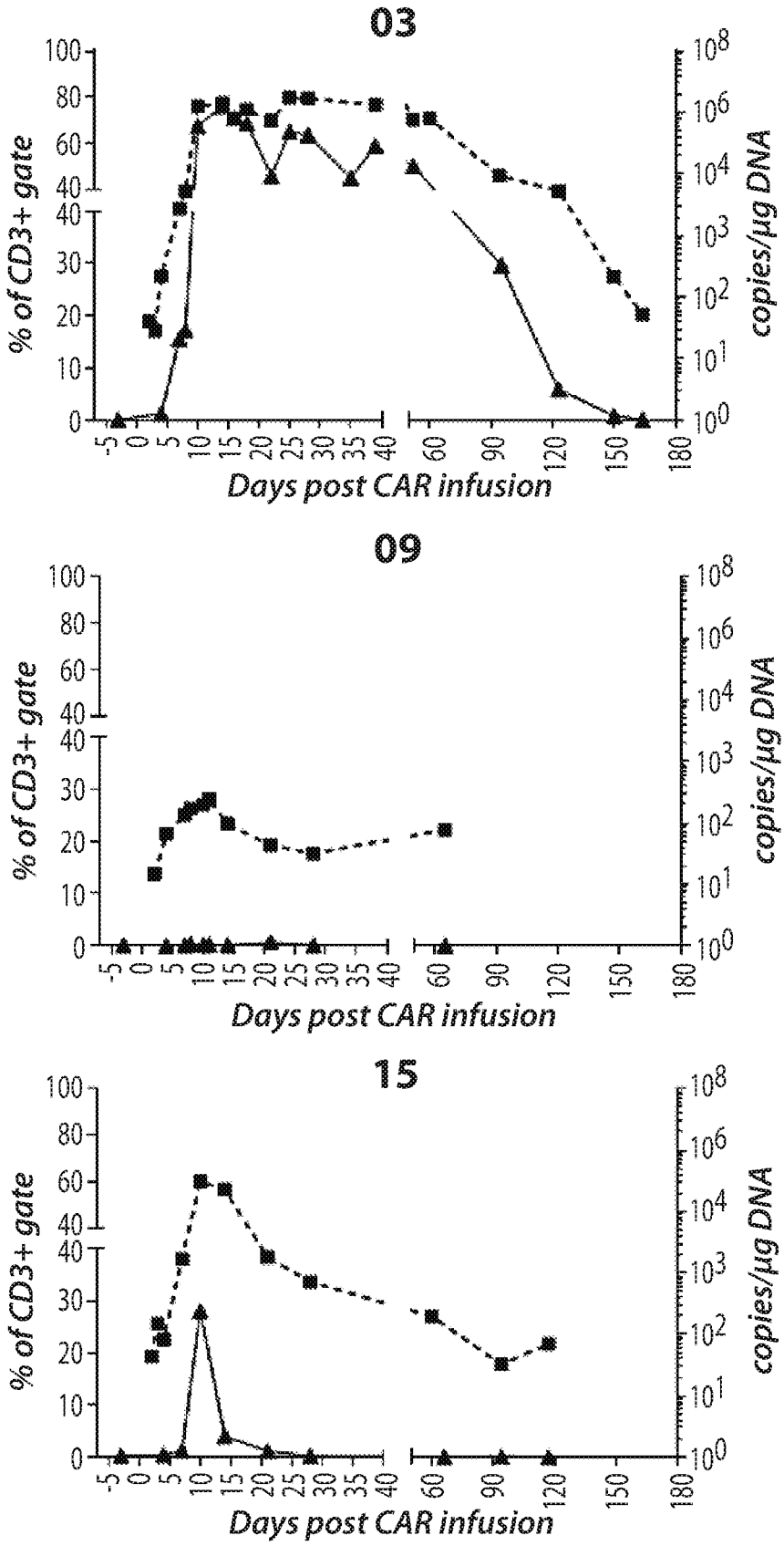

03
% of CD3+ gate
copies/µg DNA
Days post CAR infusion
09
% of CD3+ gate
copies/µg DNA
Days post CAR infusion
15
% of CD3+ gate
copies/µg DNA
Days post CAR infusion

FIG. 33A-3

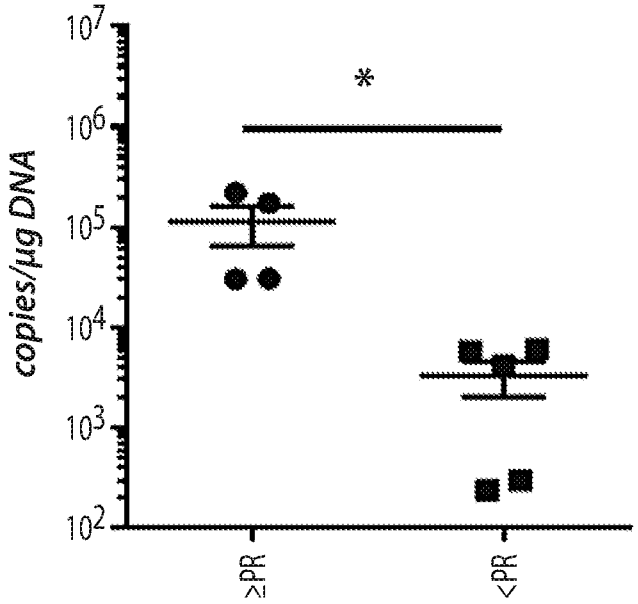


FIG. 33B

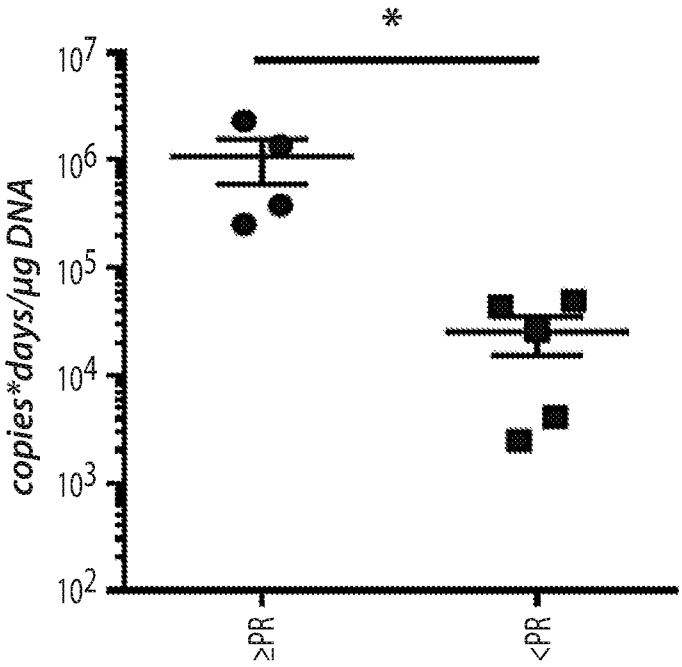
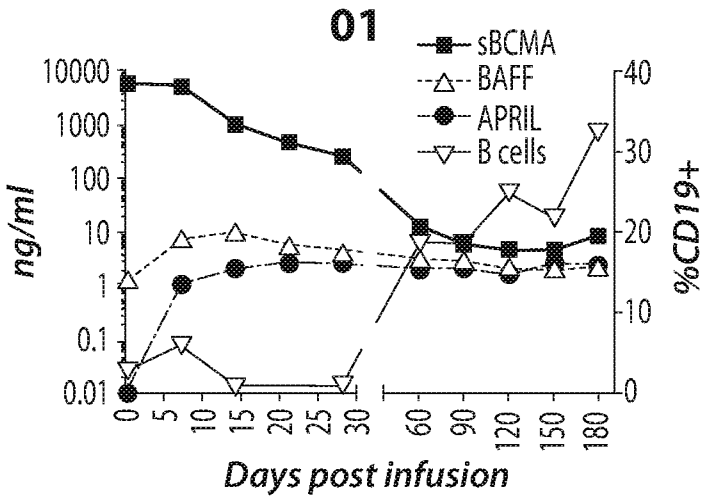
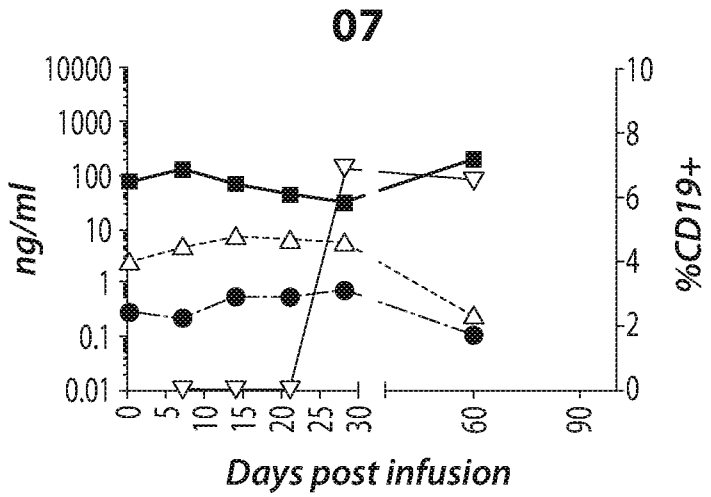


FIG. 33C


01
sBCMA
BAFF
APRIL
B cells
ng/ml
%CD19+
Days post infusion


07
ng/ml
%CD19+
Days post infusion

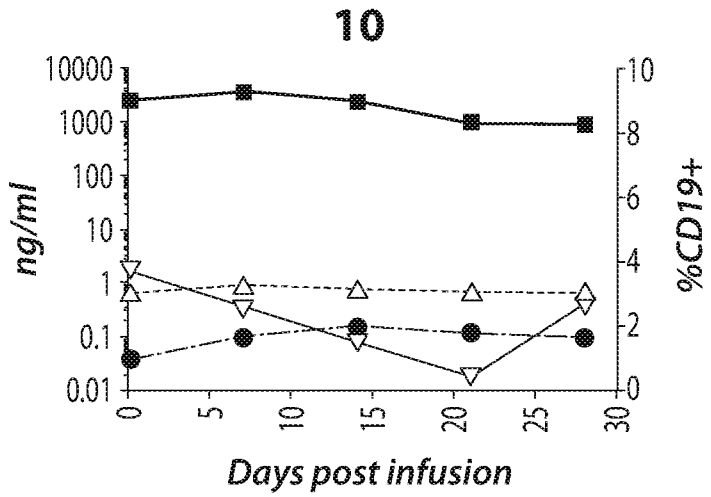
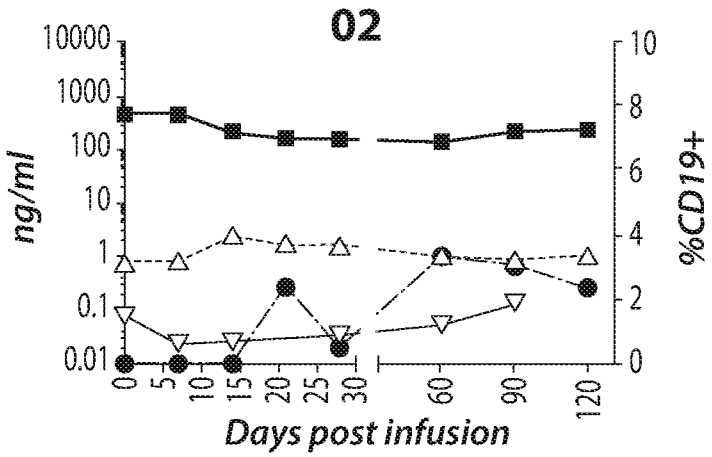
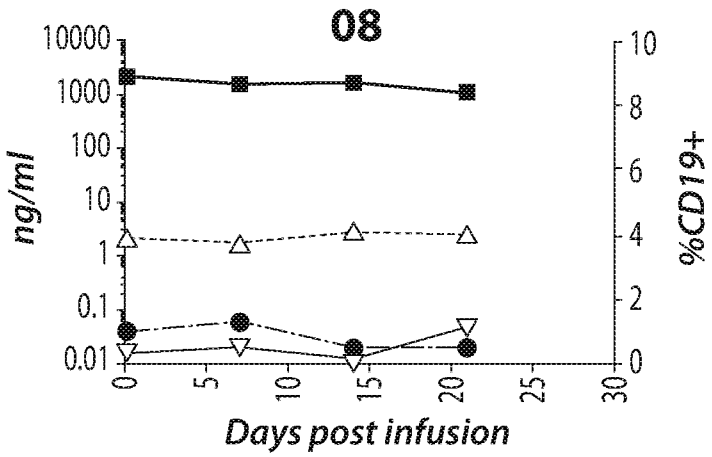

10
ng/ml
%CD19+
Days post infusion

FIG. 34-1


02
10000
1000
100
10
1
0.1
0.01
ng/ml
10
8
6
4
2
0
%CD19+
0 5 10 15 20 25 30 60 90 120
Days post infusion


08
10000
1000
100
10
1
0.1
0.01
ng/ml
10
8
6
4
2
0
%CD19+
0 5 10 15 20 25 30
Days post infusion

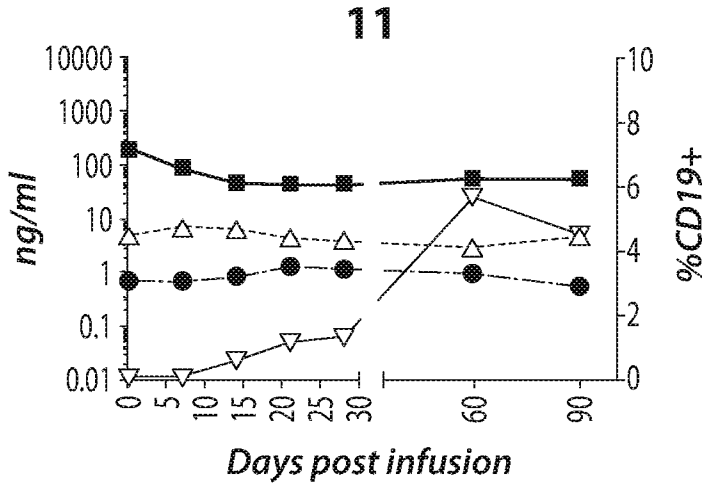
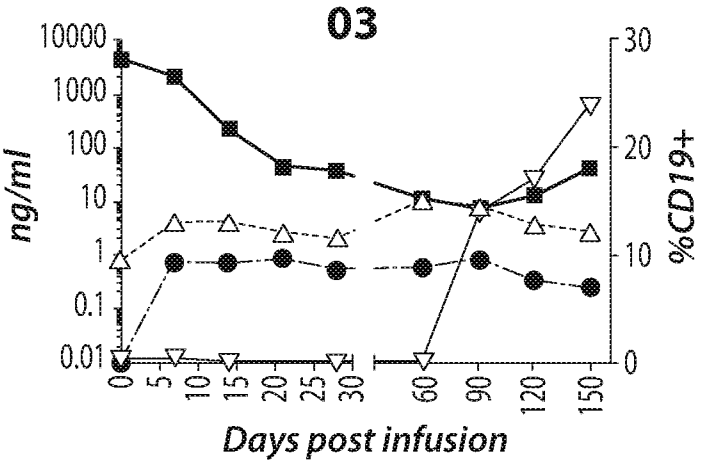
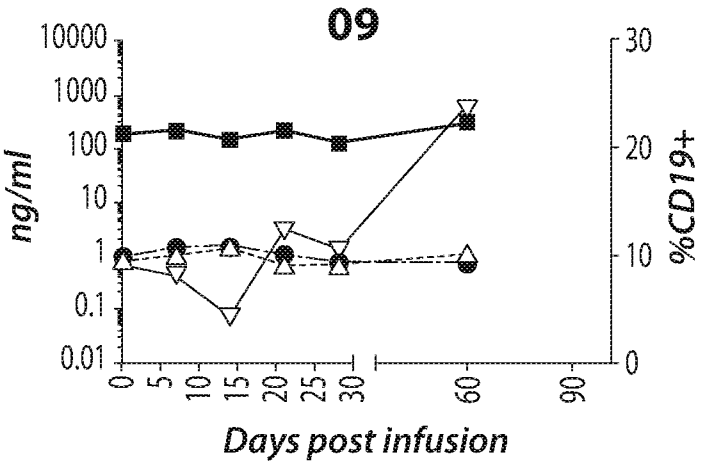

11
10000
1000
100
10
1
0.1
0.01
ng/ml
10
8
6
4
2
0
%CD19+
0 5 10 15 20 25 30 60 90
Days post infusion

FIG. 34-2


03
10000
1000
100
10
1
0.1
0.01
ng/ml
30
20
10
0
%CD19+
0 5 10 15 20 25 30 60 90 120 150
Days post infusion


09
10000
1000
100
10
1
0.1
0.01
ng/ml
30
20
10
0
%CD19+
0 5 10 15 20 25 30 60 90
Days post infusion

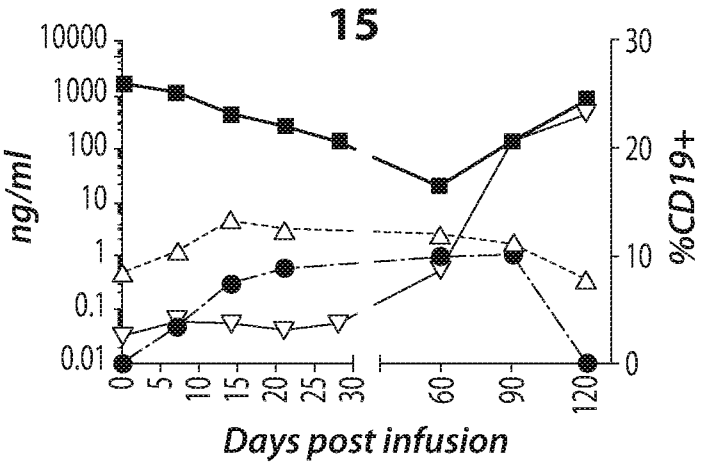

15
10000
1000
100
10
1
0.1
0.01
ng/ml
30
20
10
0
%CD19+
0 5 10 15 20 25 30 60 90 120
Days post infusion

FIG. 34-3

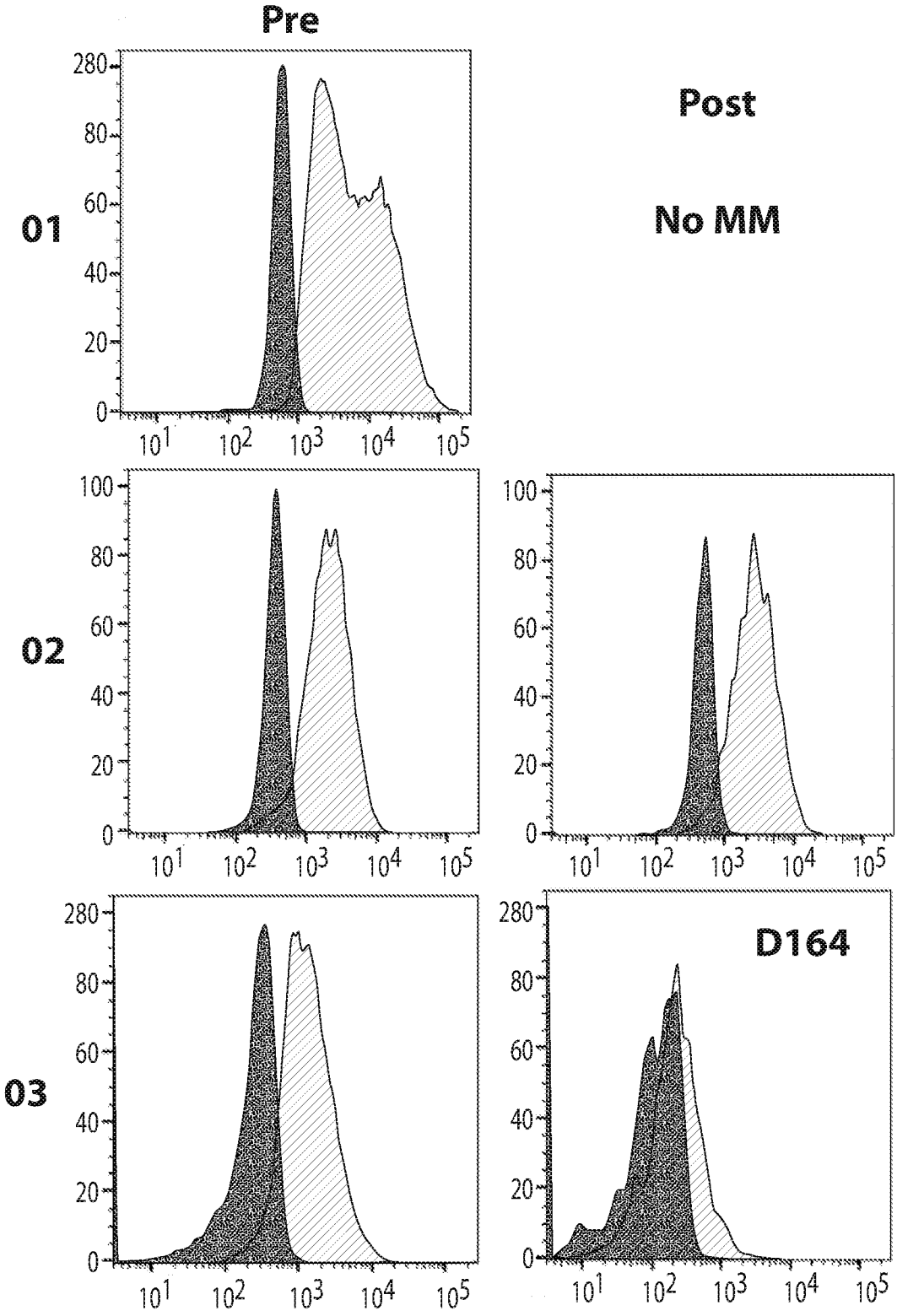

Pre
Post
No MM
01
02
03
D164
280
80
60
40
20
0
100
10^1
10^2
10^3
10^4
10^5

FIG. 35-1

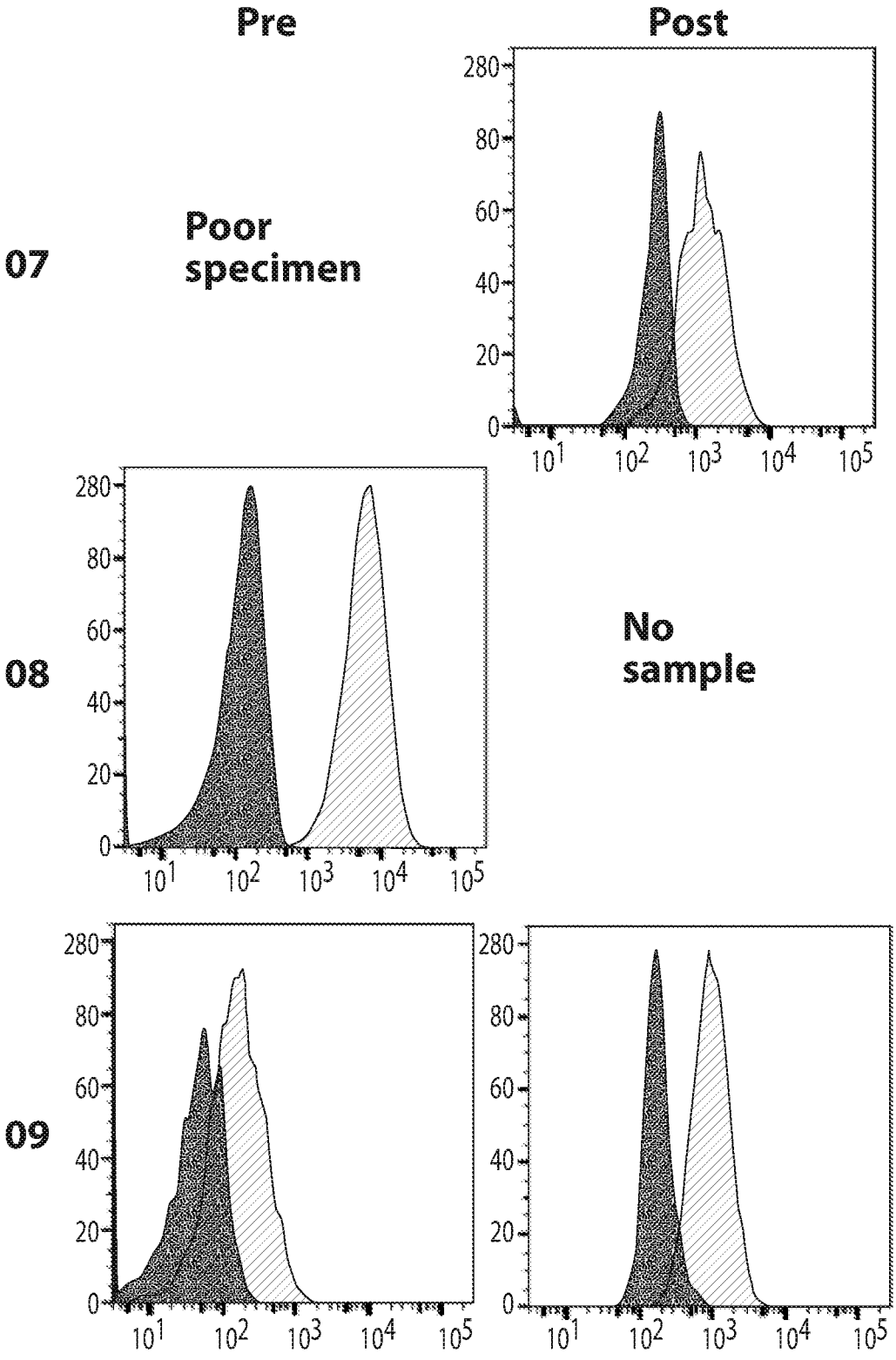

Pre
Post
07
Poor specimen
08
No sample
09
280
80
60
40
20
0
10^1
10^2
10^3
10^4
10^5

FIG. 35-2

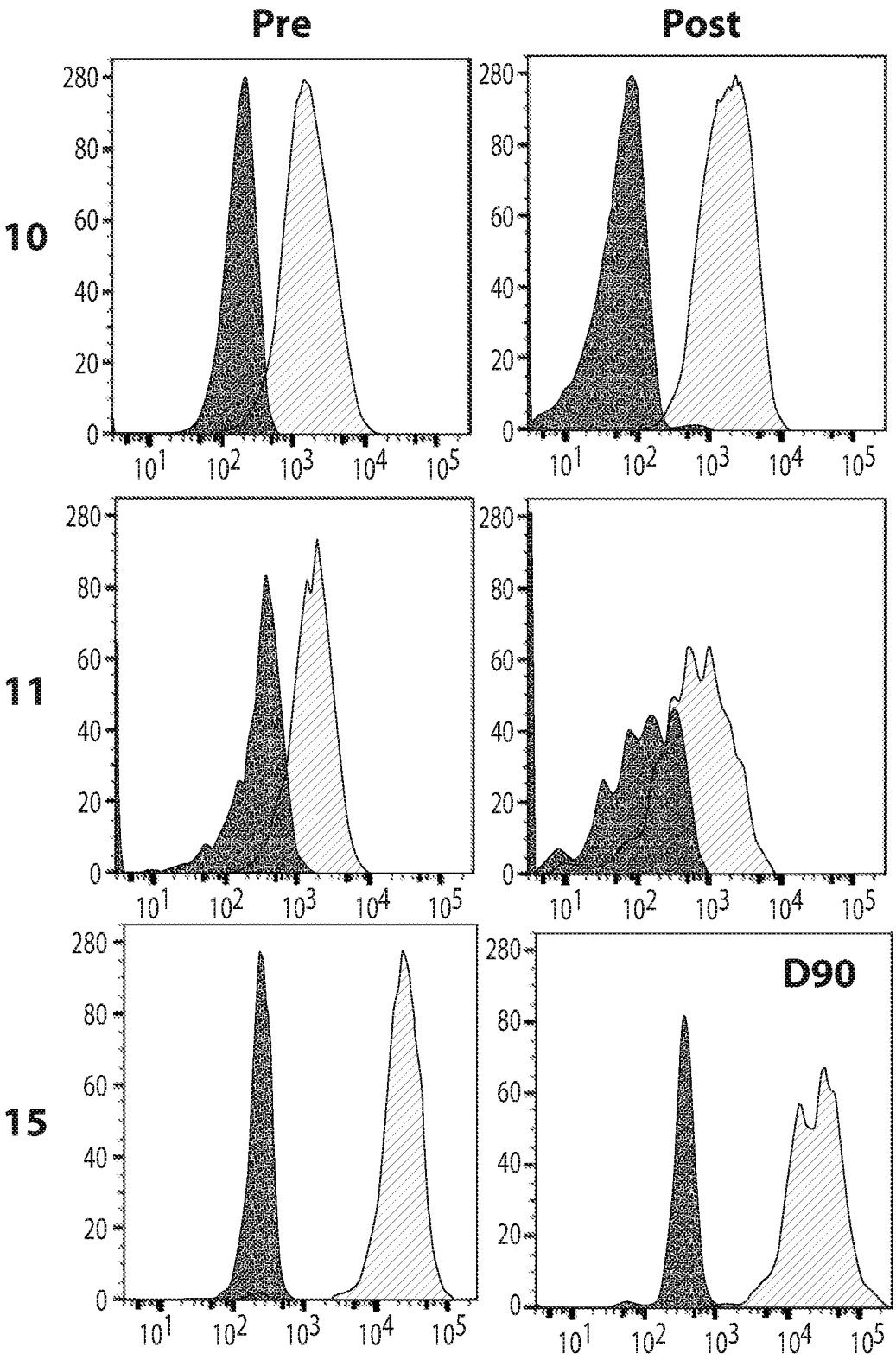


FIG. 35-3

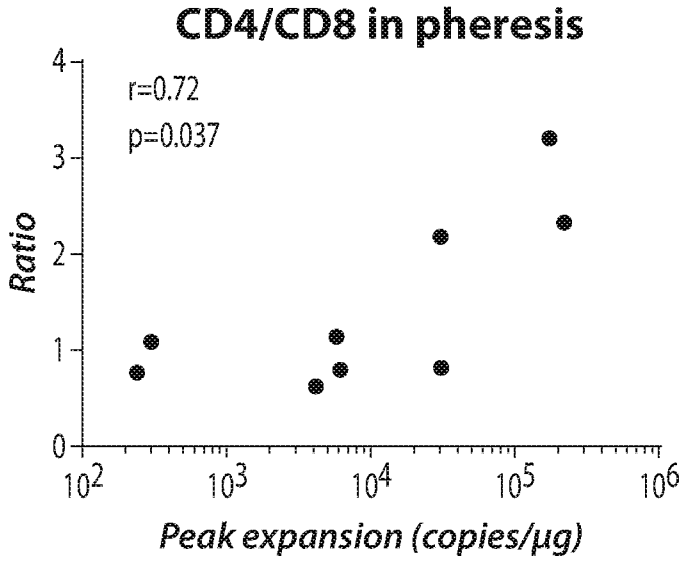


FIG. 36A

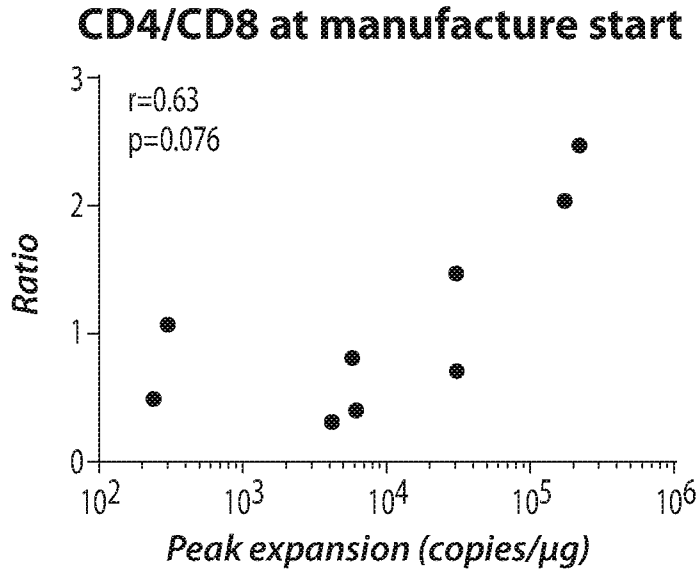


FIG. 36B

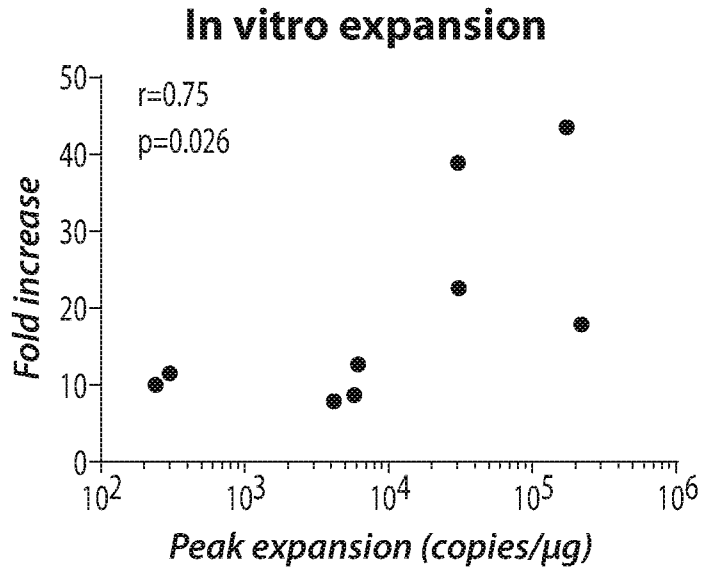


FIG. 36C

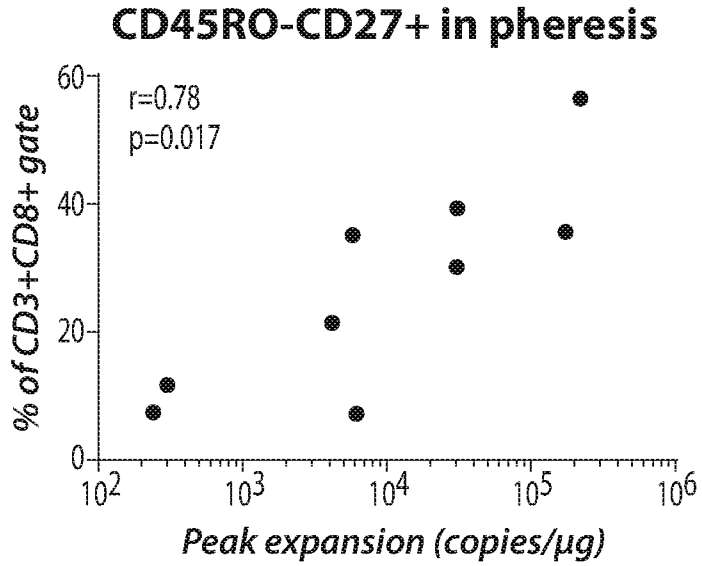


FIG. 36D

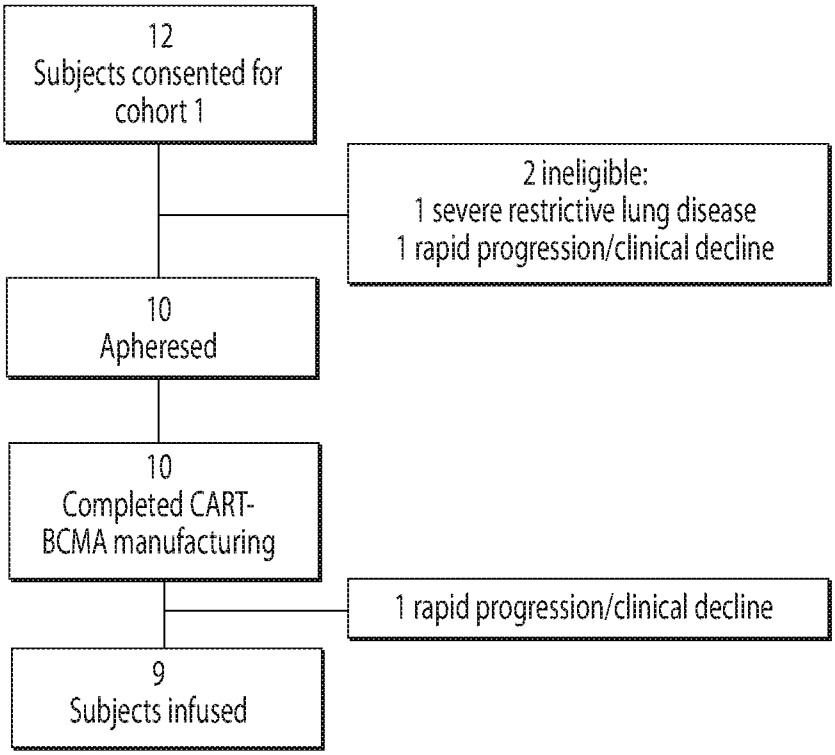

12
Subjects consented for cohort 1
2 ineligible:
1 severe restrictive lung disease
1 rapid progression/clinical decline
10
Apheresed
10
Completed CART-BCMA manufacturing
1 rapid progression/clinical decline
9
Subjects infused

FIG. 37

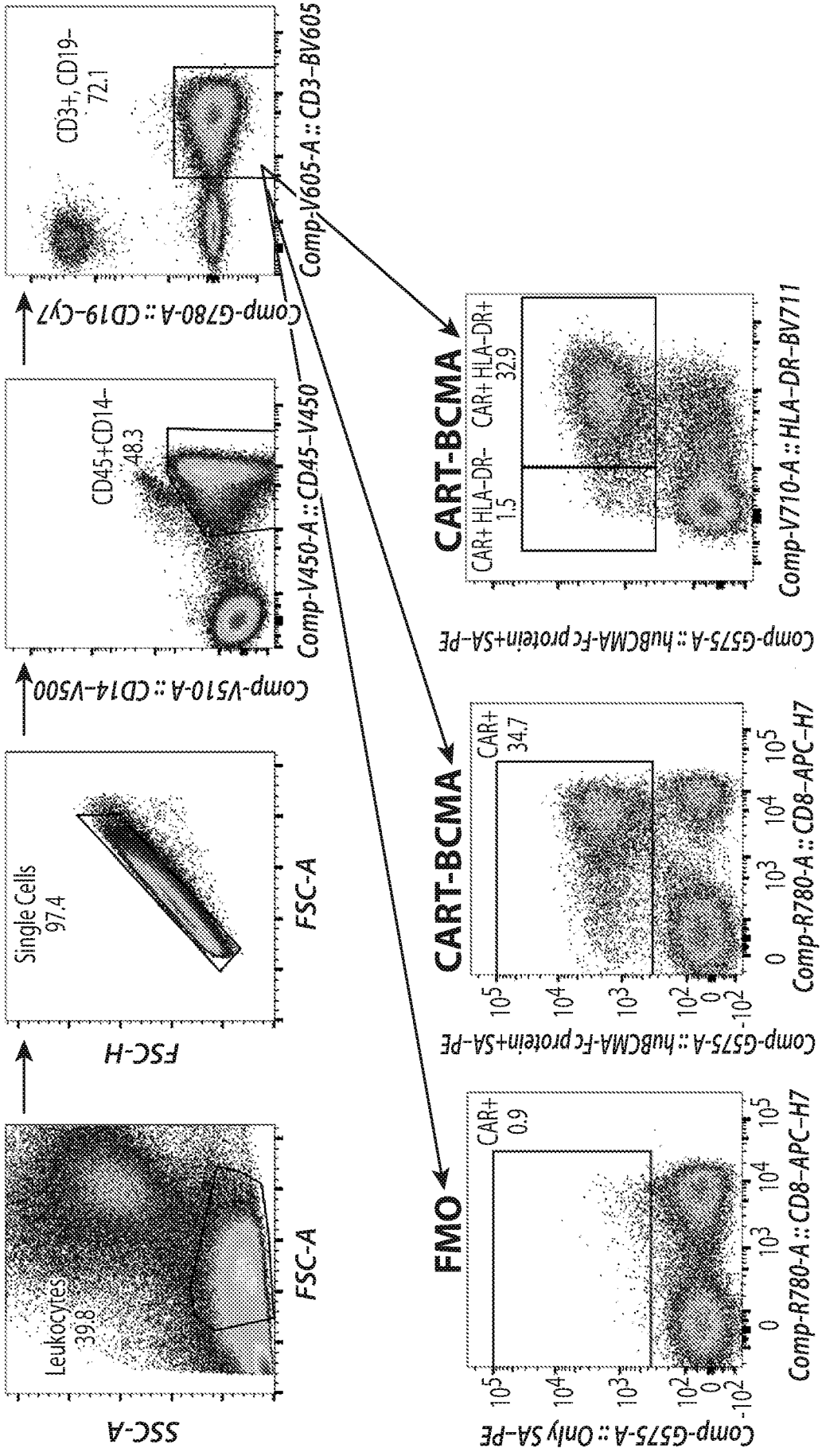
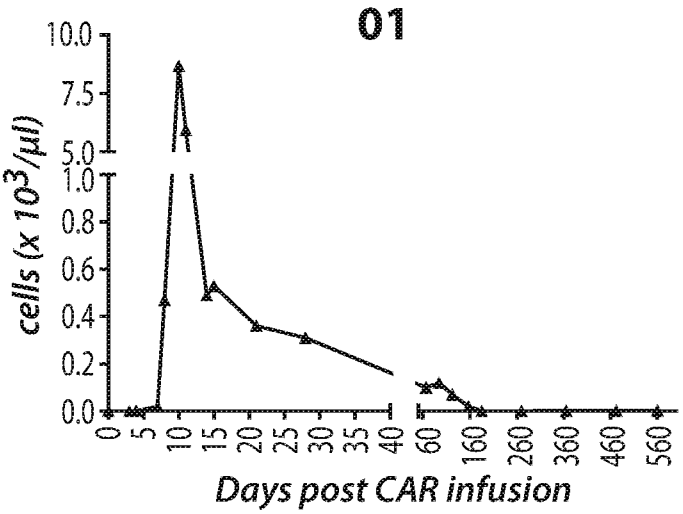
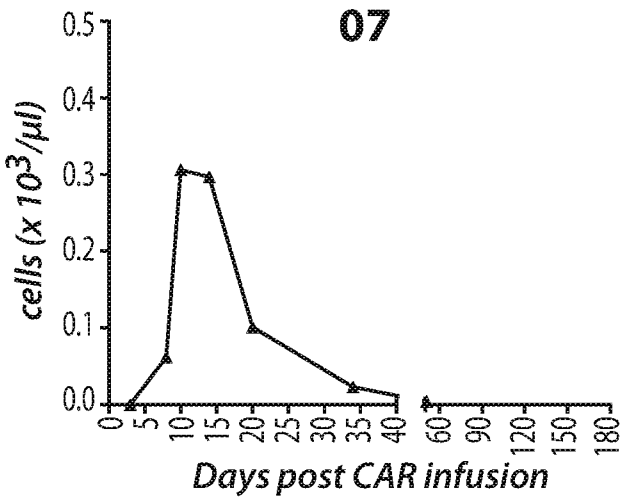

Leukocytes
39.8
SSC-A
FSC-A
Single Cells
97.4
FSC-H
FSC-A
Comp-V510-A :: CD14-V500
CD45+CD14-
48.3
Comp-V450-A :: CD45-V450
Comp-G780-A :: CD19-Cy7
CD3+, CD19-
72.1
Comp-V605-A :: CD3-BV605
FMO
CAR+
0.9
Comp-G575-A :: Only SA-PE
Comp-R780-A :: CD8-APC-H7
CART-BCMA
CAR+
34.7
Comp-G575-A :: huBCMA-Fc protein+SA-PE
Comp-R780-A :: CD8-APC-H7
CART-BCMA
CAR+ HLA-DR-
1.5
CAR+ HLA-DR+
32.9
Comp-G575-A :: huBCMA-Fc protein+SA-PE
Comp-V710-A :: HLA-DR-BV711

FIG. 38


01
cells (x 10^3/µl)
10.0
7.5
5.0
1.0
0.8
0.6
0.4
0.2
0.0
0 5 10 15 20 25 30 35 40 60 160 260 360 460 560
Days post CAR infusion


07
cells (x 10^3/µl)
0.5
0.4
0.3
0.2
0.1
0.0
0 5 10 15 20 25 30 35 40 60 90 120 150 180
Days post CAR infusion

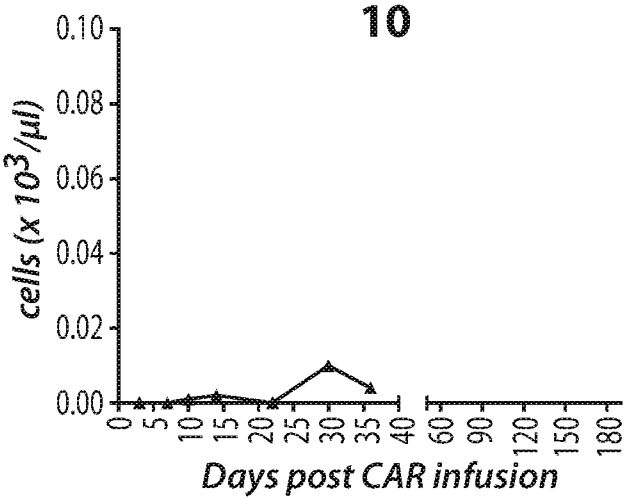

10
cells (x 10^3/µl)
0.10
0.08
0.06
0.04
0.02
0.00
0 5 10 15 20 25 30 35 40 60 90 120 150 180
Days post CAR infusion

FIG. 39-1

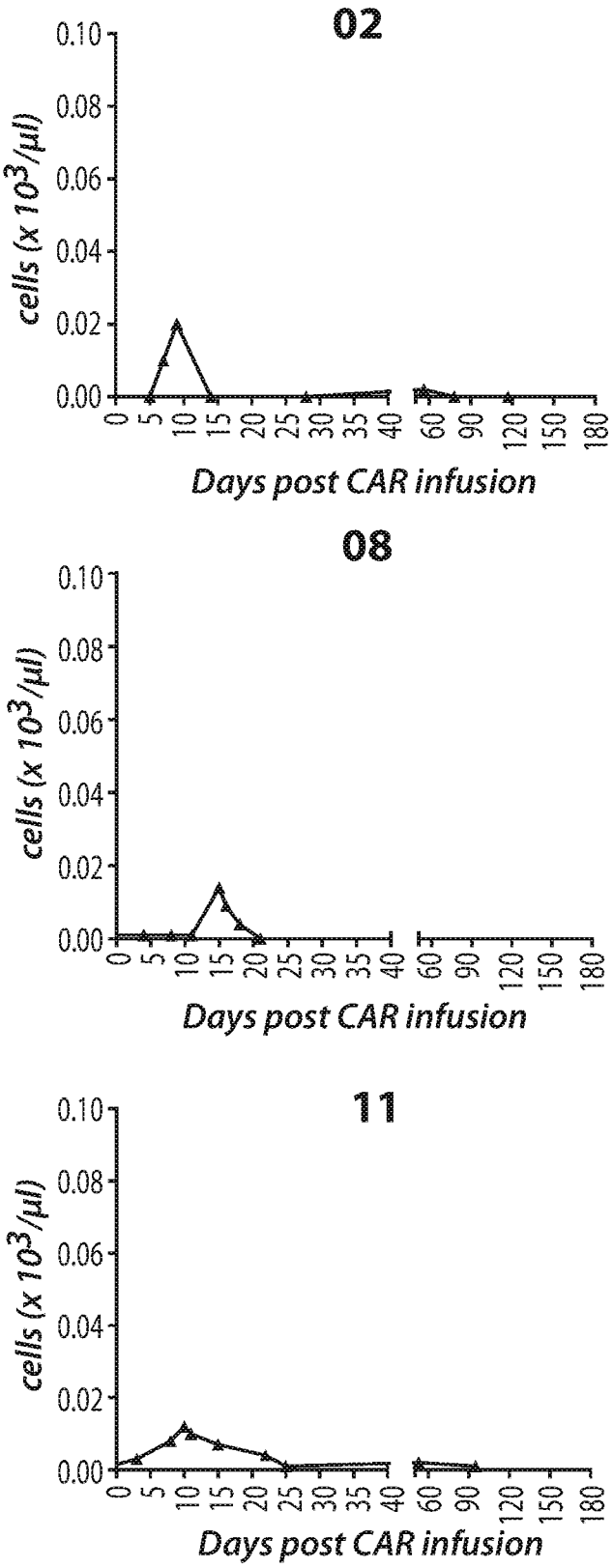

02
0.10
0.08
0.06
0.04
0.02
0.00
cells (x 10^3/μl)
0 5 10 15 20 25 30 35 40 60 90 120 150 180
Days post CAR infusion
08
0.10
0.08
0.06
0.04
0.02
0.00
cells (x 10^3/μl)
0 5 10 15 20 25 30 35 40 60 90 120 150 180
Days post CAR infusion
11
0.10
0.08
0.06
0.04
0.02
0.00
cells (x 10^3/μl)
0 5 10 15 20 25 30 35 40 60 90 120 150 180
Days post CAR infusion

FIG. 39-2

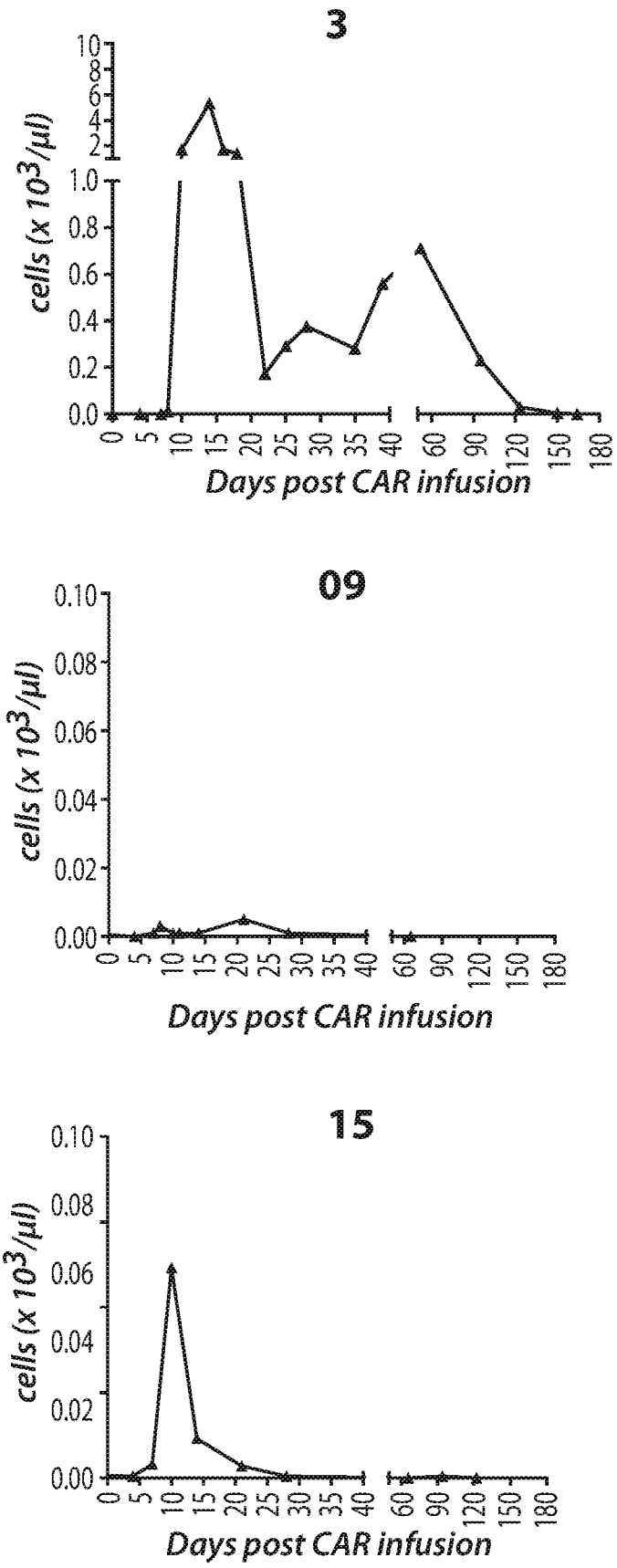

3
cells (x 10^3/μl)
Days post CAR infusion
09
cells (x 10^3/μl)
Days post CAR infusion
15
cells (x 10^3/μl)
Days post CAR infusion

FIG. 39-3

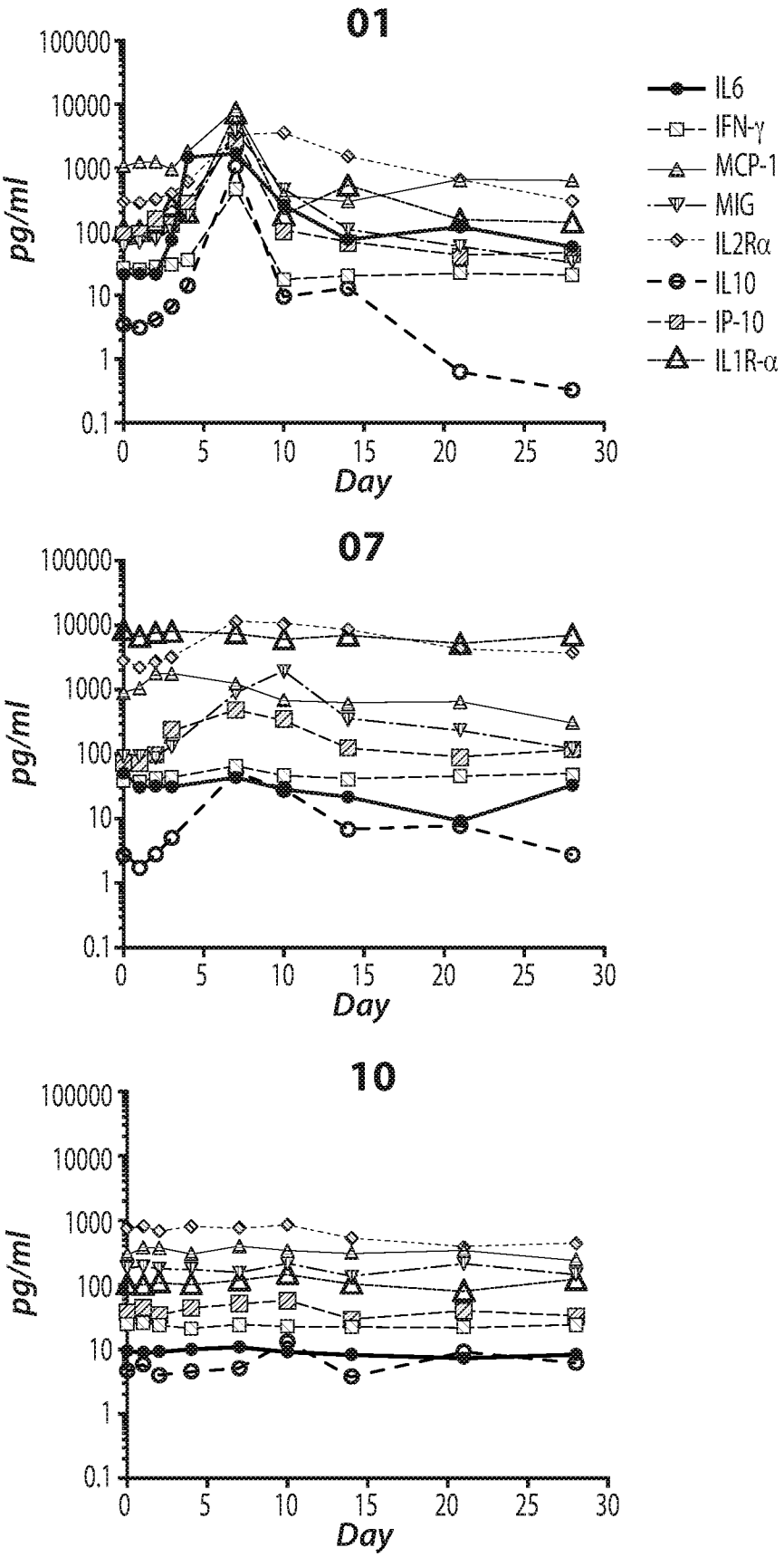

01
07
10
pg/ml
Day
100000
10000
1000
100
10
1
0.1
0
5
10
15
20
25
30
IL6
IFN-γ
MCP-1
MIG
IL2Rα
IL10
IP-10
IL1R-α

FIG. 40-1

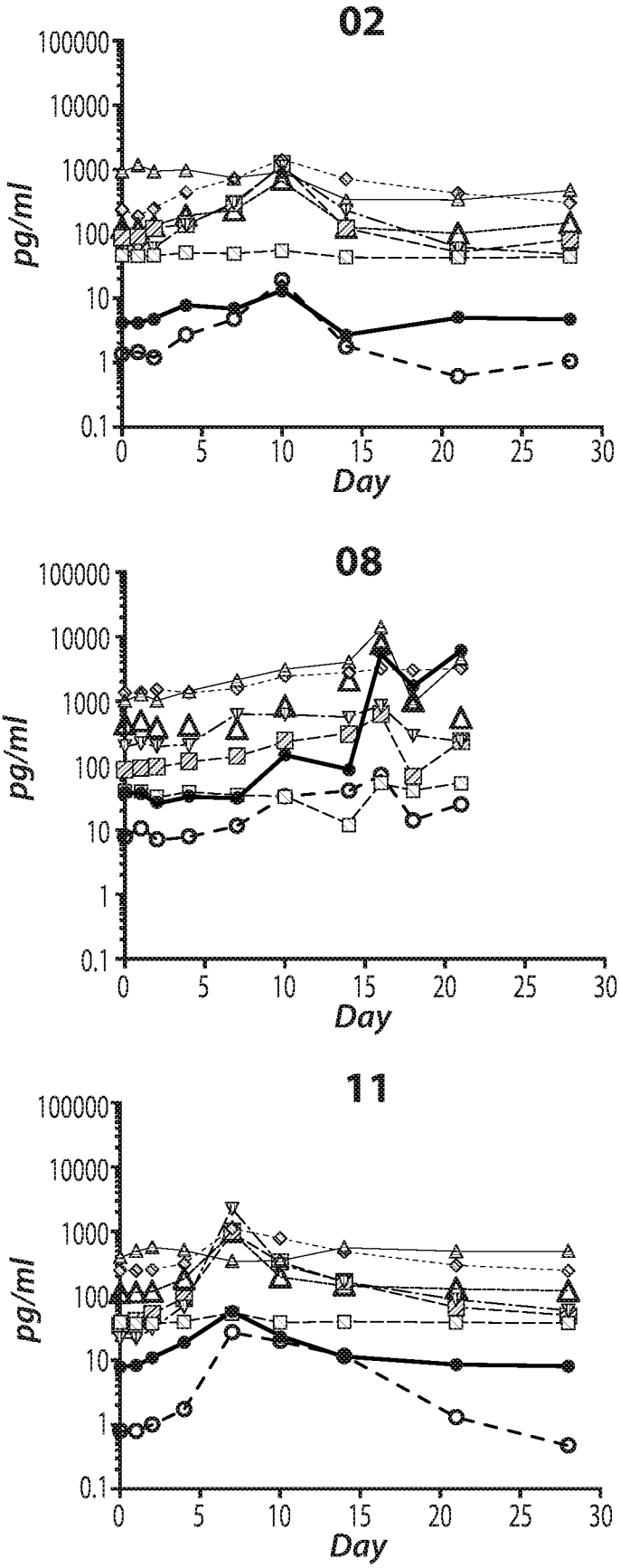

02
100000
10000
1000
100
10
1
0.1
pg/ml
0
5
10
15
20
25
30
Day
08
100000
10000
1000
100
10
1
0.1
pg/ml
0
5
10
15
20
25
30
Day
11
100000
10000
1000
100
10
1
0.1
pg/ml
0
5
10
15
20
25
30
Day

FIG. 40-2

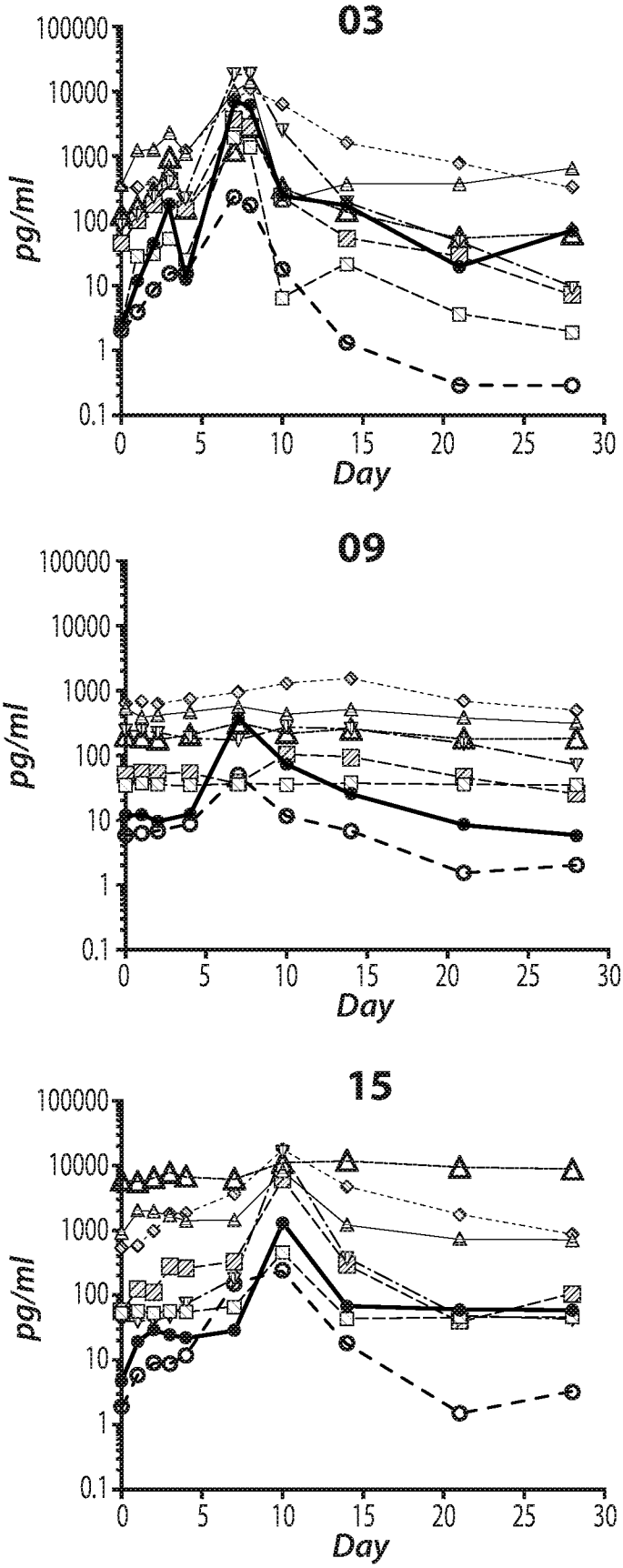

03
100000
10000
1000
100
10
1
0.1
pg/ml
0
5
10
15
20
25
30
Day
09
100000
10000
1000
100
10
1
0.1
pg/ml
0
5
10
15
20
25
30
Day
15
100000
10000
1000
100
10
1
0.1
pg/ml
0
5
10
15
20
25
30
Day

FIG. 40-3

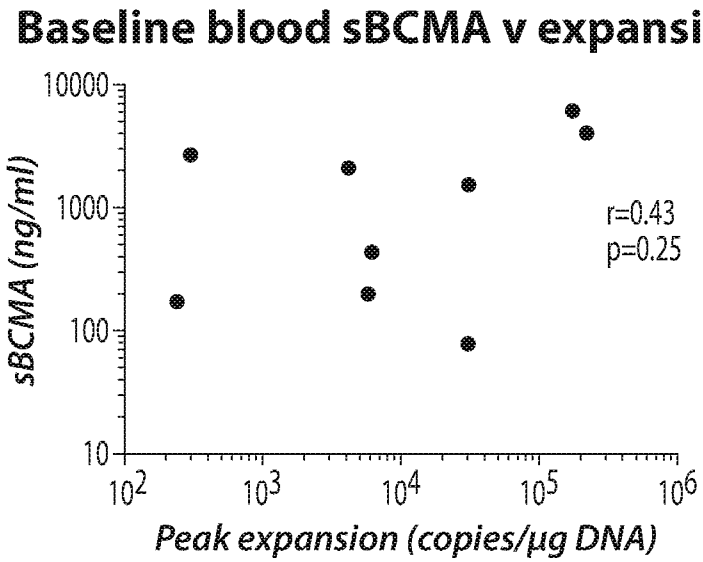


FIG. 41A

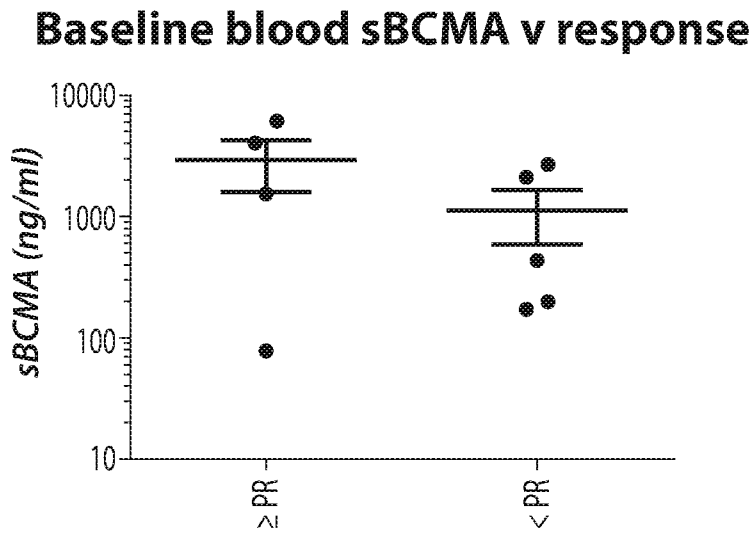


FIG. 41B

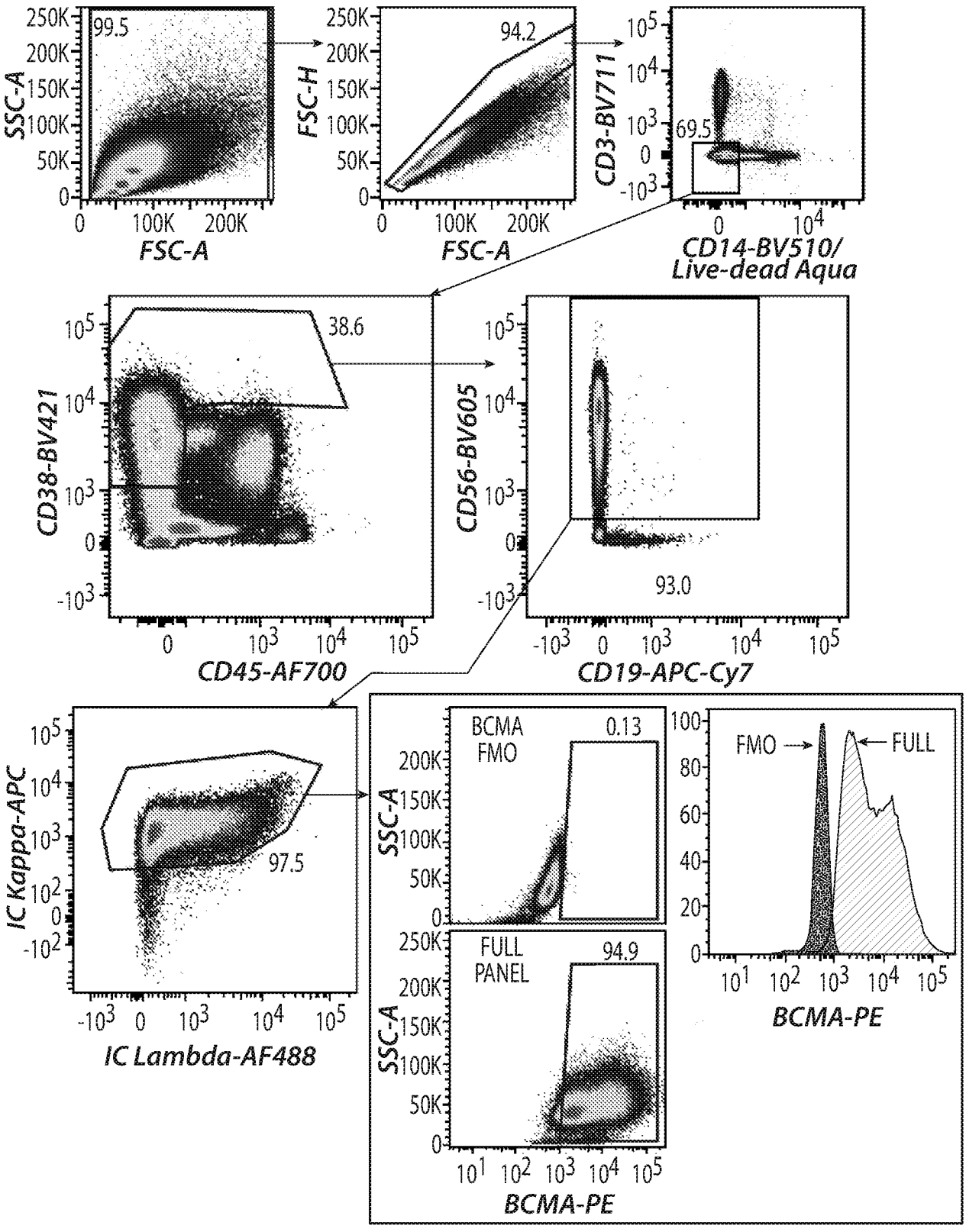

SSC-A
FSC-A
99.5
FSC-H
94.2
CD3-BV711
69.5
CD14-BV510/
Live-dead Aqua
CD38-BV421
38.6
CD45-AF700
CD56-BV605
93.0
CD19-APC-Cy7
IC Kappa-APC
97.5
IC Lambda-AF488
BCMA
FMO
0.13
FULL
PANEL
94.9
BCMA-PE
FMO
FULL

FIG. 42

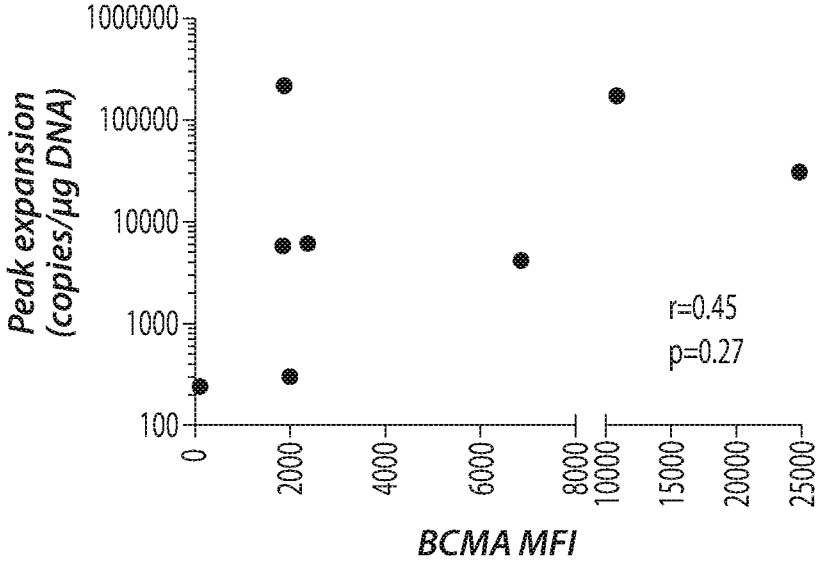


FIG. 43A

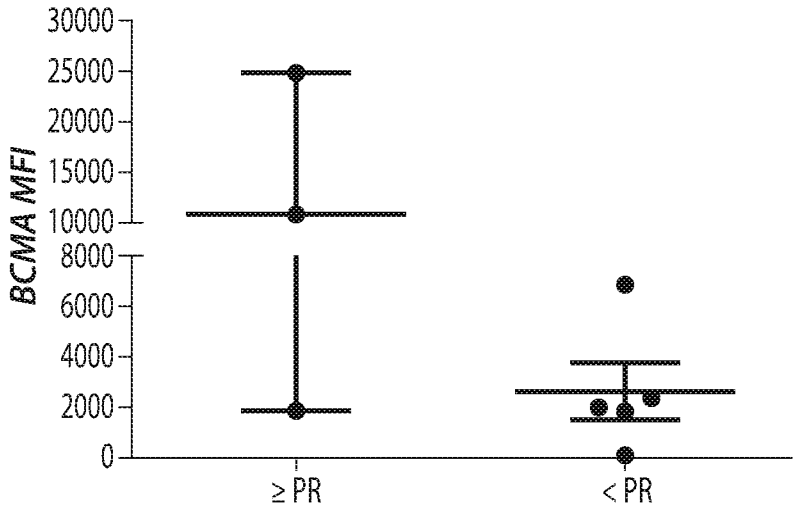


FIG. 43B

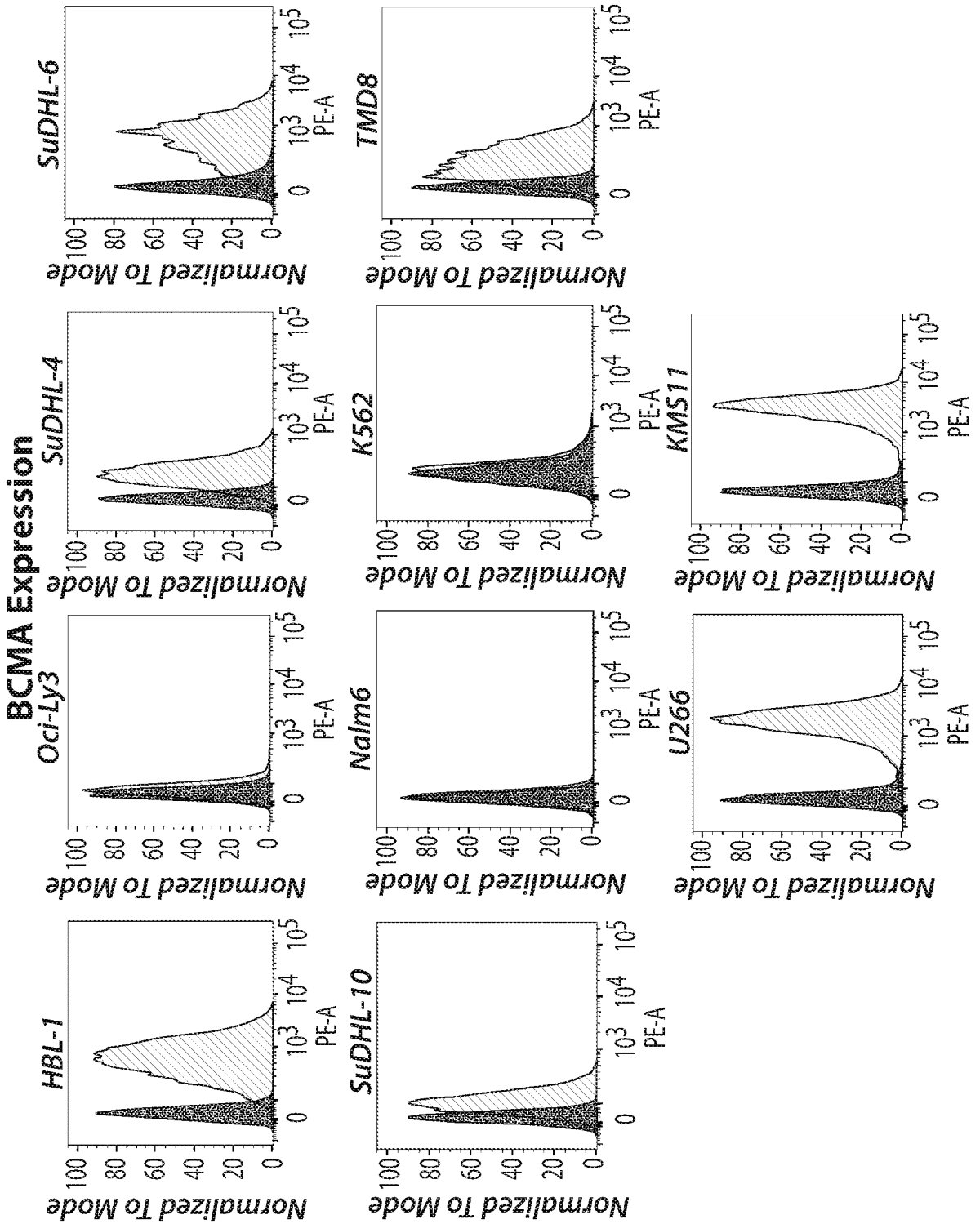

BCMA Expression
HBL-1
Oci-Ly3
SuDHL-4
SuDHL-6
SuDHL-10
Nalm6
K562
TMD8
KMS11
U266
Normalized To Mode
PE-A
0
20
40
60
80
100
10^3
10^4
10^5

FIG. 44A

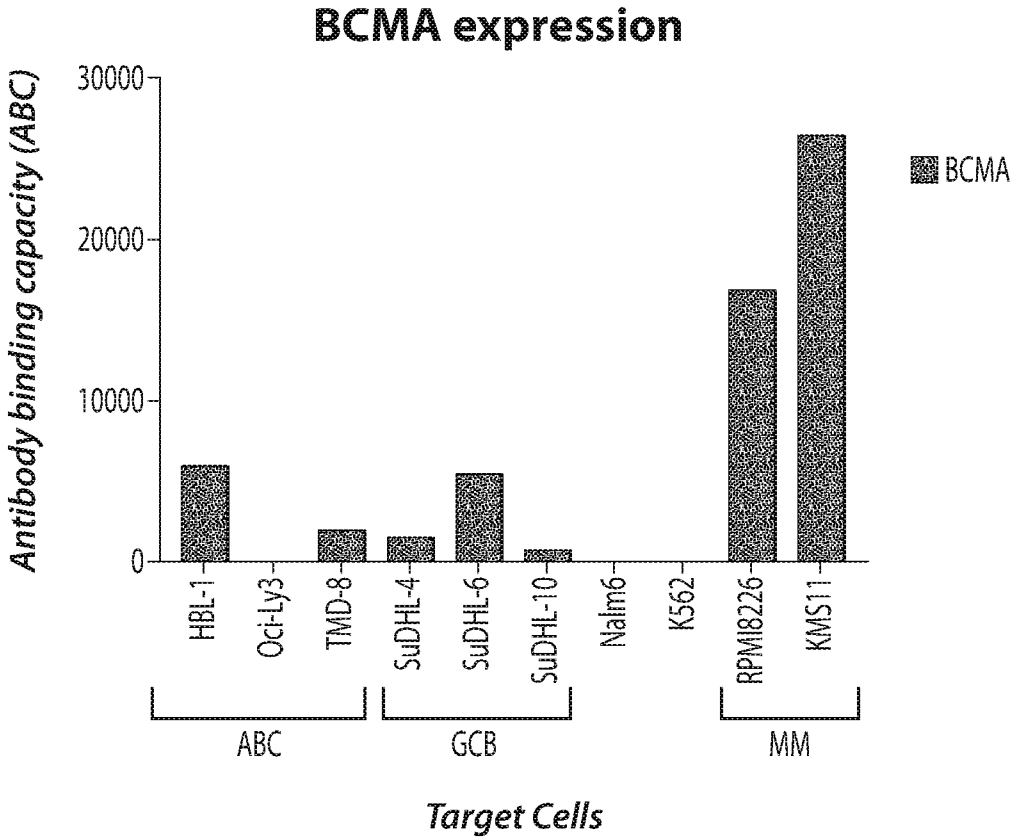

BCMA expression
Antibody binding capacity (ABC)
30000
20000
10000
0
BCMA
HBL-1
Oci-Ly3
TMD-8
SuDHL-4
SuDHL-6
SuDHL-10
Nalm6
K562
RPMI8226
KMS11
ABC
GCB
MM
Target Cells

FIG. 44B

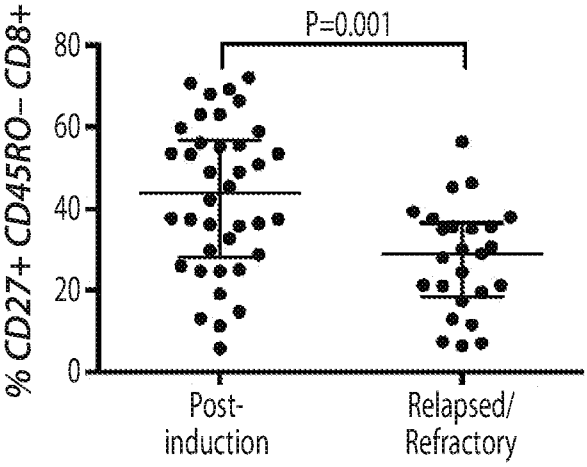


FIG. 45A

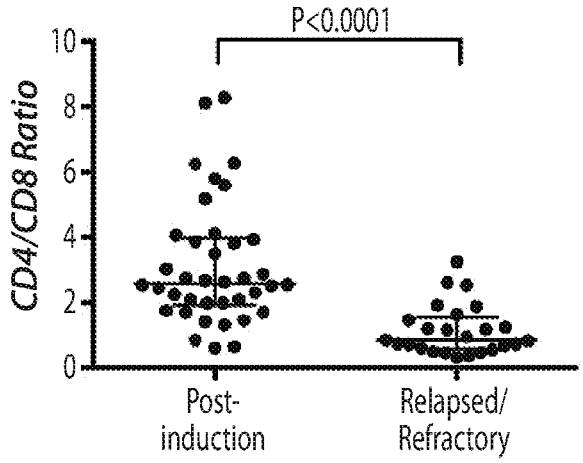


FIG. 45B

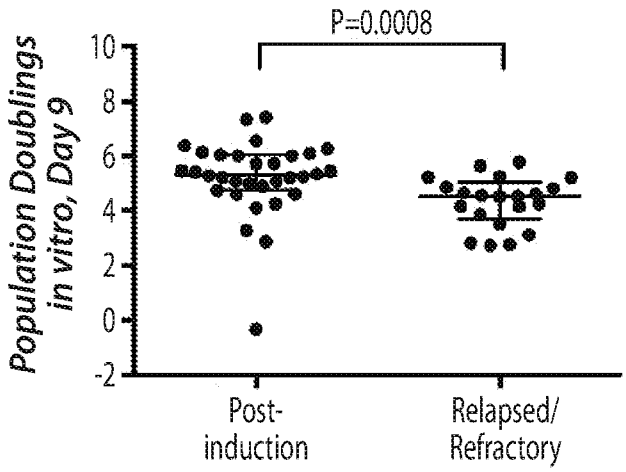
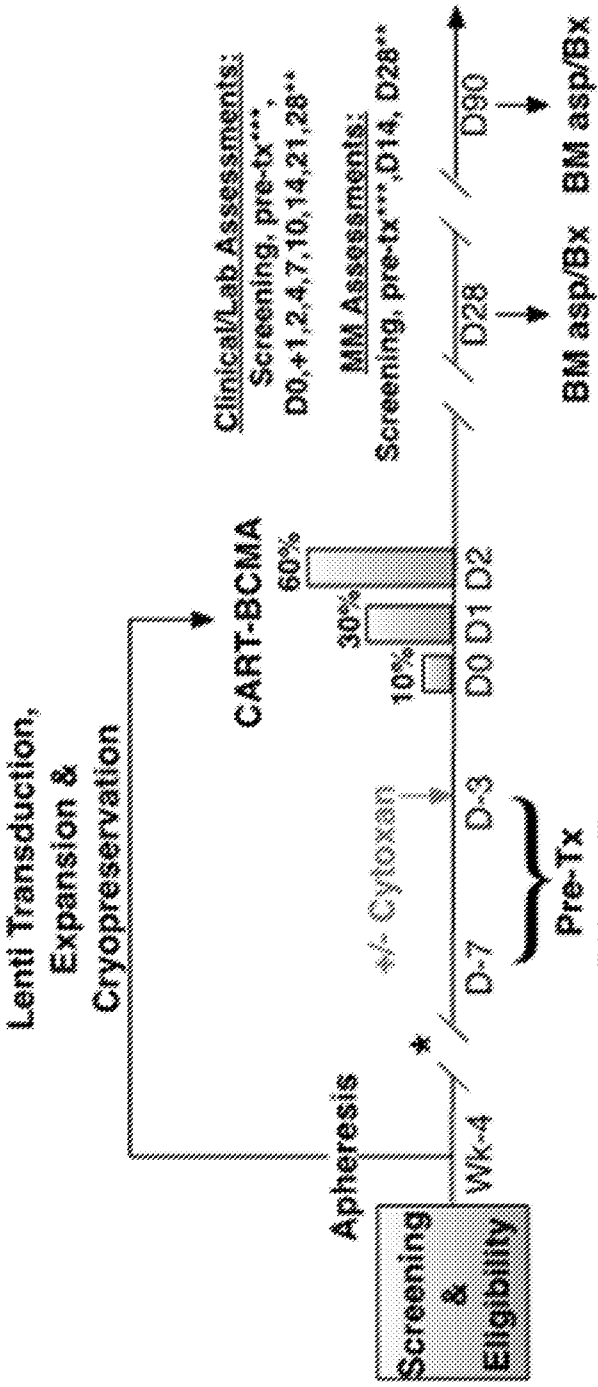


FIG. 45C

FIG. 46


Screening & Eligibility
Wk-4
Apheresis
Lenti Transduction, Expansion & Cryopreservation
CART-BCMA
+/- Cytoxan
Pre-Tx BM asp/Bx
D-7
D-3
D0 D1 D2
10%
30%
60%
Clinical/Lab Assessments: Screening, pre-tx***, D0,+1,2,4,7,10,14,21,28**
MM Assessments: Screening, pre-tx***,D14, D28**
D28
D90
BM asp/Bx
BM asp/Bx
* Patients may receive therapy during manufacturing to maintain disease control
** After first 28 days, follow-up is q4 wks up to 6 mos., then q3 mos. up to 2 years
*** Pre-tx = pre-treatment, 3 to 7 days before CAR T cell infusion

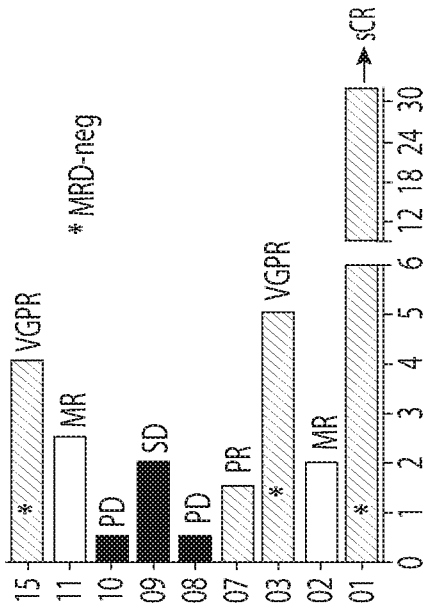


FIG. 47A

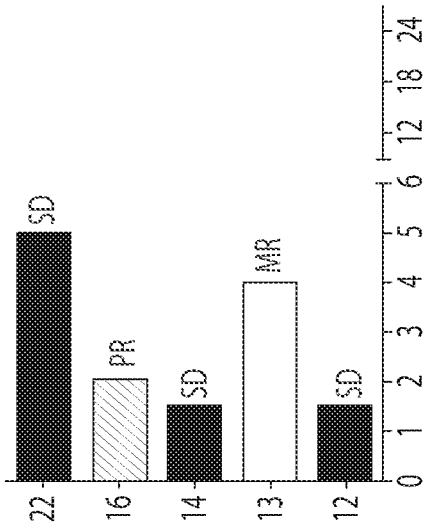


FIG. 47B

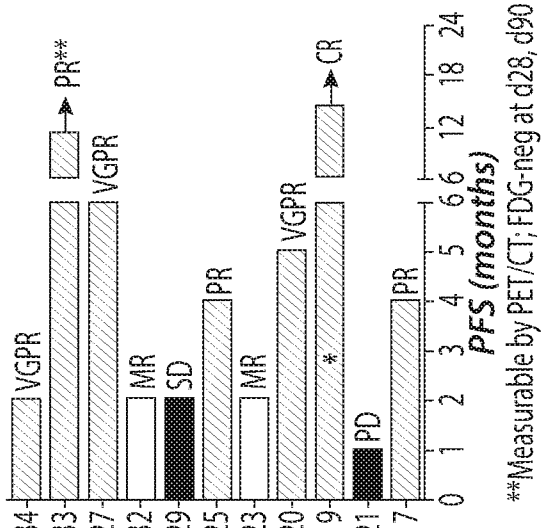


FIG. 47C

OS

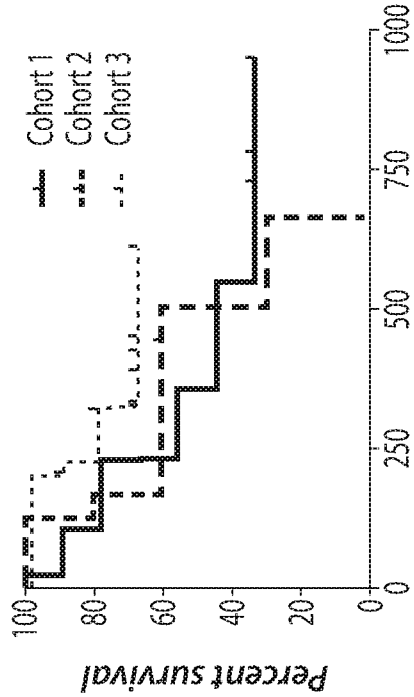


FIG. 47D

FIG. 48A

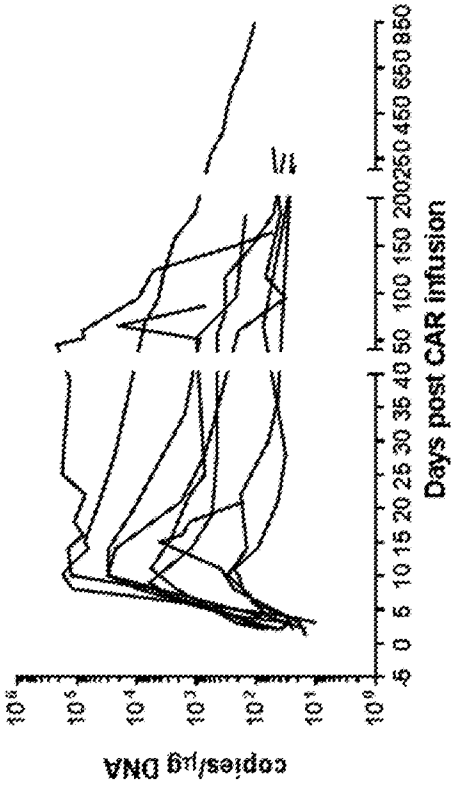


FIG. 48B

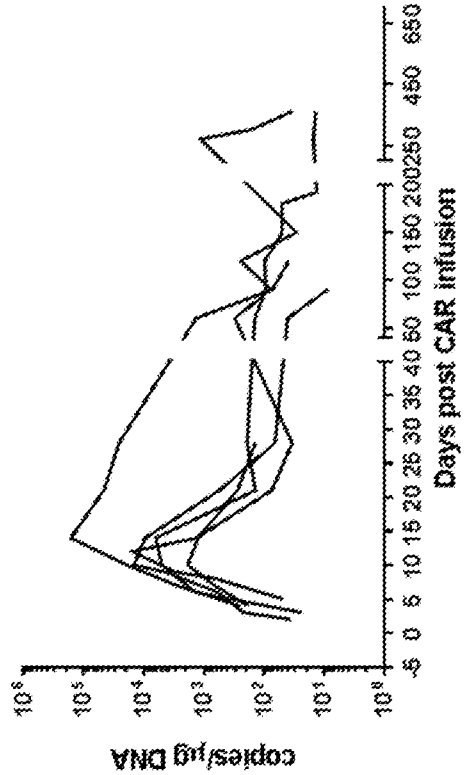


FIG. 48C

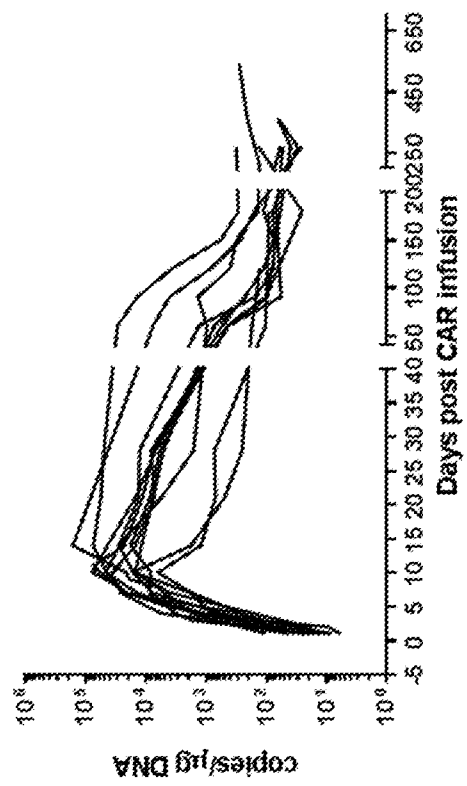


FIG. 48D

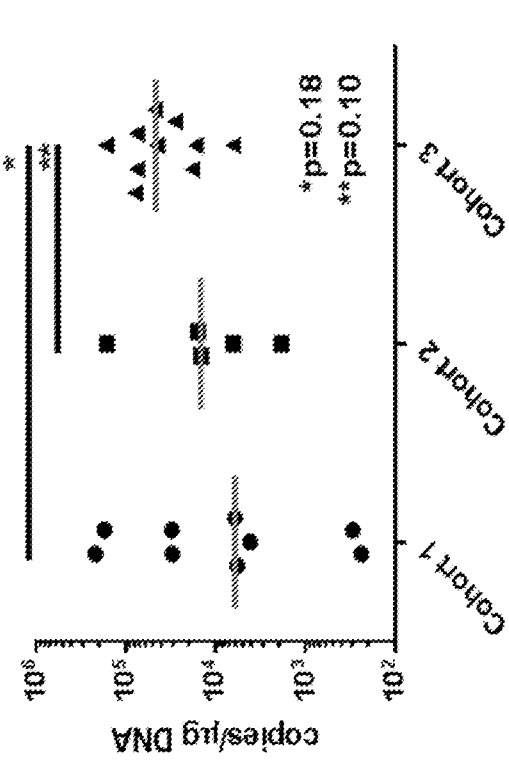


FIG. 49A

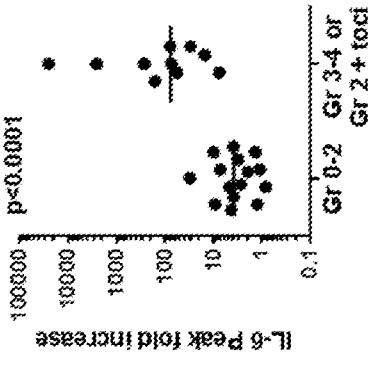


FIG. 49B

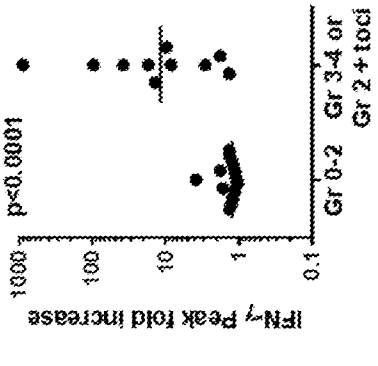


FIG. 49C

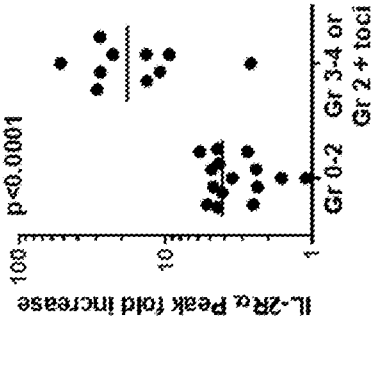


FIG. 49D

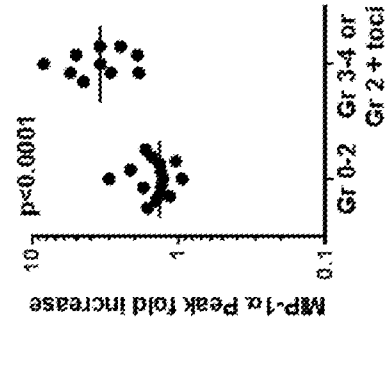


FIG. 49E

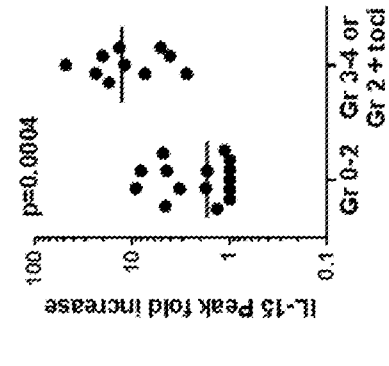


FIG. 49F

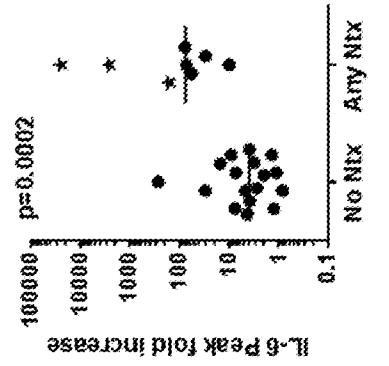


FIG. 49G

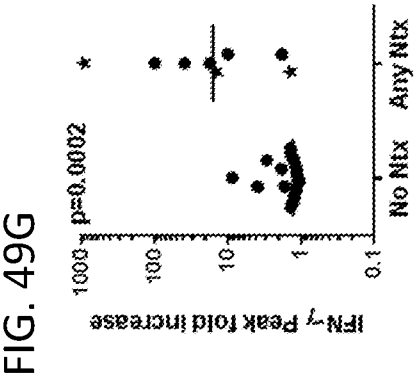


FIG. 49H

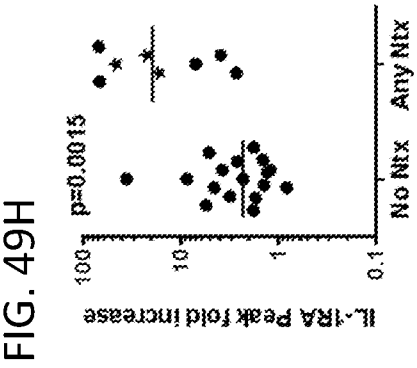
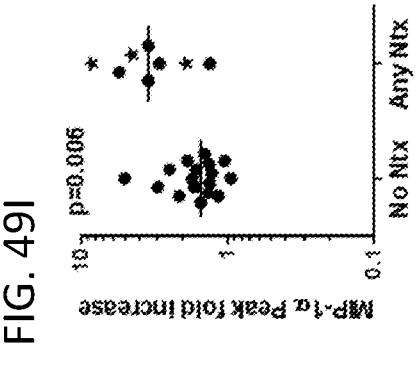


FIG. 49I



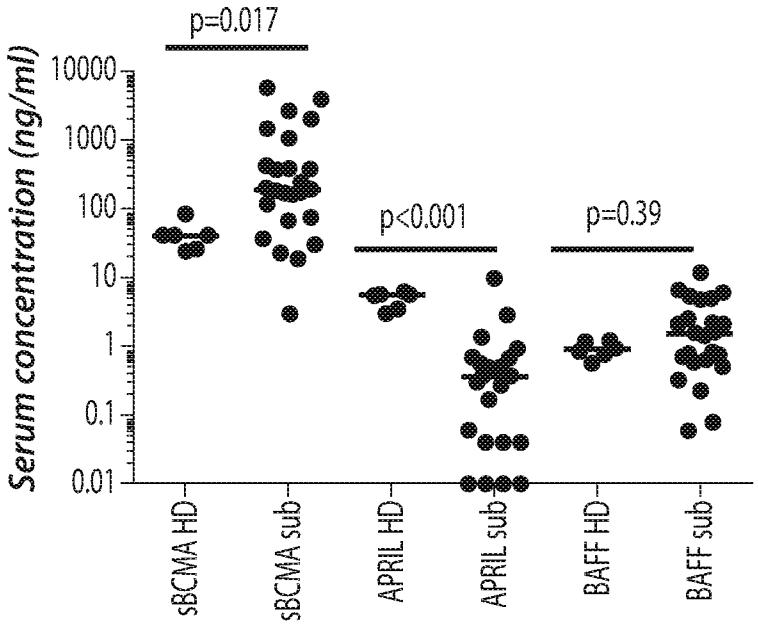


FIG. 50A

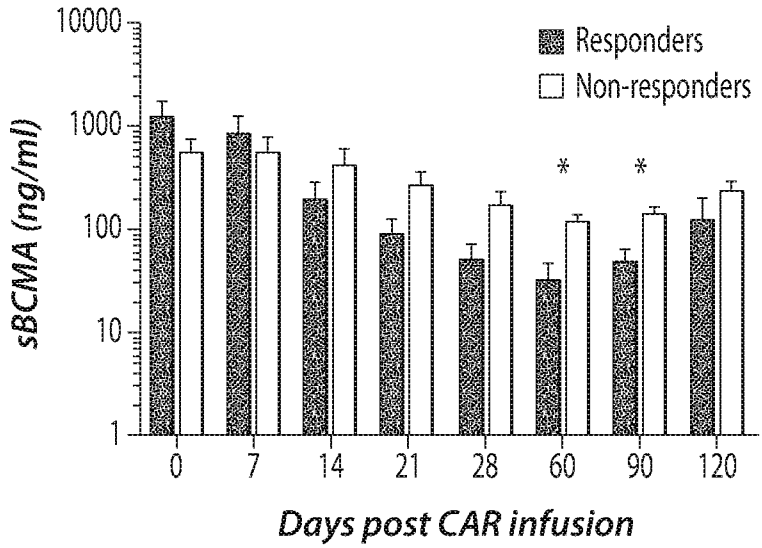


FIG. 50B

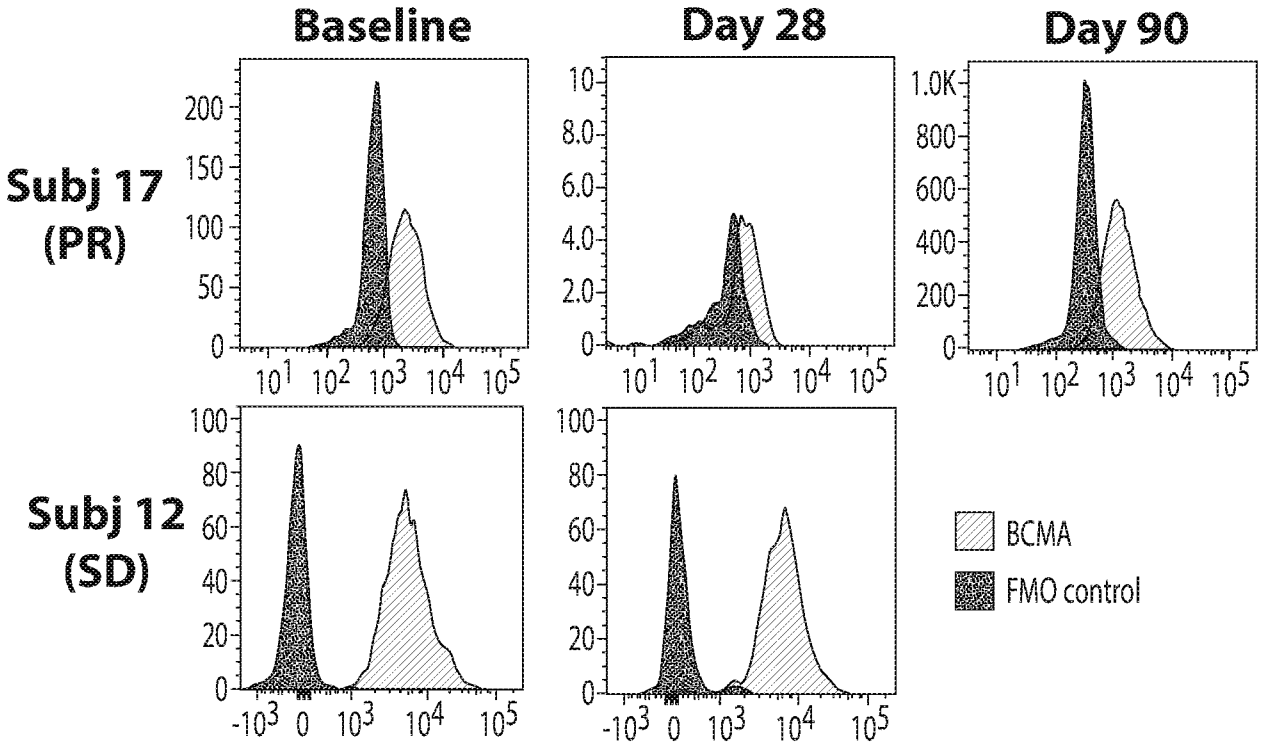


FIG. 50C

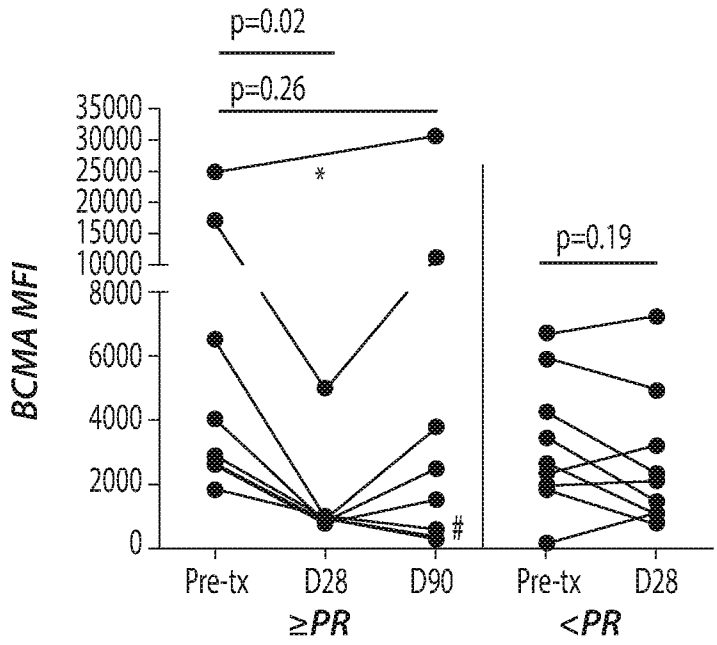


FIG. 50D

FIG. 51A

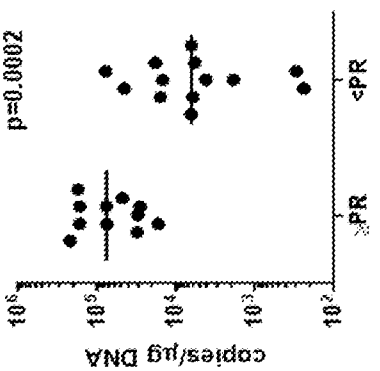


FIG. 51B

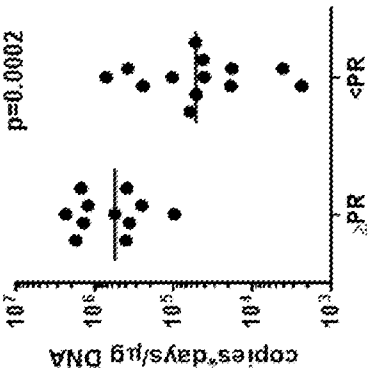


FIG. 51C

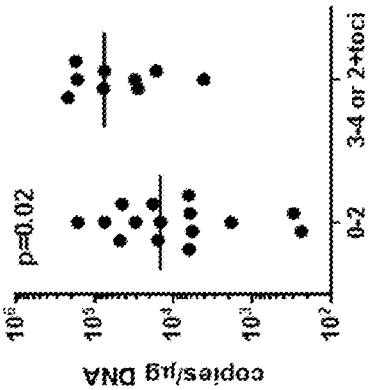


FIG. 51D

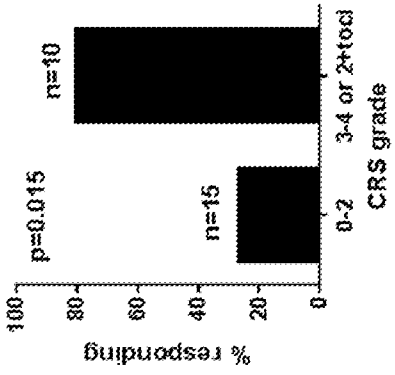


FIG. 51E

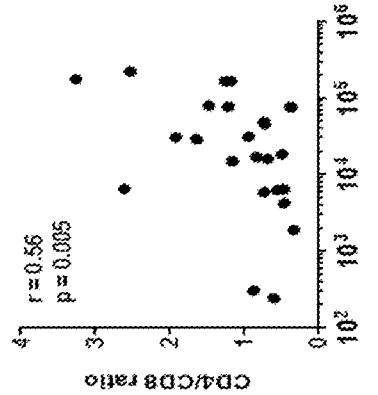


FIG. 51F

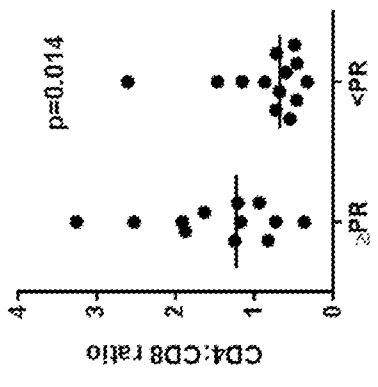


FIG. 51G

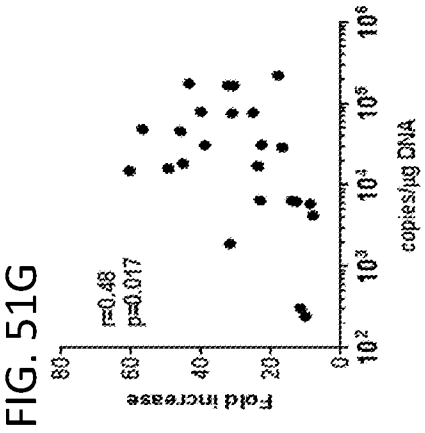


FIG. 51H

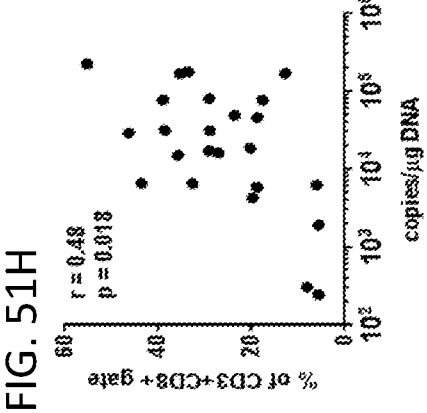


FIG. 51I

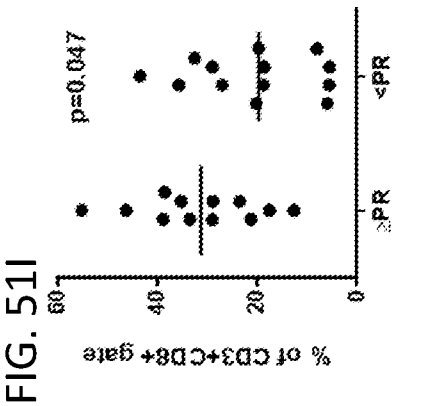


FIG. 52

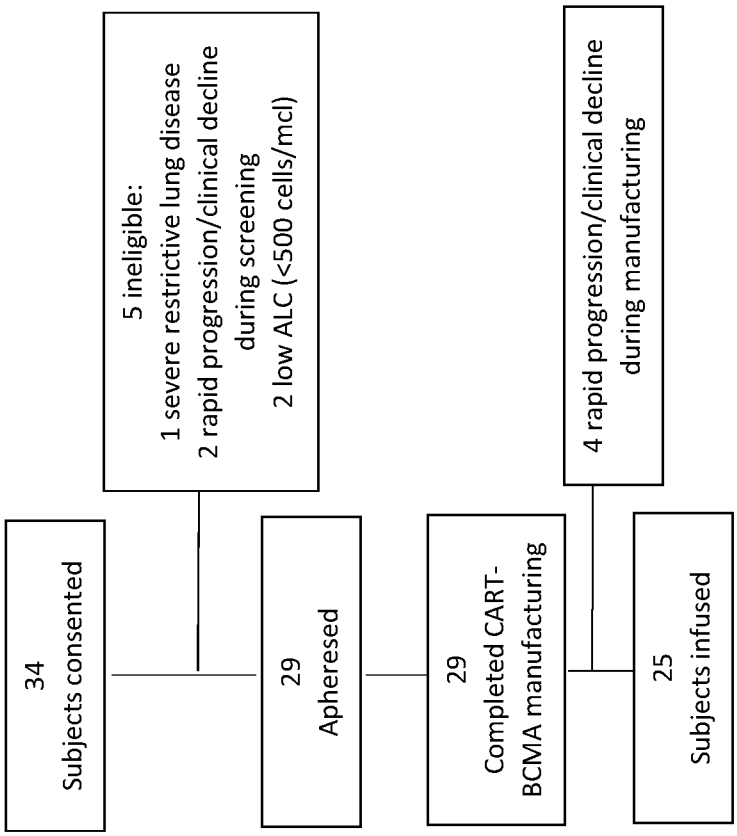

34
Subjects consented
5 ineligible:
1 severe restrictive lung disease
2 rapid progression/clinical decline during screening
2 low ALC (<500 cells/mcl)
29
Apheresed
29
Completed CART-BCMA manufacturing
4 rapid progression/clinical decline during manufacturing
25
Subjects infused

FIG. 53A

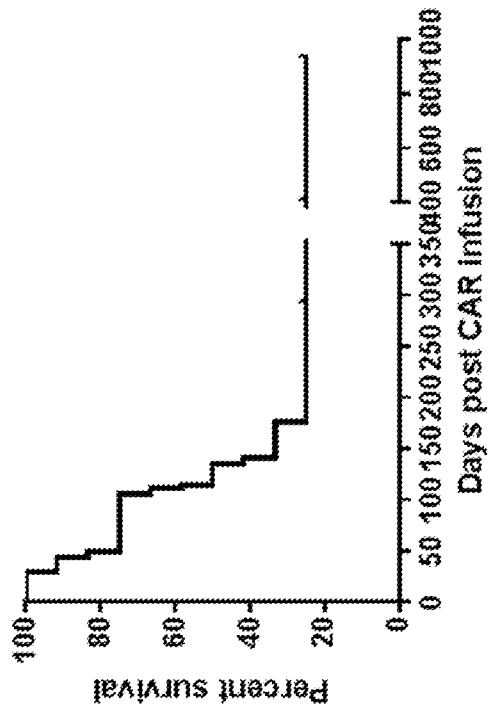


FIG. 53B

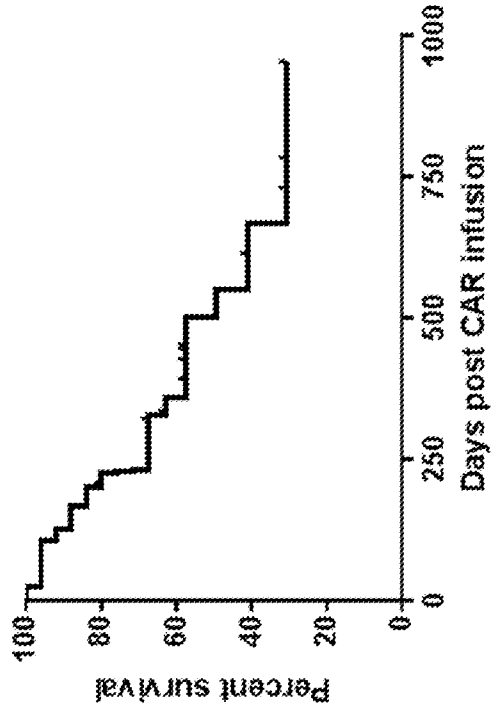


FIG. 53C

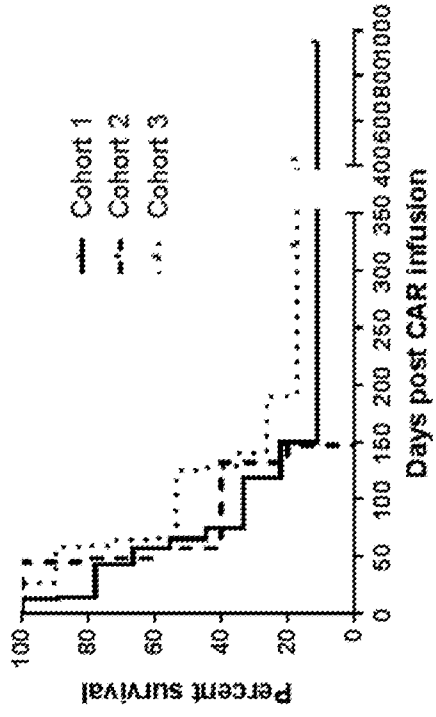


FIG. 53D

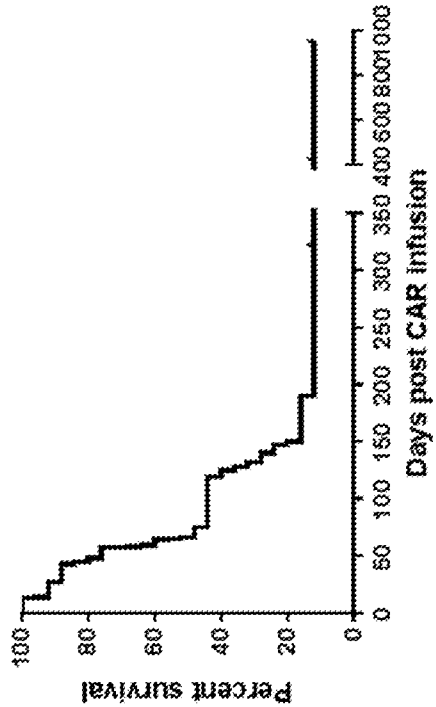


FIG. 54A

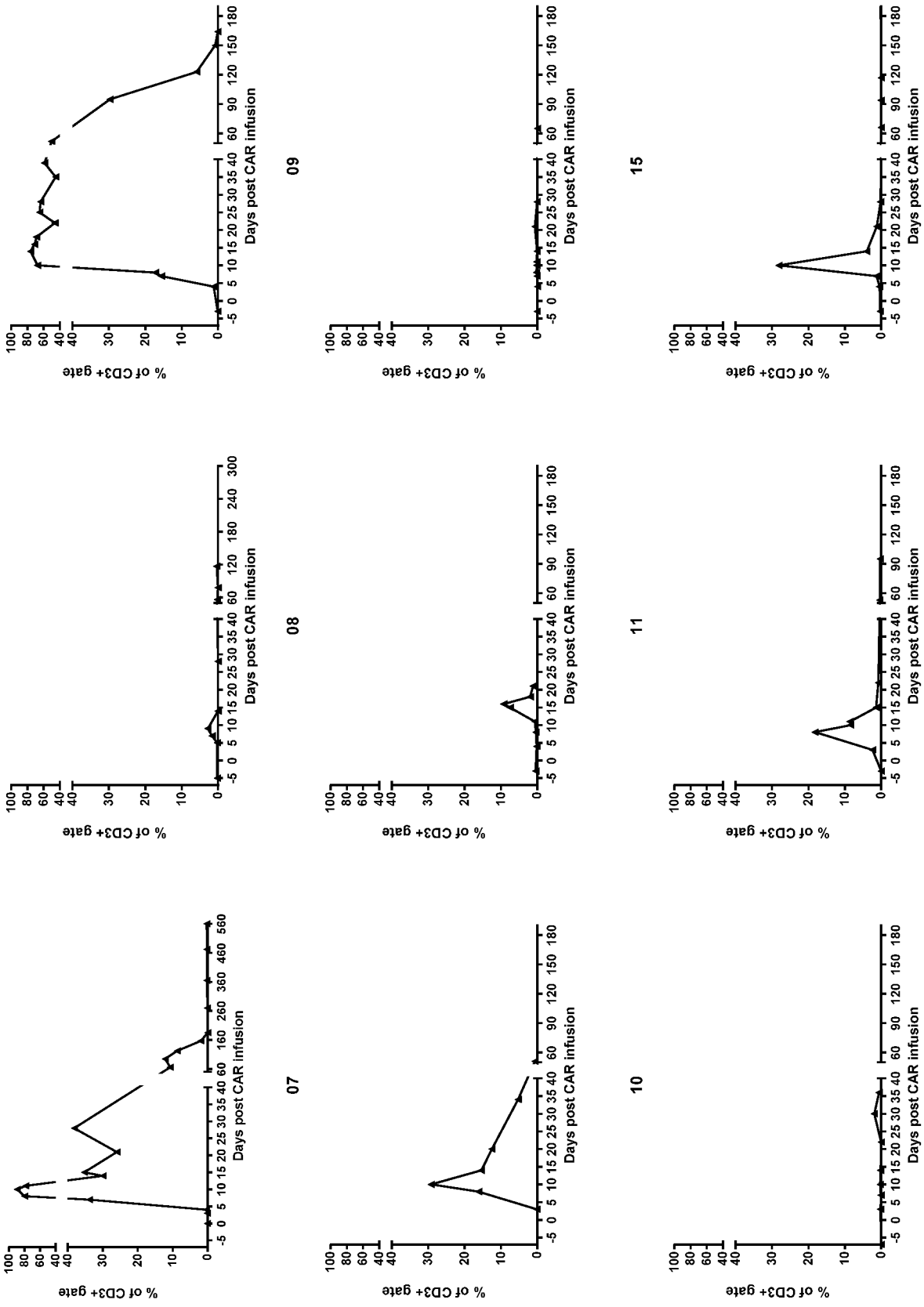
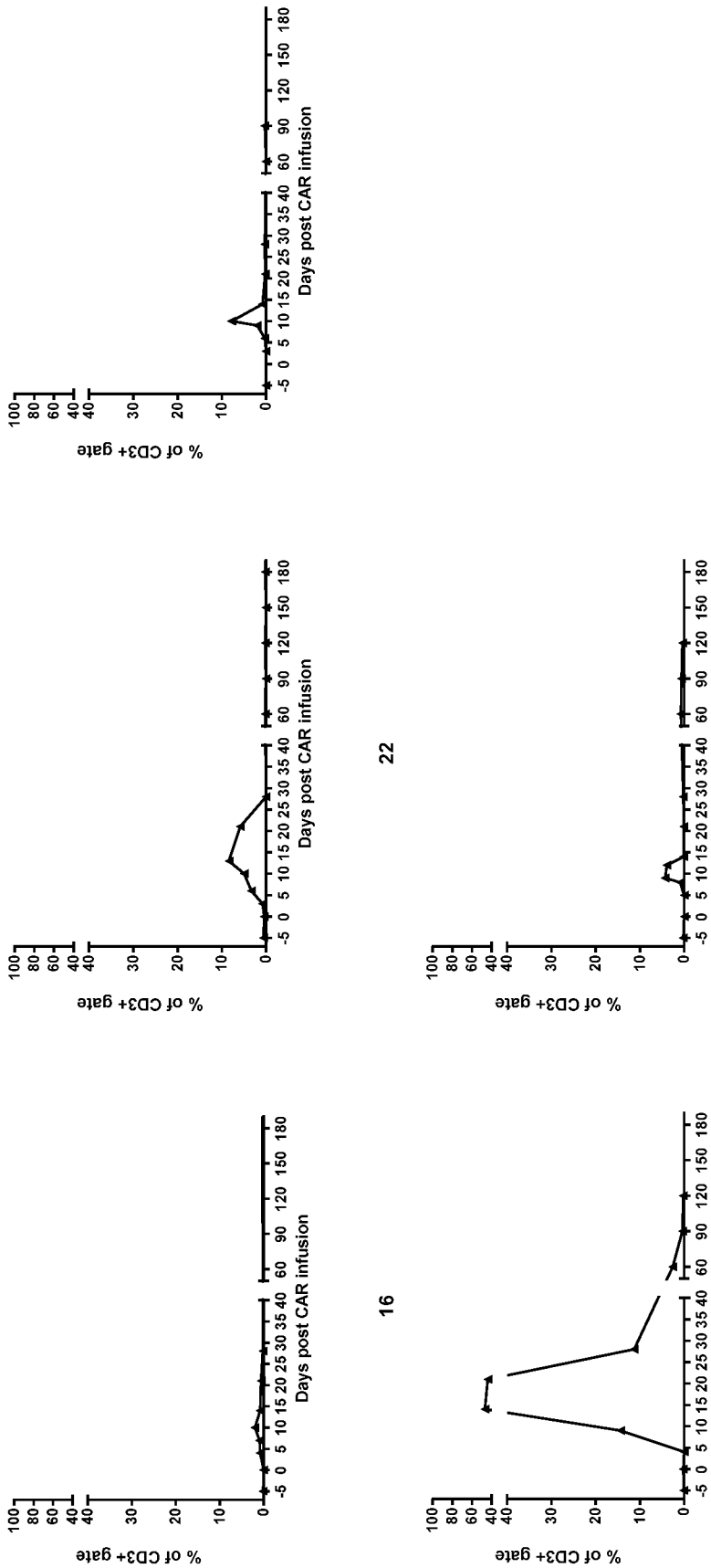


FIG. 54B



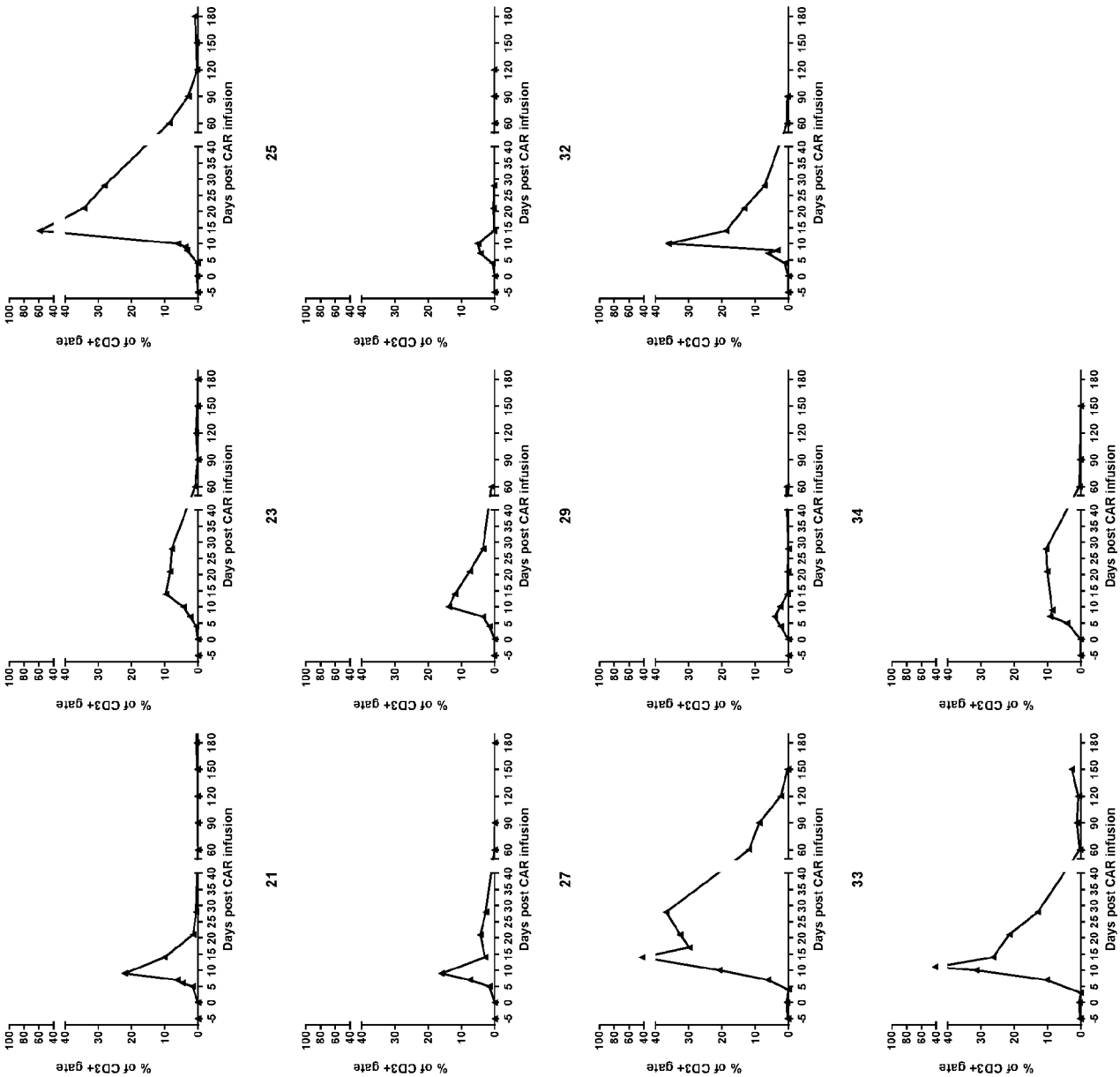

17
19
20
21
23
25
27
29
32
33
34
% of CD3+ gate
Days post CAR infusion

FIG. 54C

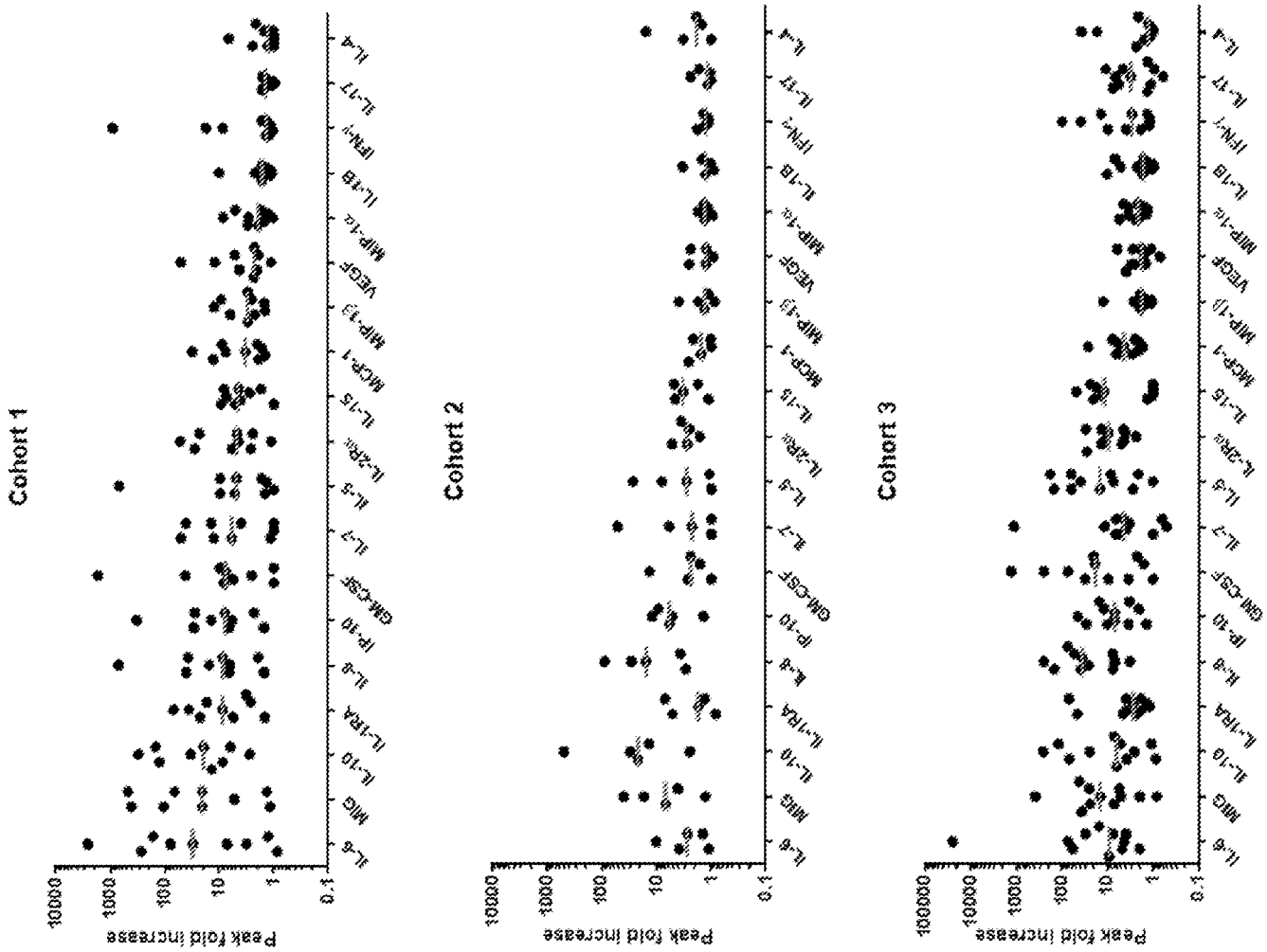

Cohort 1
Cohort 2
Cohort 3
Peak fold increase
10000
1000
100
10
1
0.1
IL-6
MIG
IL-10
IL-1RA
IL-8
IP-10
GM-CSF
IL-7
IL-5
IL-2Rα
IL-15
MCP-1
MIP-1β
VEGF
MIP-1α
IL-1β
IFNγ
IL-17
IL-4

FIG. 55

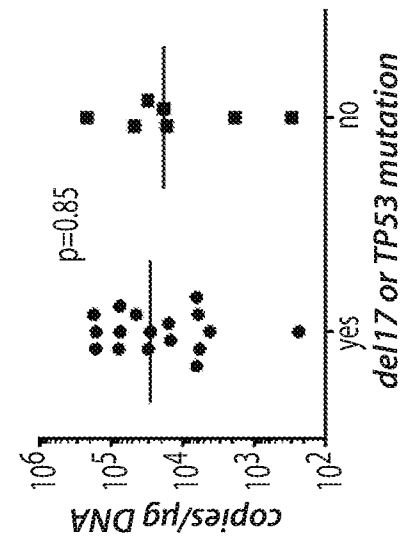


FIG. 56C

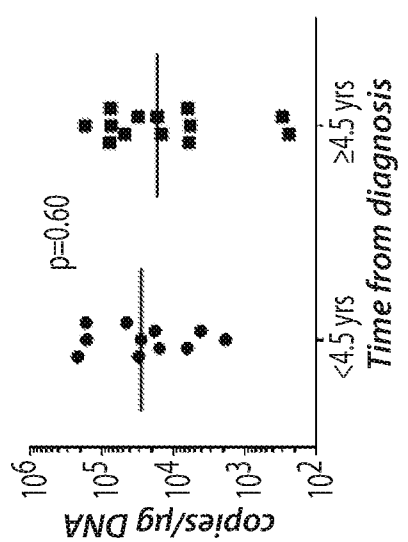


FIG. 56B

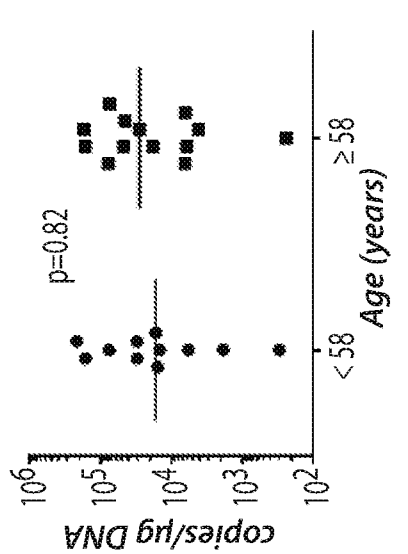


FIG. 56A

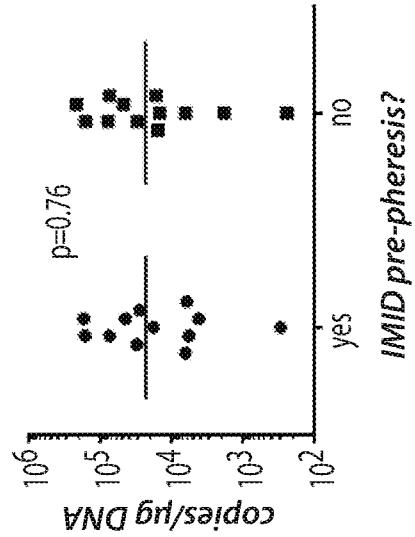


FIG. 56F

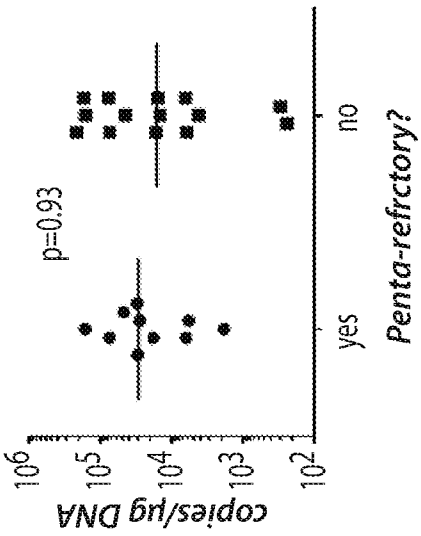


FIG. 56E

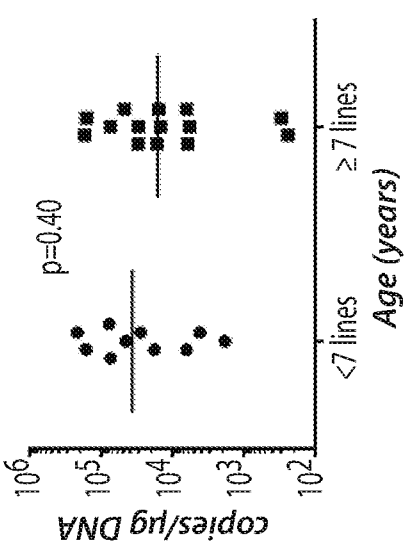


FIG. 56D

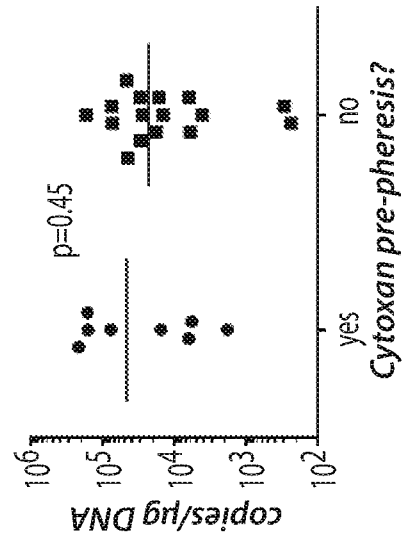


FIG. 56G

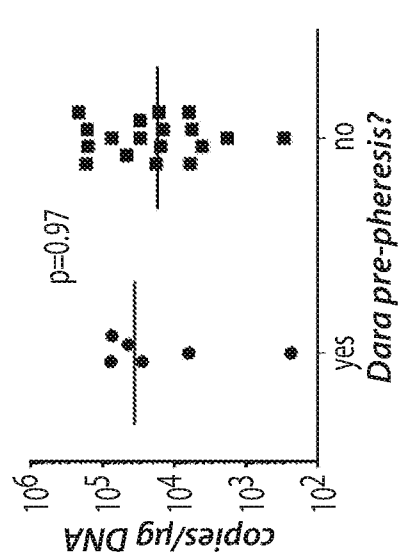


FIG. 56H

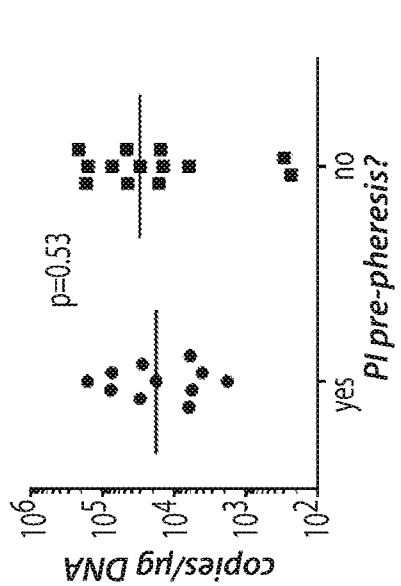


FIG. 56I

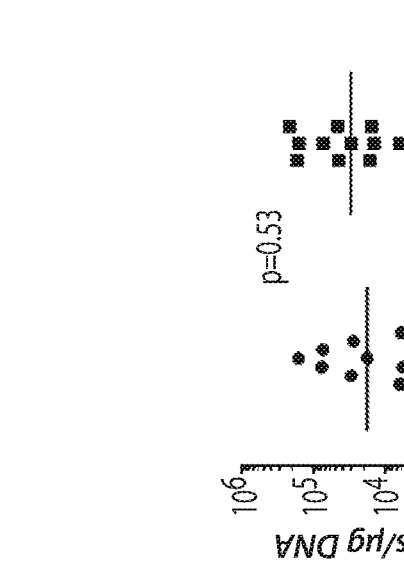


FIG. 56J

FIG. 56K

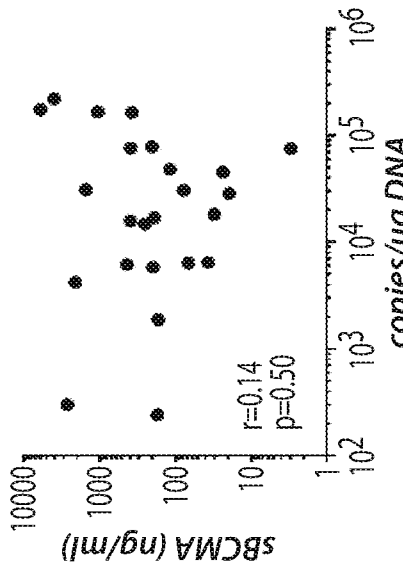


FIG. 56L

FIG. 57A

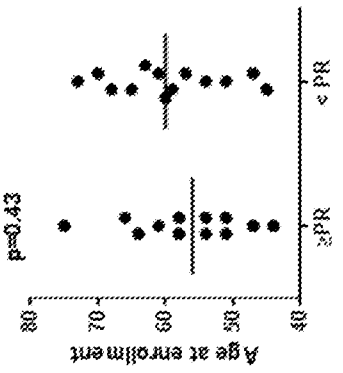


FIG. 57B

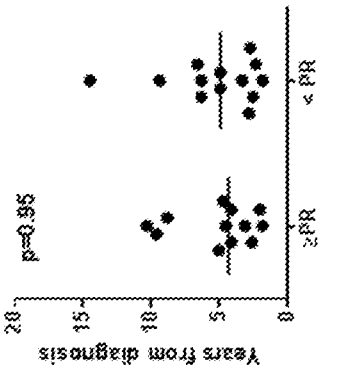


FIG. 57C

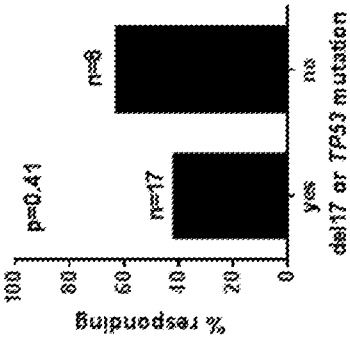


FIG. 57D

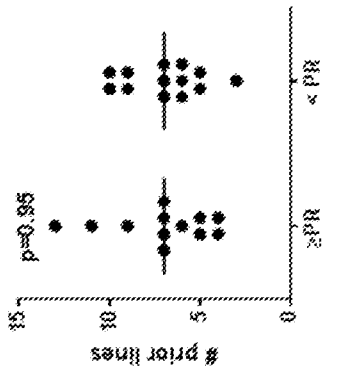


FIG. 57E

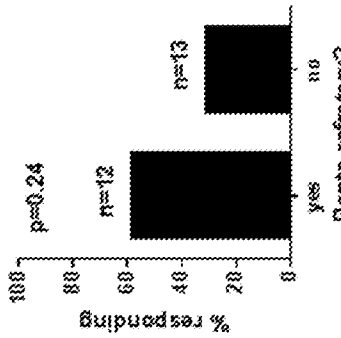


FIG. 57F

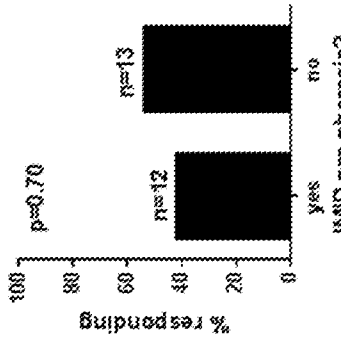


FIG. 57G

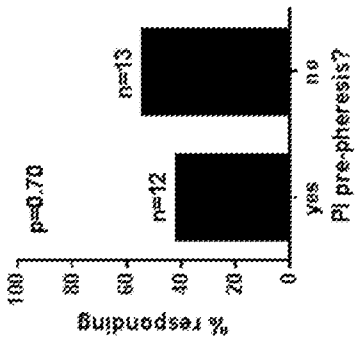


FIG. 57H

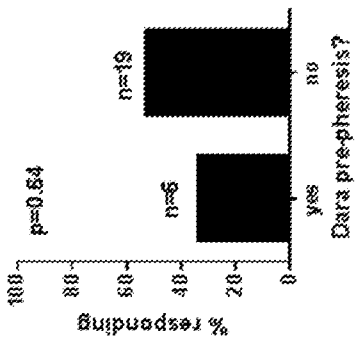


FIG. 57I

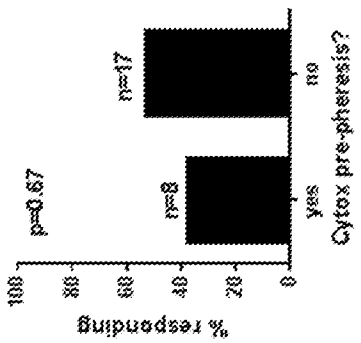


FIG. 57J

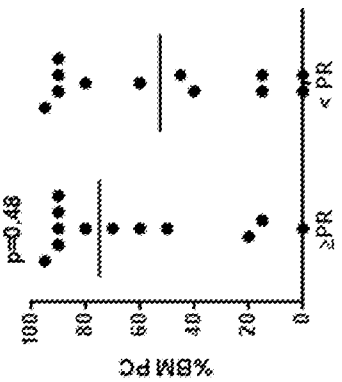


FIG. 57K

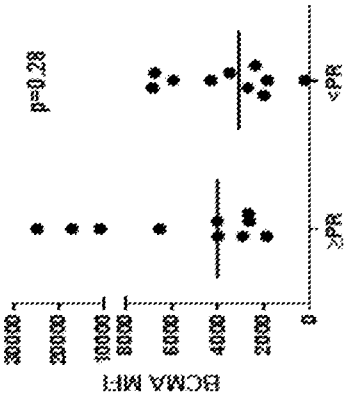
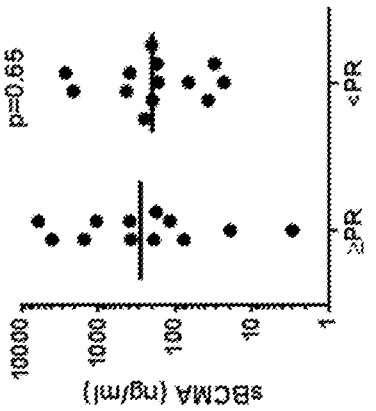


FIG. 57L



SEQUENCE LISTING

<110> NOVARTIS AG
THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA

<120> BCMA-TARGETING CHIMERIC ANTIGEN RECEPTOR, AND USES THEREOF

<130> N2067-7137WO

<140>
<141>

<150> 62/752,010
<151> 2018-10-29

<150> 62/593,043
<151> 2017-11-30

<160> 2036

<170> PatentIn version 3.5

<210> 1

<400> 1
000

<210> 2

<400> 2
000

<210> 3

<400> 3
000

<210> 4

<400> 4
000

<210> 5

<400> 5
000

<210> 6

<400> 6
000

<210> 7

<400> 7
000

<210> 8

<400> 8
000

<210> 9

<400> 9
000

<210> 10

<400> 10
000

<210> 11

<400> 11
000

<210> 12

<400> 12
000

<210> 13

<400> 13
000

<210> 14

<400> 14
000

<210> 15

<400> 15
000

<210> 16

<400> 16
000

<210> 17

<400> 17
000

<210> 18

<400> 18
000

<210> 19

<400> 19
000

<210> 20

<400> 20
000

<210> 21

<400> 21
000

<210> 22

<400> 22
000

<210> 23

<400> 23
000

<210> 24

<400> 24
000

<210> 25

<400> 25
000

<210> 26

<400> 26
000

<210> 27

<400> 27
000

<210> 28

<400> 28
000

<210> 29

<400> 29
000

<210> 30

<400> 30
000

<210> 31

<400> 31
000

<210> 32

<400> 32
000

<210> 33

<400> 33
000

<210> 34

<400> 34
000

<210> 35

<400> 35
000

<210> 36

<400> 36
000

<210> 37

<400> 37
000

<210> 38

<400> 38
000

<210> 39
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 39
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gly Trp Val
35 40 45

Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val Trp Gly Gln
100 105 110

```
Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser
    130                 135                 140


Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145                 150                 155                 160


Arg Ala Ser Gln Ser Ile Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Arg Arg
            180                 185                 190


Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala Val Tyr
    210                 215                 220


Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly
225                 230                 235                 240


Thr Lys Leu Glu Ile Lys
                245


<210> 40
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 40
```

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro
    130                 135                 140

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
145                 150                 155                 160

Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys
                165                 170                 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
            180                 185                 190
```

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
210 215 220

Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 41
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 41
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser

85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser
130 135 140

Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser
145 150 155 160

Leu Leu Arg Asn Asp Gly Lys Thr Pro Leu Tyr Trp Tyr Leu Gln Lys
165 170 175

Ala Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg Phe
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Ala Tyr Tyr
210 215 220

Cys Met Gln Asn Ile Gln Phe Pro Ser Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 42
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 42

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Lys Thr Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Asp Asn Phe
            20                  25                  30

Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65                  70                  75                  80

Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
    130                 135                 140

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
145                 150                 155                 160

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asn
                165                 170                 175
```

```
Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
            180                 185                 190


Gly Ser Lys Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
        195                 200                 205


Ser Gly Thr Asp Phe Thr Leu His Ile Thr Arg Val Gly Ala Glu Asp
    210                 215                 220


Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe
225                 230                 235                 240


Gly Gln Gly Thr Lys Leu Glu Ile Lys
                245


<210> 43
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 43
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asp
            20                  25                  30


Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu
    130                 135                 140


Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160


Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser
            180                 185                 190


Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser Glu Asp Ser Ala
    210                 215                 220


Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala Ser Phe Gly Gln Gly
225                 230                 235                 240


Thr Lys Val Glu Ile Lys
                245
```

<210> 44
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 44
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
100 105 110

Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg
115 120 125

Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Leu
130 135 140

```
Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser
145                 150                 155                 160


Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Val Asp Trp Tyr
                165                 170                 175


Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser
            180                 185                 190


Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Phe Lys Leu Gln Ile Ser Arg Val Glu Ala Glu Asp Val Gly
    210                 215                 220


Ile Tyr Tyr Cys Met Gln Gly Arg Gln Phe Pro Tyr Ser Phe Gly Gln
225                 230                 235                 240


Gly Thr Lys Val Glu Ile Lys
                245


<210> 45
<211> 238
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 45
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30


Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
```

```
        35                  40                  45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
    130                 135                 140

Val Ser Pro Gly Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Val Ser Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
                165                 170                 175

Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Ser Gly Ile Pro Asp
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
    210                 215                 220

Ser Ser Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
```

225 230 235

<210> 46
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 46
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser
130 135 140

```
Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160


Val Ser Ser Lys Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
                165                 170                 175


Arg Leu Leu Met Tyr Gly Ala Ser Ile Arg Ala Thr Gly Ile Pro Asp
            180                 185                 190


Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
        195                 200                 205


Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
    210                 215                 220


Ser Ser Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225                 230                 235


<210> 47
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 47
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30


Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
    130                 135                 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Val Gly Ser Thr Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
                165                 170                 175

Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro
            180                 185                 190

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
    210                 215                 220

Gly Ser Ser Pro Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225                 230                 235                 240
```

Lys

<210> 48
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 48
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ser Gly Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala
115 120 125

```
Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ser Tyr Thr Leu Ala Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
225                 230                 235


<210> 49
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 49
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
```

```
        35                  40                  45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
    210                 215                 220

Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
```

225 230 235

<210> 50
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 50
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Met Val Arg Glu Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala
115 120 125

Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Leu Ser
130 135 140

```
Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser
145                 150                 155                 160


Glu Ser Leu Val His Asn Ser Gly Lys Thr Tyr Leu Asn Trp Phe His
                165                 170                 175


Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Glu Val Ser Asn
            180                 185                 190


Arg Asp Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr
        195                 200                 205


Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
    210                 215                 220


Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Gly Thr Phe Gly Gln Gly
225                 230                 235                 240


Thr Lys Leu Glu Ile Lys
                245


<210> 51
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 51
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30
```

```
Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Arg Leu Thr Gln Ser Pro Ser Pro Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Glu Asp
145                 150                 155                 160

Ile Asn Lys Phe Leu Asn Trp Tyr His Gln Thr Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Asp Ala Ser Thr Leu Gln Thr Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn
        195                 200                 205

Ser Leu Gln Pro Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Glu
    210                 215                 220
```

```
Ser Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225                 230                 235


<210> 52
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 52
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30


Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60


Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80


Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95


Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110


Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125
```

```
Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro Ala Thr Leu Ser
    130                 135                 140

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Val Gly Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Gly Pro
                165                 170                 175

Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
    210                 215                 220

Asp Trp Leu Pro Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225                 230                 235                 240
```

<210> 53
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 53

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
```

```
        35                  40                  45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
    130                 135                 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Ile Gly Ser Ser Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
                165                 170                 175

Pro Arg Leu Leu Met Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro
            180                 185                 190

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
    210                 215                 220

Ala Gly Ser Pro Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
```

225 230 235 240

Lys

<210> 54
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 54
caagtgcaac tcgtggaatc tggtggagga ctcgtgcaac ccggaagatc gcttagactg 60

tcgtgtgccg ccagcgggtt cactttctcg aactacgcga tgtcctgggt ccgccaggca 120

cccggaaagg gactcggttg ggtgtccggc atttcccggt ccggcgaaaa tacctactac 180

gccgactccg tgaagggccg cttcaccatc tcaagggaca acagcaaaaa caccctgtac 240

ttgcaaatga actccctgcg ggatgaagat acagccgtgt actattgcgc ccggtcgcct 300

gcccattact acggcggaat ggacgtctgg ggacagggaa ccactgtgac tgtcagcagc 360

gcgtcgggtg gcggcggctc agggggtcgg gcctccgggg ggggagggtc cgacatcgtg 420

ctgacccagt ccccgggaac cctgagcctg agcccgggag agcgcgcgac cctgtcatgc 480

cgggcatccc agagcattag ctcctccttt ctcgcctggt atcagcagaa gcccggacag 540

gccccgaggc tgctgatcta cggcgctagc agaagggcta ccggaatccc agaccggttc 600

tccggctccg gttccgggac cgatttcacc cttactatct cgcgcctgga acctgaggac 660

tccgccgtct actactgcca gcagtaccac tcatccccgt cgtggacgtt cggacagggc 720

accaagctgg agattaag 738

<210> 55
<211> 732
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 55
caagtgcaac tcgtcgaatc cggtggaggt ctggtccaac ctggtagaag cctgagactg 60

tcgtgtgcgg ccagcggatt cacctttgat gactatgcta tgcactgggt gcggcaggcc 120

ccaggaaagg gcctggaatg ggtgtcggga attagctgga actccgggtc cattggctac 180

gccgactccg tgaagggccg cttcaccatc tcccgcgaca acgcaaagaa ctccctgtac 240

ttgcaaatga actcgctcag ggctgaggat accgcgctgt actactgctc cgtgcattcc 300

ttcctggcct actggggaca gggaactctg gtcaccgtgt cgagcgcctc cggcggcggg 360

ggctcgggtg gacgggcctc gggcggaggg gggtccgaca tcgtgatgac ccagaccccg 420

ctgagcttgc ccgtgactcc cggagagcct gcatccatct cctgccggtc atcccagtcc 480

cttctccact ccaacggata caactacctc gactggtacc tccagaagcc gggacagagc 540

cctcagcttc tgatctacct ggggtcaaat agagcctcag gagtgccgga tcggttcagc 600

ggatctggtt cgggaactga tttcactctg aagatttccc gcgtggaagc cgaggacgtg 660

ggcgtctact actgtatgca ggcgctgcag acccccctata ccttcggcca agggacgaaa 720

gtggagatca ag 732

<210> 56
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 56
gaagtgcaat tgttggaatc tggaggagga cttgtgcagc ctggaggatc actgagactt 60

tcgtgtgcgg tgtcaggctt cgccctgagc aaccacggca tgagctgggt gcggagagcc 120

ccggggaagg gtctggaatg ggtgtccggg atcgtctact ccggttcaac ttactacgcc 180

gcaagcgtga agggtcgctt caccatttcc cgcgataact cccggaacac cctgtacctc 240

caaatgaact ccctgcggcc cgaggacacc gccatctact actgttccgc gcatggagga 300

gagtccgatg tctggggaca gggcactacc gtgaccgtgt cgagcgcctc gggggggagga 360

ggctccggcg gtcgcgcctc cgggggggggt ggcagcgaca ttgtgatgac gcagactcca 420

ctctcgctgt ccgtgacccc gggacagccc gcgtccatct cgtgcaagag ctcccagagc 480

ctgctgagga acgacggaaa gactcctctg tattggtacc tccagaaggc tggacagccc 540

ccgcaactgc tcatctacga agtgtcaaat cgcttctccg gggtgccgga tcggttttcc 600

ggctcgggat cgggcaccga cttcaccctg aaaatctcca gggtcgaggc cgaggacgtg 660

ggagcctact actgcatgca aaacatccag ttcccttcct tcggcggcgg cacaaagctg 720

gagattaag 729

<210> 57
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 57
caagtccaac tcgtccagtc cggcgcagaa gtcagaaaaa ccggtgctag cgtgaaagtg 60

tcctgcaagg cctccggcta cattttcgat aacttcggaa tcaactgggt cagacaggcc 120

ccgggccagg ggctggaatg gatgggatgg atcaacccca agaacaacaa caccaactac 180

gcacagaagt tccagggccg cgtgactatc accgccgatg aatcgaccaa taccgcctac 240

atggaggtgt cctccctgcg gtcggaggac actgccgtgt attactgcgc gaggggccca 300

tactactacc aaagctacat ggacgtctgg ggacagggaa ccatggtgac cgtgtcatcc 360

gcctccggtg gtggaggctc ggggggcgg gcttcaggag gcggaggaag cgatattgtg 420

atgacccaga ctccgcttag cctgcccgtg actcctggag aaccggcctc catttcctgc 480

cggtcctcgc aatcactcct gcattccaac ggttacaact acctgaattg gtacctccag 540

aagcctggcc agtcgcccca gttgctgatc tatctgggct cgaagcgcgc ctccggggtg 600

cctgaccggt ttagcggatc tgggagcggc acggacttca ctctccacat cacccgcgtg 660

ggagcggagg acgtgggagt gtactactgt atgcaggcgc tgcagactcc gtacacattc 720

ggacagggca ccaagctgga gatcaag 747

<210> 58
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 58
caagtgcaac ttcaagaatc aggcggagga ctcgtgcagc ccggaggatc attgcggctc 60

tcgtgcgccg cctcgggctt caccttctcg agcgacgcca tgacctgggt ccgccaggcc 120

ccggggaagg ggctggaatg ggtgtctgtg atttccggct ccgggggaac tacgtactac 180

gccgattccg tgaaaggtcg cttcactatc tcccgggaca acagcaagaa cacccтttat 240

ctgcaaatga attccctccg cgccgaggac accgccgtgt actactgcgc caagctggac 300

tcctcgggct actactatgc ccggggtccg agatactggg gacagggaac cctcgtgacc 360

gtgtcctccg cgtccggcgg aggagggtcg ggagggcggg cctccggcgg cggcggttcg 420

gacatccagc tgacccagtc cccatcctca ctgagcgcaa gcgtgggcga cagagtcacc 480

attacatgca gggcgtccca gagcatcagc tcctacctga actggtacca acagaagcct 540

ggaaaggctc ctaagctgtt gatctacggg gcttcgaccc tggcatccgg ggtgcccgcg 600

aggtttagcg gaagcggtag cggcactcac ttcactctga ccattaacag cctccagtcc 660

gaggattcag ccacttacta ctgtcagcag tcctacaagc gggccagctt cggacagggc 720

actaaggtcg agatcaag 738

<210> 59
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 59
caagtccaac tggtccagag cggtgcagaa gtgaagaagc ccggagcgag cgtgaaagtg 60

tcctgcaagg cttccgggta caccttctcc aactacggca tcacttgggt gcgccaggcc 120

ccgggacagg gcctggaatg gatggggtgg atttccgcgt acaacggcaa tacgaactac 180

gctcagaagt tccagggtag agtgaccatg actaggaaca cctccatttc caccgcctac 240

atggaactgt cctccctgcg gagcgaggac accgccgtgt actattgcgc ccggggacca 300

tactactact acatggatgt ctgggggaag gggactatgg tcaccgtgtc atccgcctcg 360

ggaggcggcg gatcaggagg acgcgcctct ggtggtggag gatcggagat cgtgatgacc 420

cagagccctc tctccttgcc cgtgactcct ggggagcccg catccatttc atgccggagc 480

tcccagtcac ttctctactc caacggctat aactacgtgg attggtacct ccaaaagccg 540

ggccagagcc cgcagctgct gatctacctg ggctcgaaca gggccagcgg agtgcctgac 600

cggttctccg ggtcgggaag cgggaccgac ttcaagctgc aaatctcgag agtggaggcc 660

gaggacgtgg gaatctacta ctgtatgcag ggccgccagt ttccgtactc gttcggacag 720

ggcaccaaag tggaaatcaa g 741

<210> 60
<211> 714
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 60
gaagtgcaat tgctcgaaac tggaggaggt ctggtgcaac ctggaggatc acttcgcctg 60

tcctgcgccg tgtcgggctt tgccctgtcc aaccatggaa tgagctgggt ccgccgcgcg 120

ccggggaagg gcctcgaatg ggtgtccggc atcgtctact ccggctccac ctactacgcc 180

gcgtccgtga agggccggtt cacgatttca cgggacaact cgcggaacac cctgtacctc 240

caaatgaatt cccttcggcc ggaggatact gccatctact actgctccgc ccacggtggc 300

gaatccgacg tctggggcca gggaaccacc gtgaccgtgt ccagcgcgtc cgggggagga 360

ggaagcgggg gtagagcatc gggtggaggc ggatcagaga tcgtgctgac ccagtccccc 420

gccaccttga gcgtgtcacc aggagagtcc gccaccctgt catgccgcgc cagccagtcc 480

gtgtcctcca acctggcttg gtaccagcag aagccggggc aggcccctag actcctgatc 540

tatggggcgt cgacccgggc atctggaatt cccgataggt tcagcggatc gggctcgggc 600

actgacttca ctctgaccat ctcctcgctg caagccgagg acgtggctgt gtactactgt 660

cagcagtacg gaagctccct gactttcggt ggcgggacca aagtcgagat taag 714

<210> 61
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 61
gaagtgcaat tggtggaaac tggaggagga cttgtgcaac ctggaggatc attgagactg 60

agctgcgcag tgtcgggatt cgccctgagc aaccatggaa tgtcctgggt cagaagggcc 120

cctggaaaag gcctcgaatg ggtgtcaggg atcgtgtact ccggttccac ttactacgcc 180

gcctccgtga aggggcgctt cactatctca cgggataact cccgcaatac cctgtacctc 240

caaatgaaca gcctgcggcc ggaggatacc gccatctact actgttccgc ccacggtgga 300

gagtctgacg tctggggcca gggaactacc gtgaccgtgt cctccgcgtc cggcggtgga 360

gggagcggcg gccgcgccag cggcggcgga ggctccgaga tcgtgatgac ccagagcccc 420

gctactctgt cggtgtcgcc cggagaaagg gcgaccctgt cctgccgggc gtcgcagtcc 480

gtgagcagca agctggcttg gtaccagcag aagccgggcc aggcaccacg cctgcttatg 540

tacggtgcct ccattcgggc caccggaatc ccggaccggt tctcggggtc ggggtccggt 600

accgagttca cactgaccat ttcctcgctc gagcccgagg actttgccgt ctattactgc 660

cagcagtacg gctcctcctc atggacgttc ggccagggga ccaaggtcga aatcaag 717

<210> 62
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 62
gaagtgcaat tggtggagac tggaggagga gtggtgcaac ctggaggaag cctgagactg 60

tcatgcgcgg tgtcgggctt cgccctctcc aaccacggaa tgtcctgggt ccgccgggcc 120

cctgggaaag gacttgaatg ggtgtccggc atcgtgtact cgggttccac ctactacgcg 180

gcctcagtga agggccggtt tactattagc cgcgacaact ccagaaacac actgtacctc 240

caaatgaact cgctgcggcc ggaagatacc gctatctact actgctccgc ccatggggga 300

gagtcggacg tctggggaca gggcaccact gtcactgtgt ccagcgcttc cggcggtggt 360

ggaagcgggg gacgggcctc aggaggcggt ggcagcgaga ttgtgctgac ccagtccccc 420

gggaccctga gcctgtcccc gggagaaagg gccaccctct cctgtcgggc atcccagtcc 480

gtggggtcta ctaaccttgc atggtaccag cagaagcccg gccaggcccc tcgcctgctg 540

atctacgacg cgtccaatag agccaccggc atcccggatc gcttcagcgg aggcggatcg 600

ggcaccgact tcaccctcac catttcaagg ctggaaccgg aggacttcgc cgtgtactac 660

tgccagcagt atggttcgtc cccaccctgg acgttcggcc aggggactaa ggtcgagatc 720

aag 723

<210> 63
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 63
caagtgcaac tcgtggaatc tggtggagga ctcgtgaaac ctggaggatc attgagactg 60

tcatgcgcgg cctcgggatt cacgttctcc gattactaca tgagctggat tcgccaggct 120

ccggggaagg gactggaatg ggtgtcctac atttcctcat ccggctccac catctactac 180

gcggactccg tgaaggggag attcaccatt agccgcgata acgccaagaa cagcctgtac 240

cttcagatga actccctgcg ggctgaagat actgccgtct actactgcgc aagggagagc 300

ggagatggga tggacgtctg gggacagggt accactgtga ccgtgtcgtc ggcctccggc 360

ggagggggtt cgggtggaag ggccagcggc ggcggaggca gcgacatcca gatgacccag 420

tccccctcat cgctgtccgc ctccgtgggc gaccgcgtca ccatcacatg ccgggcctca 480

cagtcgatct cctcctacct caattggtat cagcagaagc ccggaaaggc ccctaagctt 540

ctgatctacg cagcgtcctc cctgcaatcc ggggtcccat ctcggttctc cggctcgggc 600

agcggtaccg acttcactct gaccatctcg agcctgcagc cggaggactt cgccacttac 660

tactgtcagc aaagctacac cctcgcgttt ggccagggca ccaaagtgga catcaag 717

<210> 64
<211> 717
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 64
gaagtgcaat tggtggaatc agggggagga cttgtgcagc ctggaggatc gctgagactg 60

tcatgtgccg tgtccggctt tgccctgtcc aaccacggga tgtcctgggt ccgccgcgcg 120

cctggaaagg gcctcgaatg ggtgtcgggt attgtgtaca gcggtagcac ctactatgcc 180

gcatccgtga aggggagatt caccatcagc cgggacaact ccaggaacac tctgtacctc 240

caaatgaatt cgctgaggcc agaggacact gccatctact actgctccgc gcatggcgga 300

gagtccgacg tctggggaca ggggaccacc gtgaccgtgt ctagcgcgtc cggcggaggc 360

ggcagcgggg gtcgggcatc agggggcggc ggatcggaca tccagctcac ccagtccccg 420

agctcgctgt ccgcctccgt gggagatcgg gtcaccatca cgtgccgcgc cagccagtcg 480

atttcctcct acctgaactg gtaccaacag aagcccggaa aagccccgaa gcttctcatc 540

tacgccgcct cgagcctgca gtcaggagtg ccctcacggt tctccggctc cggttccggt 600

actgatttca ccctgaccat ttcctccctg caaccggagg acttcgctac ttactactgc 660

cagcagtcgt actccacccc ctacactttc ggacaaggca ccaaggtcga aatcaag 717

<210> 65
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 65
caagtgcaac tggtgcaaag cggaggagga ttggtcaaac ccggaggaag cctgagactg 60

tcatgcgcgg cctctggatt caccttctcc gattactaca tgtcatggat cagacaggcc 120

ccggggaagg gcctcgaatg ggtgtcctac atctcgtcct ccgggaacac catctactac 180

gccgacagcg tgaagggccg ctttaccatt tcccgcgaca acgcaaagaa ctcgctgtac 240

cttcagatga attccctgcg ggctgaagat accgcggtgt actattgcgc ccggtccact 300

atggtccggg aggactactg gggacagggc acactcgtga ccgtgtccag cgcgagcggg 360

ggtggaggca gcggtggacg cgcctccggc ggcggcggtt cagacatcgt gctgactcag 420

tcgcccctgt cgctgccggt caccctgggc caaccggcct caattagctg caagtcctcg 480

gagagcctgg tgcacaactc aggaaagact tacctgaact ggttccatca gcggcctgga 540

cagtccccac ggaggctcat ctatgaagtg tccaacaggg attcgggggt gcccgaccgc 600

ttcactggct ccgggtccgg caccgacttc accttgaaaa tctccagagt ggaagccgag 660

gacgtgggcg tgtactactg tatgcagggt acccactggc ctggaacctt tggacaagga 720

actaagctcg agattaag 738

<210> 66
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 66
caagtgcaac tcgtggaatc tggtggagga ctcgtgcaac ccggtggaag ccttaggctg 60

tcgtgcgccg tcagcgggtt tgctctgagc aaccatggaa tgtcctgggt ccgccgggca 120

ccgggaaaag ggctggaatg ggtgtccggc atcgtgtaca gcgggtcaac ctattacgcc 180

gcgtccgtga agggcagatt cactatctca agagacaaca gccggaacac cctgtacttg 240

caaatgaatt ccctgcgccc cgaggacacc gccatctact actgctccgc ccacggagga 300

gagtcggacg tgtggggcca gggaacgact gtgactgtgt ccagcgcatc aggagggggt 360

ggttcgggcg gccgggcctc ggggggagga ggttccgaca ttcggctgac ccagtccccg 420

tccccactgt cggcctccgt cggcgaccgc gtgaccatca cttgtcaggc gtccgaggac 480

attaacaagt tcctgaactg gtaccaccag acccctggaa aggcccccaa gctgctgatc 540

tacgatgcct cgacccttca aactggagtg cctagccggt tctccgggtc cggctccggc 600

actgatttca ctctgaccat caactcattg cagccggaag atatcgggac ctactattgc 660

cagcagtacg aatccctccc gctcacattc ggcgggggaa ccaaggtcga gattaag 717

<210> 67
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 67
gaagtgcaat tggtggaaac tggaggagga cttgtgcaac ctggaggatc attgcggctc 60

tcatgcgctg tctccggctt cgccctgtca aatcacggga tgtcgtgggt cagacgggcc 120

ccgggaaagg gtctggaatg ggtgtcgggg attgtgtaca gcggctccac ctactacgcc 180

gcttcggtca agggccgctt cactatttca cgggacaaca gccgcaacac cctctatctg 240

caaatgaact ctctccgccc ggaggatacc gccatctact actgctccgc acacggcggc 300

gaatccgacg tgtggggaca gggaaccact gtcaccgtgt cgtccgcatc cggtggcgga 360

ggatcgggtg gccgggcctc cgggggcggc ggcagcgaga ctaccctgac ccagtcccct 420

gccactctgt ccgtgagccc gggagagaga gccaccctta gctgccgggc cagccagagc 480

gtgggctcca acctggcctg gtaccagcag aagccaggac agggtcccag gctgctgatc 540

tacggagcct ccactcgcgc gaccggcatc cccgcgaggt tctccgggtc gggttccggg 600

accgagttca ccctgaccat ctcctccctc caaccggagg acttcgcggt gtactactgt 660

cagcagtaca acgattggct gcccgtgaca tttggacagg ggacgaaggt ggaaatcaaa 720

<210> 68

<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 68
gaagtgcaat tggtggaatc tggtggagga cttgtgcaac ctggaggatc actgagactg 60

tcatgcgcgg tgtccggttt tgccctgagc aatcatggga tgtcgtgggt ccggcgcgcc 120

cccggaaagg gtctggaatg ggtgtcgggt atcgtctact ccgggagcac ttactacgcc 180

gcgagcgtga agggccgctt caccatttcc cgcgataact cccgcaacac cctgtacttg 240

caaatgaact cgctccggcc tgaggacact gccatctact actgctccgc acacggagga 300

gaatccgacg tgtggggcca gggaactacc gtgaccgtca gcagcgcctc cggcggcggg 360

ggctcaggcg gacgggctag cggcggcggt ggctccgaga tcgtgctgac ccagtcgcct 420

ggcactctct cgctgagccc cggggaaagg gcaaccctgt cctgtcgggc cagccagtcc 480

attggatcat cctccctcgc ctggtatcag cagaaaccgg gacaggctcc gcggctgctt 540

atgtatgggg ccagctcaag agcctccggc attcccgacc ggttctccgg gtccggttcc 600

ggcaccgatt tcaccctgac tatctcgagg ctggagccag aggacttcgc cgtgtactac 660

tgccagcagt acgcggggtc cccgccgttc acgttcggac agggaaccaa ggtcgagatc 720

aag 723

<210> 69
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 69

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gly Trp Val
        35                  40                  45


Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 70
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 70
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
```

20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 71
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 71
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50   55   60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65   70   75   80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85   90   95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100   105   110

Val Ser Ser
        115

<210> 72
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 72
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Lys Thr Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Asp Asn Phe
            20   25   30

Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn Tyr Ala Gln Lys Phe
    50   55   60

```
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65                  70                  75                  80


Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val Trp Gly Gln
            100                 105                 110


Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210> 73
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 73
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asp
            20                  25                  30


Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
```

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 74
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 74
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr

100 105 110

Met Val Thr Val Ser Ser
115

<210> 75
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 75
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 76
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 76
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 77
<211> 115
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 77
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 78
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 78
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ser Gly Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 79
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 79
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30


Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60


Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80


Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95


Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110


Val Ser Ser
        115


<210> 80
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 80
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30
```

```
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Thr Met Val Arg Glu Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 81
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 81
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30


Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 82
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 82
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu

65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 83
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 83
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 84
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 84
Asp Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 85
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 85
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 86
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 86
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Arg Asn
20 25 30

Asp Gly Lys Thr Pro Leu Tyr Trp Tyr Leu Gln Lys Ala Gly Gln Pro
35 40 45

Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Ala Tyr Tyr Cys Met Gln Asn
85 90 95

Ile Gln Phe Pro Ser Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 87
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 87
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

```
Asn Gly Tyr Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Lys Arg Ala Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu His Ile
65                  70                  75                  80

Thr Arg Val Gly Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 88
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 88

```
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Gly Ala Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
    50                  55                  60
```

```
Ser Gly Ser Gly Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65                  70                  75                  80


Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala Ser
                85                  90                  95


Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 89
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 89
Glu Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1               5                   10                  15


Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser
            20                  25                  30


Asn Gly Tyr Asn Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Lys Leu Gln Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly
                85                  90                  95
```

Arg Gln Phe Pro Tyr Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 90
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 90
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 91
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 91
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Lys
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Met
35 40 45

Tyr Gly Ala Ser Ile Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Ser Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 92
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 92
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

```
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Thr
            20                  25                  30


Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60


Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95


Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 93
<211> 105
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 93
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

```
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Thr Leu Ala Phe
                85                  90                  95

Gly Gln Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 94
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 94

```
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Tyr
```

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 95
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 95
Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Glu Ser Leu Val His Asn
20 25 30

Ser Gly Lys Thr Tyr Leu Asn Trp Phe His Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Glu Val Ser Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Gly Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 96
<211> 107

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 96
Asp Ile Arg Leu Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Glu Asp Ile Asn Lys Phe
20 25 30

Leu Asn Trp Tyr His Gln Thr Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Thr Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Glu Ser Leu Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 97
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 97

Glu Thr Thr Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Gly Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asp Trp Leu Pro
85 90 95

Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 98
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 98
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu

35 40 45

Met Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Gly Ser Pro
85 90 95

Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 99
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 99
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Asn Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Gly Trp Val Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr
65 70 75 80

```
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met
        115                 120                 125

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Ser Phe Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        195                 200                 205

Gly Ala Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
225                 230                 235                 240

Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp
                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270
```

```
Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460
```

```
Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480


Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 100
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 100
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45


Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly
65                  70                  75                  80


Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95


Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110
```

```
Ala Leu Tyr Tyr Cys Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
145                 150                 155                 160

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
                165                 170                 175

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
            180                 185                 190

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
        195                 200                 205

Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
    210                 215                 220

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
225                 230                 235                 240

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe
                245                 250                 255

Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300
```

```
Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320


Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335


Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350


Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365


Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380


Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400


Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415


Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430


Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
        435                 440                 445


Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
    450                 455                 460


Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465                 470                 475                 480


His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 101
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 101
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
35 40 45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
100 105 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
130 135 140

```
Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
145                 150                 155                 160


Pro Leu Ser Leu Ser Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys
                165                 170                 175


Lys Ser Ser Gln Ser Leu Leu Arg Asn Asp Gly Lys Thr Pro Leu Tyr
            180                 185                 190


Trp Tyr Leu Gln Lys Ala Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu
        195                 200                 205


Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
    210                 215                 220


Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
225                 230                 235                 240


Val Gly Ala Tyr Tyr Cys Met Gln Asn Ile Gln Phe Pro Ser Phe Gly
                245                 250                 255


Gly Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270


Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285


Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300


Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320


Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335
```

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
340 345 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
355 360 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
370 375 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385 390 395 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
405 410 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
420 425 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
435 440 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 102
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 102

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Arg Lys Thr Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Ile Phe Asp Asn Phe Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser
                85                  90                  95

Thr Asn Thr Ala Tyr Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met
        115                 120                 125

Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile
145                 150                 155                 160

Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
                165                 170                 175

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly
```

```
            180                 185                 190

Tyr Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
        195                 200                 205

Leu Leu Ile Tyr Leu Gly Ser Lys Arg Ala Ser Gly Val Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu His Ile Thr Arg
225                 230                 235                 240

Val Gly Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln
                245                 250                 255

Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
```

370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 103
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 103
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu
20 25 30

```
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Asp Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala
        115                 120                 125

Arg Gly Pro Arg Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    130                 135                 140

Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
                165                 170                 175

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
        195                 200                 205

Ile Tyr Gly Ala Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
    210                 215                 220
```

```
Gly Ser Gly Ser Gly Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln
225                 230                 235                 240

Ser Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala
                245                 250                 255

Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415
```

```
Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430


Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445


Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460


Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480


Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 104
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 104
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Ser Asn Tyr Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60
```

```
Gly Leu Glu Trp Met Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Pro Tyr Tyr Tyr Tyr Met Asp Val
        115                 120                 125

Trp Gly Lys Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145                 150                 155                 160

Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser
                165                 170                 175

Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn
            180                 185                 190

Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu
        195                 200                 205

Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Lys Leu Gln Ile Ser Arg Val Glu
225                 230                 235                 240

Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly Arg Gln Phe Pro
                245                 250                 255
```

```
Tyr Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445
```

```
Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460


His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480


Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 105
<211> 482
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 105
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45


Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80


Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95
```

```
Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Ser Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala
        195                 200                 205

Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Gly Ser Ser Leu Thr Phe Gly Gly Gly Thr Lys Val
                245                 250                 255

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
            260                 265                 270

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
        275                 280                 285
```

```
Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
    290                 295                 300

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
305                 310                 315                 320

Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu
                325                 330                 335

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
            340                 345                 350

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
        355                 360                 365

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
    370                 375                 380

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
385                 390                 395                 400

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
                405                 410                 415

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
            420                 425                 430

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
        435                 440                 445

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
    450                 455                 460

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
465                 470                 475                 480
```

Pro Arg

<210> 106
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 106

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
```

```
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser
145                 150                 155                 160

Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Ser Ser Lys Leu Ala Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Gln Ala Pro Arg Leu Leu Met Tyr Gly Ala Ser Ile Arg Ala
        195                 200                 205

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Gly Ser Ser Ser Trp Thr Phe Gly Gln Gly Thr Lys
                245                 250                 255

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
```

325 330 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
340 345 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
355 360 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
370 375 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385 390 395 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
405 410 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
420 425 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
435 440 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
450 455 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465 470 475 480

Pro Pro Arg

<210> 107
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 107

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175
```

```
Arg Ala Ser Gln Ser Val Gly Ser Thr Asn Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg
        195                 200                 205

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Pro Trp Thr Phe Gly Gln Gly
                245                 250                 255

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365
```

```
Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385                 390                 395                 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
                405                 410                 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
            420                 425                 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
        435                 440                 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
    450                 455                 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465                 470                 475                 480

Ala Leu Pro Pro Arg
                485


<210> 108
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 108
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Glu Ser Gly Asp Gly Met Asp Val Trp
        115                 120                 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
145                 150                 155                 160

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
                165                 170                 175

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
            180                 185                 190

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
        195                 200                 205
```

```
Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
    210                 215                 220

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
225                 230                 235                 240

Tyr Tyr Cys Gln Gln Ser Tyr Thr Leu Ala Phe Gly Gln Gly Thr Lys
                245                 250                 255

Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400
```

```
Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415


Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430


Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        435                 440                 445


Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    450                 455                 460


Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480


Pro Pro Arg
```

<210> 109
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 109

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45
```

```
Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
145                 150                 155                 160

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
        195                 200                 205

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
225                 230                 235                 240
```

```
Cys Gln Gln Ser Tyr Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys
                245                 250                 255

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430
```

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
435 440 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
450 455 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465 470 475 480

Pro Pro Arg

<210> 110
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 110
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala

```
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Thr Met Val Arg Glu Asp Tyr Trp
        115                 120                 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr
145                 150                 155                 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile
                165                 170                 175

Ser Cys Lys Ser Ser Glu Ser Leu Val His Asn Ser Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Phe His Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile
        195                 200                 205

Tyr Glu Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Thr Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Gly
                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
```

```
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
```

465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 111
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 111
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
35 40 45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
100 105 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
115 120 125

```
Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Arg Leu Thr Gln Ser
145                 150                 155                 160

Pro Ser Pro Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175

Gln Ala Ser Glu Asp Ile Asn Lys Phe Leu Asn Trp Tyr His Gln Thr
            180                 185                 190

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Thr Leu Gln
        195                 200                 205

Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Asn Ser Leu Gln Pro Glu Asp Ile Gly Thr Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Glu Ser Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys
                245                 250                 255

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320
```

```
Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        435                 440                 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    450                 455                 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480

Pro Pro Arg
```

<210> 112
<211> 484

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 112

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45


Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80


Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95


Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110


Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125


Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser
145                 150                 155                 160
```

```
Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Gly Ser Asn Leu Ala Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Gln Gly Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala
        195                 200                 205

Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Asn Asp Trp Leu Pro Val Thr Phe Gly Gln Gly Thr
                245                 250                 255

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
            260                 265                 270

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
        275                 280                 285

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
    290                 295                 300

Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu
305                 310                 315                 320

Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys
                325                 330                 335

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
            340                 345                 350
```

```
Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
        355                 360                 365


Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
    370                 375                 380


Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
385                 390                 395                 400


Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
                405                 410                 415


Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
            420                 425                 430


Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
        435                 440                 445


Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
    450                 455                 460


Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
465                 470                 475                 480


Leu Pro Pro Arg



<210> 113
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 113
```

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Ile Gly Ser Ser Ser Leu Ala Trp Tyr Gln Gln
            180                 185                 190
```

```
Lys Pro Gly Gln Ala Pro Arg Leu Leu Met Tyr Gly Ala Ser Ser Arg
        195                 200                 205

Ala Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Ala Gly Ser Pro Pro Phe Thr Phe Gly Gln Gly
                245                 250                 255

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380
```

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 114
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 114
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atctggtgga ggactcgtgc aacccggaag atcgcttaga 120

ctgtcgtgtg ccgccagcgg gttcactttc tcgaactacg cgatgtcctg ggtccgccag 180

gcacccggaa agggactcgg ttgggtgtcc ggcatttccc ggtccggcga aaatacctac 240

tacgccgact ccgtgaaggg ccgcttcacc atctcaaggg acaacagcaa aaacaccctg 300

tacttgcaaa tgaactccct gcgggatgaa gatacagccg tgtactattg cgcccggtcg 360

cctgcccatt actacggcgg aatggacgtc tggggacagg gaaccactgt gactgtcagc 420

agcgcgtcgg gtggcggcgg ctcaggggggt cgggcctccg gggggggagg gtccgacatc 480

gtgctgaccc agtccccggg aaccctgagc ctgagcccgg gagagcgcgc gaccctgtca 540

tgccgggcat cccagagcat tagctcctcc tttctcgcct ggtatcagca gaagcccgga 600

caggccccga ggctgctgat ctacggcgct agcagaaggg ctaccggaat cccagaccgg 660

ttctccggct ccggttccgg gaccgatttc acccttacta tctcgcgcct ggaacctgag 720

gactccgccg tctactactg ccagcagtac cactcatccc cgtcgtggac gttcggacag 780

ggcaccaagc tggagattaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 115
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 115
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcga atccggtgga ggtctggtcc aacctggtag aagcctgaga 120

ctgtcgtgtg cggccagcgg attcaccttt gatgactatg ctatgcactg ggtgcggcag 180

gccccaggaa agggcctgga atgggtgtcg ggaattagct ggaactccgg gtccattggc 240

tacgccgact ccgtgaaggg ccgcttcacc atctcccgcg acaacgcaaa gaactccctg 300

tacttgcaaa tgaactcgct cagggctgag gataccgcgc tgtactactg ctccgtgcat 360

tccttcctgg cctactgggg acagggaact ctggtcaccg tgtcgagcgc ctccggcggc 420

gggggctcgg gtggacgggc ctcgggcgga ggggggtccg acatcgtgat gacccagacc 480

ccgctgagct tgcccgtgac tcccggagag cctgcatcca tctcctgccg gtcatcccag 540

tcccttctcc actccaacgg atacaactac ctcgactggt acctccagaa gccgggacag 600

agccctcagc ttctgatcta cctggggtca aatagagcct caggagtgcc ggatcggttc 660

agcggatctg gttcgggaac tgatttcact ctgaagattt cccgcgtgga agccgaggac 720

gtgggcgtct actactgtat gcaggcgctg cagacccccc ataccttcgg ccaagggacg 780

aaagtggaga tcaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 116
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 116
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattgttgga atctggagga ggacttgtgc agcctggagg atcactgaga 120

ctttcgtgtg cggtgtcagg cttcgccctg agcaaccacg gcatgagctg ggtgcggaga 180

gccccgggga agggtctgga atgggtgtcc gggatcgtct actccggttc aacttactac 240

gccgcaagcg tgaagggtcg cttcaccatt tcccgcgata actcccggaa caccctgtac 300

ctccaaatga actccctgcg gcccgaggac accgccatct actactgttc cgcgcatgga 360

ggagagtccg atgtctgggg acagggcact accgtgaccg tgtcgagcgc ctcgggggga 420

ggaggctccg gcggtcgcgc ctccgggggg ggtggcagcg acattgtgat gacgcagact 480

ccactctcgc tgtccgtgac cccgggacag cccgcgtcca tctcgtgcaa gagctcccag 540

agcctgctga ggaacgacgg aaagactcct ctgtattggt acctccagaa ggctggacag 600

cccccgcaac tgctcatcta cgaagtgtca aatcgcttct ccggggtgcc ggatcggttt 660

tccggctcgg gatcgggcac cgacttcacc ctgaaaatct ccagggtcga ggccgaggac 720

gtgggagcct actactgcat gcaaaacatc cagttccctt ccttcggcgg cggcacaaag 780

ctggagatta agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 117
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 117
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtccggcgca gaagtcagaa aaaccggtgc tagcgtgaaa 120

gtgtcctgca aggcctccgg ctacattttc gataacttcg gaatcaactg ggtcagacag 180

gccccgggcc aggggctgga atggatggga tggatcaacc ccaagaacaa caacaccaac 240

tacgcacaga agttccaggg ccgcgtgact atcaccgccg atgaatcgac caataccgcc 300

tacatggagg tgtcctccct gcggtcggag gacactgccg tgtattactg cgcgaggggc 360

ccatactact accaaagcta catggacgtc tggggacagg gaaccatggt gaccgtgtca 420

tccgcctccg gtggtggagg ctccgggggg cgggcttcag gaggcggagg aagcgatatt 480

gtgatgaccc agactccgct tagcctgccc gtgactcctg gagaaccggc ctccatttcc 540

tgccggtcct cgcaatcact cctgcattcc aacggttaca actacctgaa ttggtacctc 600

cagaagcctg gccagtcgcc ccagttgctg atctatctgg gctcgaagcg cgcctccggg 660

gtgcctgacc ggtttagcgg atctgggagc ggcacggact tcactctcca catcacccgc 720

gtgggagcgg aggacgtggg agtgtactac tgtatgcagg cgctgcagac tccgtacaca 780

ttcggacagg gcaccaagct ggagatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 118
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 118
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aacttcaaga atcaggcgga ggactcgtgc agcccggagg atcattgcgg 120

ctctcgtgcg ccgcctcggg cttcaccttc tcgagcgacg ccatgacctg ggtccgccag 180

gccccgggga aggggctgga atgggtgtct gtgatttccg gctccggggg aactacgtac 240

tacgccgatt ccgtgaaagg tcgcttcact atctcccggg acaacagcaa gaacaccctt 300

tatctgcaaa tgaattccct ccgcgccgag gacaccgccg tgtactactg cgccaagctg 360

gactcctcgg gctactacta tgcccggggt ccgagatact ggggacaggg aaccctcgtg 420

accgtgtcct ccgcgtccgg cggaggaggg tcgggagggc gggcctccgg cggcggcggt 480

tcggacatcc agctgaccca gtccccatcc tcactgagcg caagcgtggg cgacagagtc 540

accattacat gcagggcgtc ccagagcatc agctcctacc tgaactggta ccaacagaag 600

cctggaaagg ctcctaagct gttgatctac ggggcttcga ccctggcatc cggggtgccc 660

gcgaggttta gcggaagcgg tagcggcact cacttcactc tgaccattaa cagcctccag 720

tccgaggatt cagccactta ctactgtcag cagtcctaca agcgggccag cttcggacag 780

ggcactaagg tcgagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 119
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 119
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactggtcca gagcggtgca gaagtgaaga agcccggagc gagcgtgaaa 120

gtgtcctgca aggcttccgg gtacaccttc tccaactacg gcatcacttg ggtgcgccag 180

gccccgggac agggcctgga atggatgggg tggatttccg cgtacaacgg caatacgaac 240

tacgctcaga agttccaggg tagagtgacc atgactagga acacctccat ttccaccgcc 300

tacatggaac tgtcctccct gcggagcgag gacaccgccg tgtactattg cgcccgggga 360

ccatactact actacatgga tgtctggggg aaggggacta tggtcaccgt gtcatccgcc 420

tcgggaggcg gcggatcagg aggacgcgcc tctggtggtg gaggatcgga gatcgtgatg 480

acccagagcc ctctctcctt gcccgtgact cctggggagc ccgcatccat ttcatgccgg 540

agctcccagt cacttctcta ctccaacggc tataactacg tggattggta cctccaaaag 600

ccgggccaga gcccgcagct gctgatctac ctgggctcga acagggccag cggagtgcct 660

gaccggttct ccgggtcggg aagcgggacc gacttcaagc tgcaaatctc gagagtggag 720

gccgaggacg tgggaatcta ctactgtatg cagggccgcc agtttccgta ctcgttcgga 780

cagggcacca aagtggaaat caagaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 120
<211> 1446
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 120
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattgctcga aactggagga ggtctggtgc aacctggagg atcacttcgc 120

ctgtcctgcg ccgtgtcggg ctttgccctg tccaaccatg gaatgagctg ggtccgccgc 180

gcgccgggga agggcctcga atgggtgtcc ggcatcgtct actccggctc cacctactac 240

gccgcgtccg tgaagggccg gttcacgatt tcacgggaca actcgcggaa caccctgtac 300

ctccaaatga attcccttcg gccggaggat actgccatct actactgctc cgcccacggt 360

ggcgaatccg acgtctgggg ccagggaacc accgtgaccg tgtccagcgc gtccggggga 420

ggaggaagcg ggggtagagc atcgggtgga ggcggatcag agatcgtgct gacccagtcc 480

cccgccacct tgagcgtgtc accaggagag tccgccaccc tgtcatgccg cgccagccag 540

tccgtgtcct ccaacctggc ttggtaccag cagaagccgg ggcaggcccc tagactcctg 600

atctatgggg cgtcgacccg ggcatctgga attcccgata ggttcagcgg atcgggctcg 660

ggcactgact tcactctgac catctcctcg ctgcaagccg aggacgtggc tgtgtactac 720

tgtcagcagt acggaagctc cctgactttc ggtggcggga ccaaagtcga gattaagacc 780

actaccccag caccgaggcc acccaccccg gctcctacca tcgcctccca gcctctgtcc 840

ctgcgtccgg aggcatgtag acccgcagct ggtggggccg tgcatacccg gggtcttgac 900

ttcgcctgcg atatctacat ttgggcccct ctggctggta cttgcggggt cctgctgctt 960

tcactcgtga tcactcttta ctgtaagcgc ggtcggaaga agctgctgta catctttaag 1020

caacccttca tgaggcctgt gcagactact caagaggagg acggctgttc atgccggttc 1080

ccagaggagg aggaaggcgg ctgcgaactg cgcgtgaaat tcagccgcag cgcagatgct 1140

ccagcctaca agcaggggca gaaccagctc tacaacgaac tcaatcttgg tcggagagag 1200

gagtacgacg tgctggacaa gcggagagga cgggacccag aaatgggcgg gaagccgcgc 1260

agaaagaatc cccaagaggg cctgtacaac gagctccaaa aggataagat ggcagaagcc 1320

tatagcgaga ttggtatgaa aggggaacgc agaagaggca aaggccacga cggactgtac 1380

cagggactca gcaccgccac caaggacacc tatgacgctc ttcacatgca ggccctgccg 1440

cctcgg 1446

<210> 121
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 121
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga aactggagga ggacttgtgc aacctggagg atcattgaga 120

ctgagctgcg cagtgtcggg attcgccctg agcaaccatg gaatgtcctg ggtcagaagg 180

gcccctggaa aaggcctcga atgggtgtca gggatcgtgt actccggttc cacttactac 240

gccgcctccg tgaaggggcg cttcactatc tcacgggata actcccgcaa taccctgtac 300

ctccaaatga acagcctgcg gccggaggat accgccatct actactgttc cgcccacggt 360

ggagagtctg acgtctgggg ccagggaact accgtgaccg tgtcctccgc gtccggcggt 420

ggagggagcg gcggccgcgc cagcggcggc ggaggctccg agatcgtgat gacccagagc 480

cccgctactc tgtcggtgtc gcccggagaa agggcgaccc tgtcctgccg ggcgtcgcag 540

tccgtgagca gcaagctggc ttggtaccag cagaagccgg gccaggcacc acgcctgctt 600

atgtacggtg cctccattcg ggccaccgga atcccggacc ggttctcggg gtcggggtcc 660

ggtaccgagt tcacactgac catttcctcg ctcgagcccg aggactttgc cgtctattac 720

tgccagcagt acggctcctc ctcatggacg ttcggccagg ggaccaaggt cgaaatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 122
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 122
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga gactggagga ggagtggtgc aacctggagg aagcctgaga 120

ctgtcatgcg cggtgtcggg cttcgccctc tccaaccacg gaatgtcctg ggtccgccgg 180

gcccctggga aaggacttga atgggtgtcc ggcatcgtgt actcgggttc cacctactac 240

gcggcctcag tgaagggccg gtttactatt agccgcgaca actccagaaa cacactgtac 300

ctccaaatga actcgctgcg gccggaagat accgctatct actactgctc cgcccatggg 360

ggagagtcgg acgtctgggg acagggcacc actgtcactg tgtccagcgc ttccggcggt 420

ggtggaagcg ggggacgggc ctcaggaggc ggtggcagcg agattgtgct gacccagtcc 480

cccgggaccc tgagcctgtc cccgggagaa agggccaccc tctcctgtcg ggcatcccag 540

tccgtggggt ctactaacct tgcatggtac cagcagaagc ccggccaggc ccctcgcctg 600

ctgatctacg acgcgtccaa tagagccacc ggcatcccgg atcgcttcag cggaggcgga 660

tcgggcaccg acttcaccct caccatttca aggctggaac cggaggactt cgccgtgtac 720

tactgccagc agtatggttc gtccccaccc tggacgttcg gccaggggac taaggtcgag 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 123
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 123
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atctggtgga ggactcgtga aacctggagg atcattgaga 120

ctgtcatgcg cggcctcggg attcacgttc tccgattact acatgagctg gattcgccag 180

gctccgggga agggactgga atgggtgtcc tacatttcct catccggctc caccatctac 240

tacgcggact ccgtgaaggg gagattcacc attagccgcg ataacgccaa gaacagcctg 300

taccttcaga tgaactccct gcgggctgaa gatactgccg tctactactg cgcaagggag 360

agcggagatg ggatggacgt ctggggacag ggtaccactg tgaccgtgtc gtcggcctcc 420

ggcggagggg gttcgggtgg aagggccagc ggcggcggag gcagcgacat ccagatgacc 480

cagtcccccc catcgctgtc cgcctccgtg ggcgaccgcg tcaccatcac atgccgggcc 540

tcacagtcga tctcctccta cctcaattgg tatcagcaga agcccggaaa ggcccctaag 600

cttctgatct acgcagcgtc ctccctgcaa tccggggtcc catctcggtt ctccggctcg 660

ggcagcggta ccgacttcac tctgaccatc tcgagcctgc agccggagga cttcgccact 720

tactactgtc agcaaagcta caccctcgcg tttggccagg gcaccaaagt ggacatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 124
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 124
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga atcaggggga ggacttgtgc agcctggagg atcgctgaga 120

ctgtcatgtg ccgtgtccgg ctttgccctg tccaaccacg ggatgtcctg ggtccgccgc 180

gcgcctggaa agggcctcga atgggtgtcg ggtattgtgt acagcggtag cacctactat 240

gccgcatccg tgaaggggag attcaccatc agccgggaca actccaggaa cactctgtac 300

ctccaaatga attcgctgag gccagaggac actgccatct actactgctc cgcgcatggc 360

ggagagtccg acgtctgggg acaggggacc accgtgaccg tgtctagcgc gtccggcgga 420

ggcggcagcg ggggtcgggc atcagggggc ggcggatcgg acatccagct cacccagtcc 480

ccgagctcgc tgtccgcctc cgtgggagat cgggtcacca tcacgtgccg cgccagccag 540

tcgatttcct cctacctgaa ctggtaccaa cagaagcccg gaaaagcccc gaagcttctc 600

atctacgccg cctcgagcct gcagtcagga gtgccctcac ggttctccgg ctccggttcc 660

ggtactgatt tcaccctgac catttcctcc ctgcaaccgg aggacttcgc tacttactac 720

tgccagcagt cgtactccac cccctacact ttcggacaag gcaccaaggt cgaaatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 125
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 125

atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactggtgca aagcggagga ggattggtca aacccggagg aagcctgaga 120

ctgtcatgcg cggcctctgg attcaccttc tccgattact acatgtcatg gatcagacag 180

gccccgggga agggcctcga atgggtgtcc tacatctcgt cctccgggaa caccatctac 240

tacgccgaca gcgtgaaggg ccgctttacc atttcccgcg acaacgcaaa gaactcgctg 300

taccttcaga tgaattccct gcgggctgaa gataccgcgg tgtactattg cgcccggtcc 360

actatggtcc gggaggacta ctggggacag ggcacactcg tgaccgtgtc cagcgcgagc 420

gggggtggag gcagcggtgg acgcgcctcc ggcggcggcg gttcagacat cgtgctgact 480

cagtcgcccc tgtcgctgcc ggtcaccctg ggccaaccgg cctcaattag ctgcaagtcc 540

tcggagagcc tggtgcacaa ctcaggaaag acttacctga actggttcca tcagcggcct 600

ggacagtccc cacggaggct catctatgaa gtgtccaaca gggattcggg ggtgcccgac 660

cgcttcactg gctccgggtc cggcaccgac ttcaccttga aaatctccag agtggaagcc 720

gaggacgtgg gcgtgtacta ctgtatgcag ggtacccact ggcctggaac ctttggacaa 780

ggaactaagc tcgagattaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 126
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 126
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atctggtgga ggactcgtgc aacccggtgg aagccttagg 120

ctgtcgtgcg ccgtcagcgg gtttgctctg agcaaccatg gaatgtcctg ggtccgccgg 180

gcaccgggaa aagggctgga atgggtgtcc ggcatcgtgt acagcgggtc aacctattac 240

gccgcgtccg tgaagggcag attcactatc tcaagagaca acagccggaa caccctgtac 300

ttgcaaatga attccctgcg ccccgaggac accgccatct actactgctc cgcccacgga 360

ggagagtcgg acgtgtgggg ccagggaacg actgtgactg tgtccagcgc atcaggaggg 420

ggtggttcgg gcggccgggc ctcgggggga ggaggttccg acattcggct gacccagtcc 480

ccgtccccac tgtcggcctc cgtcggcgac cgcgtgacca tcacttgtca ggcgtccgag 540

gacattaaca agttcctgaa ctggtaccac cagacccctg gaaaggcccc caagctgctg 600

atctacgatg cctcgaccct tcaaactgga gtgcctagcc ggttctccgg gtccggctcc 660

ggcactgatt tcactctgac catcaactca ttgcagccgg aagatatcgg gacctactat 720

tgccagcagt acgaatccct cccgctcaca ttcggcgggg gaaccaaggt cgagattaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 127
<211> 1452
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 127
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga aactggagga ggacttgtgc aacctggagg atcattgcgg 120

ctctcatgcg ctgtctccgg cttcgccctg tcaaatcacg ggatgtcgtg ggtcagacgg 180

gccccgggaa agggtctgga atgggtgtcg gggattgtgt acagcggctc cacctactac 240

gccgcttcgg tcaagggccg cttcactatt tcacgggaca acagccgcaa caccctctat 300

ctgcaaatga actctctccg cccggaggat accgccatct actactgctc cgcacacggc 360

ggcgaatccg acgtgtgggg acagggaacc actgtcaccg tgtcgtccgc atccggtggc 420

ggaggatcgg gtggccgggc ctccgggggc ggcggcagcg agactaccct gacccagtcc 480

cctgccactc tgtccgtgag cccgggagag agagccaccc ttagctgccg ggccagccag 540

agcgtgggct ccaacctggc ctggtaccag cagaagccag gacagggtcc caggctgctg 600

atctacggag cctccactcg cgcgaccggc atccccgcga ggttctccgg gtcgggttcc 660

gggaccgagt tcaccctgac catctcctcc ctccaaccgg aggacttcgc ggtgtactac 720

tgtcagcagt acaacgattg gctgcccgtg acatttggac aggggacgaa ggtggaaatc 780

aaaaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 840

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 900

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 960

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1020

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1080

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1140

gatgctccag cctacaagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1200

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 1260

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 1320

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 1380

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 1440

ctgccgcctc gg 1452

<210> 128
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 128
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga atctggtgga ggacttgtgc aacctggagg atcactgaga 120

ctgtcatgcg cggtgtccgg ttttgccctg agcaatcatg ggatgtcgtg ggtccggcgc 180

gcccccggaa agggtctgga atgggtgtcg ggtatcgtct actccgggag cacttactac 240

gccgcgagcg tgaagggccg cttcaccatt tcccgcgata actcccgcaa caccctgtac 300

ttgcaaatga actcgctccg gcctgaggac actgccatct actactgctc cgcacacgga 360

ggagaatccg acgtgtgggg ccagggaact accgtgaccg tcagcagcgc ctccggcggc 420

gggggctcag gcggacgggc tagcggcggc ggtggctccg agatcgtgct gacccagtcg 480

cctggcactc tctcgctgag ccccggggaa agggcaaccc tgtcctgtcg ggccagccag 540

tccattggat catcctccct cgcctggtat cagcagaaac cgggacaggc tccgcggctg 600

cttatgtatg gggccagctc aagagcctcc ggcattcccg accggttctc cgggtccggt 660

tccggcaccg atttcaccct gactatctcg aggctggagc cagaggactt cgccgtgtac 720

tactgccagc agtacgcggg gtccccgccg ttcacgttcg gacagggaac caaggtcgag 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 129
<211> 243

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 129

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                  10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
            20                  25                  30


Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile Trp Gly
            100                 105                 110


Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro
    130                 135                 140


Ala Phe Met Ser Ala Thr Pro Gly Asp Lys Val Ile Ile Ser Cys Lys
145                 150                 155                 160
```

```
Ala Ser Gln Asp Ile Asp Asp Ala Met Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Glu Ala Pro Leu Phe Ile Ile Gln Ser Ala Thr Ser Pro Val Pro
            180                 185                 190


Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Phe Gly Thr Asp Phe Ser
        195                 200                 205


Leu Thr Ile Asn Asn Ile Glu Ser Glu Asp Ala Ala Tyr Tyr Phe Cys
    210                 215                 220


Leu Gln His Asp Asn Phe Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu
225                 230                 235                 240


Glu Ile Lys



<210> 130
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 130
Val Asn Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr
1               5                   10                  15


Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Arg Thr Ser Gly
            20                  25                  30


Met Cys Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp
        35                  40                  45
```

```
Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys Phe Tyr Ser Thr Ser Leu
    50                  55                  60

Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Asp Asn Gln Val Val
65                  70                  75                  80

Leu Arg Met Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile Trp
            100                 105                 110

Gly Pro Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Asp Ile Tyr Asn Asn Leu Ala Trp Phe Gln Leu Lys
                165                 170                 175

Pro Gly Ser Ala Pro Arg Ser Leu Met Tyr Ala Ala Asn Lys Ser Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln His Tyr Tyr Arg Phe Pro Tyr Ser Phe Gly Gln Gly Thr Lys
225                 230                 235                 240
```

Leu Glu Ile Lys

<210> 131
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 131
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Leu Ser

130 135 140

Leu Pro Val Thr Pro Glu Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser
145 150 155 160

Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu
165 170 175

Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn
180 185 190

Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
210 215 220

Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Leu Glu Ile Lys
245

<210> 132
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 132
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

```
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Leu Arg Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Ser Pro Ser Val Ser Ala
    130                 135                 140

Ala Pro Gly Tyr Thr Ala Thr Ile Ser Cys Gly Gly Asn Asn Ile Gly
145                 150                 155                 160

Thr Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu
                165                 170                 175

Leu Val Ile Arg Asp Asp Ser Val Arg Pro Ser Lys Ile Pro Gly Arg
            180                 185                 190

Phe Ser Gly Ser Asn Ser Gly Asn Met Ala Thr Leu Thr Ile Ser Gly
        195                 200                 205

Val Gln Ala Gly Asp Glu Ala Asp Phe Tyr Cys Gln Val Trp Asp Ser
    210                 215                 220
```

```
Asp Ser Glu His Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
225                 230                 235                 240


<210> 133
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 133
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr Thr Val Thr Ser His
            20                  25                  30


Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ser Ser Thr Val Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe Trp Gly Arg
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Pro Pro Ser
    130                 135                 140


Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile Thr Cys Ser Gly Asp
145                 150                 155                 160


Gly Leu Ser Lys Lys Tyr Val Ser Trp Tyr Gln Gln Lys Ala Gly Gln
                165                 170                 175


Ser Pro Val Val Leu Ile Ser Arg Asp Lys Glu Arg Pro Ser Gly Ile
            180                 185                 190


Pro Asp Arg Phe Ser Gly Ser Asn Ser Ala Asp Thr Ala Thr Leu Thr
        195                 200                 205


Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Tyr Cys Gln Ala
    210                 215                 220


Trp Asp Asp Thr Thr Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val
225                 230                 235                 240


Leu



<210> 134
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 134
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
            100                 105                 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Ile Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Ala Ala Ser Asn Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp
        195                 200                 205
```

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr
210 215 220

Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe Thr Phe Gly Pro Gly Thr
225 230 235 240

Lys Val Asp Ile Lys
245

<210> 135
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 135
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu

100 105 110

Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130 135 140

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
145 150 155 160

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
165 170 175

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Leu Tyr
180 185 190

Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
210 215 220

Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Ser Ser Gly Asp His
225 230 235 240

Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
245 250

<210> 136
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 136
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1   5   10   15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
            20   25   30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35   40   45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala
    50   55   60

Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Lys Asn
65   70   75   80

Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro Glu Asp Thr Ala Val
                85   90   95

Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe
            100   105   110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Asp
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu
    130   135   140

Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Ile Arg Ile
145   150   155   160

Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala Thr Trp Tyr Gln
                165   170   175

Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Thr Asn Asn
            180   185   190

```
Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala Ser Ser Ser Gly Asn
        195                 200                 205


Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp
    210                 215                 220


Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His His Leu Leu Phe Gly
225                 230                 235                 240


Thr Gly Thr Lys Val Thr Val Leu
                245


<210> 137
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 137
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu
    130                 135                 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145                 150                 155                 160

Ser Val Ser Ser Ala Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
                165                 170                 175

Pro Pro Arg Leu Leu Ile Ser Gly Ala Ser Thr Arg Ala Thr Gly Ile
            180                 185                 190

Pro Asp Arg Phe Gly Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His
    210                 215                 220

Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe Thr Phe Gly Gln Gly
225                 230                 235                 240

Thr Arg Leu Glu Ile Lys
                245
```

<210> 138
<211> 241
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 138

```
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Ser Arg Tyr
            20                  25                  30


Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr Tyr Ala Asp Ser Ala
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80


Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
    130                 135                 140


Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145                 150                 155                 160
```

Ser Val Ser Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Ile Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Phe
210 215 220

Gly Thr Ser Ser Gly Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys

<210> 139
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 139
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val

```
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
    130                 135                 140

Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
145                 150                 155                 160

Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser
            180                 185                 190

Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala
    210                 215                 220

Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Arg Leu Glu Ile Lys
```

245

<210> 140
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 140
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Thr Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
130 135 140

```
Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly Glu Ser Ala Thr Leu
145                 150                 155                 160


Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr Phe Leu Ala Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ser Ser
            180                 185                 190


Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu Pro Glu Asp Phe Ala
    210                 215                 220


Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly
225                 230                 235                 240


Gln Gly Thr Lys Val Glu Ile Lys
                245


<210> 141
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 141
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
```

```
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Ser Ser Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
    210                 215                 220
```

```
Ser Thr Pro Tyr Ser Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
225                 230                 235


<210> 142
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 142
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30


Ala Met His Trp Val Arg Gln Arg Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala Tyr Gly Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Phe
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val Trp
            100                 105                 110


Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125
```

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu Ala Trp Tyr Gln Gln
165 170 175

Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Gln Arg
180 185 190

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Arg Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Val Glu Pro Glu Asp Ser Ala Val Tyr
210 215 220

Tyr Cys Gln His Tyr Glu Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 143
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 143
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

```
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Val Arg Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
    130                 135                 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
                165                 170                 175

Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro
            180                 185                 190

Asp Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
```

210 215 220

Gly Ser Pro Pro Arg Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile
225 230 235 240

Lys

<210> 144
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 144
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

```
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
    130                 135                 140


Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145                 150                 155                 160


Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
                165                 170                 175


Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
            180                 185                 190


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205


Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His
    210                 215                 220


Tyr Gly Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu
225                 230                 235                 240


Ile Lys
```

<210> 145
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 145

```
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Met Ser Arg Glu Asn Asp Lys Asn Ser Val Phe
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
    130                 135                 140

Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Ser Ala Thr Leu
145                 150                 155                 160

Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn Tyr Leu Ala Trp Tyr
                165                 170                 175

Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu Ile Ser Gly Ala Ser
            180                 185                 190
```

```
Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala
    210                 215                 220


Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro Ser Trp Thr Phe Gly
225                 230                 235                 240


Gln Gly Thr Lys Val Glu Ile Lys
                245


<210> 146
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 146
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
```

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Gln Ala Pro Gly Leu Leu Ile Tyr Gly Ala Ser Asn Trp Ala Thr
            180                 185                 190

Gly Thr Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Thr Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
    210                 215                 220

Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr Phe Gly Gln Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 147
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 147
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro
130 135 140

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
145 150 155 160

Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys

165 170 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
210 215 220

Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Asp Ile Lys

<210> 148
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 148
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly
            100                 105                 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
    130                 135                 140

Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145                 150                 155                 160

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly
            180                 185                 190

Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp
    210                 215                 220

Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn Ser Pro Pro Lys Phe
225                 230                 235                 240

Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
                245                 250
```

<210> 149
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 149
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
130 135 140

```
Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145                 150                 155                 160


Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Gly Arg
            180                 185                 190


Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
    210                 215                 220


Tyr Cys Gln His Tyr Gly Gly Ser Pro Arg Leu Thr Phe Gly Gly Gly
225                 230                 235                 240


Thr Lys Val Asp Ile Lys
                245
```

<210> 150
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 150
caagtgcagc ttcaggaaag cggaccgggc ctggtcaagc catccgaaac tctctccctg 60

acttgcactg tgtctggcgg ttccatctca tcgtcgtact actactgggg ctggattagg 120

cagccgcccg gaaagggact ggagtggatc ggaagcatct actattccgg ctcggcgtac 180

tacaacccta gcctcaagtc gagagtgacc atctccgtgg atacctccaa gaaccagttt 240

tccctgcgcc tgagctccgt gaccgccgct gacaccgccg tgtactactg tgctcggcat 300

tggcaggaat ggcccgatgc cttcgacatt tggggccagg gcactatggt cactgtgtca 360

tccgggggtg gaggcagcgg gggaggaggg tccgggggggg gaggttcaga gacaaccttg 420

acccagtcac ccgcattcat gtccgccact ccgggagaca aggtcatcat ctcgtgcaaa 480

gcgtcccagg atatcgacga tgccatgaat tggtaccagc agaagcctgg cgaagcgccg 540

ctgttcatta tccaatccgc aacctcgccc gtgcctggaa tcccaccgcg gttcagcggc 600

agcggtttcg gaaccgactt ttccctgacc attaacaaca ttgagtccga ggacgccgcc 660

tactacttct gcctgcaaca cgacaacttc cctctcacgt tcggccaggg aaccaagctg 720

gaaatcaag 729

<210> 151
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 151
caagtcaatc tgcgcgaatc cggccccgcc ttggtcaagc ctacccagac cctcactctg 60

acctgtactt tctccggctt ctccctgcgg acttccggga tgtgcgtgtc ctggatcaga 120

cagcctccgg gaaaggccct ggagtggctc gctcgcattg actgggatga ggacaagttc 180

tactccacct cactcaagac caggctgacc atcagcaaag atacctctga caaccaagtg 240

gtgctccgca tgaccaacat ggacccagcc gacactgcca cttactactg cgcgaggagc 300

ggagcgggcg gaacctccgc caccgccttc gatatttggg gcccgggtac catggtcacc 360

gtgtcaagcg gaggaggggg gtccgggggc ggcggttccg ggggaggcgg atcggacatt 420

cagatgactc agtcaccatc gtccctgagc gctagcgtgg gcgacagagt gacaatcact 480

tgccgggcat cccaggacat ctataacaac cttgcgtggt tccagctgaa gcctggttcc 540

gcaccgcggt cacttatgta cgccgccaac aagagccagt cgggagtgcc gtcccggttt 600

tccggttcgg cctcgggaac tgacttcacc ctgacgatct ccagcctgca acccgaggat 660

ttcgccacct actactgcca gcactactac cgctttccct actcgttcgg acagggaacc 720

aagctggaaa tcaag 735

<210> 152
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 152
gaagtgcagc ttgtcgaatc cgggggggga ctggtcaagc cgggcggatc actgagactg 60

tcctgcgccg cgagcggctt cacgttctcc tcctactcca tgaactgggt ccgccaagcc 120

cccgggaagg gactggaatg ggtgtcctct atctcctcgt cgtcgtccta catctactac 180

gccgactccg tgaagggaag attcaccatt tcccgcgaca acgcaaagaa ctcactgtac 240

ttgcaaatga actcactccg ggccgaagat actgctgtgt actattgcgc caagactatt 300

gccgccgtct acgctttcga catctggggc cagggaacca ccgtgactgt gtcgtccggt 360

ggtggtggct cgggcggagg aggaagcggc ggcggggggt ccgagattgt gctgacccag 420

tcgccactga gcctccctgt gacccccgag gaacccgcca gcatcagctg ccggtccagc 480

cagtccctgc tccactccaa cggatacaat tacctcgatt ggtaccttca gaagcctgga 540

caaagcccgc agctgctcat ctacttggga tcaaaccgcg cgtcaggagt gcctgaccgg 600

ttctccggct cgggcagcgg taccgatttc accctgaaaa tctccagggt ggaggcagag 660

gacgtgggag tgtattactg tatgcaggcg ctgcagactc cgtacacatt tgggcagggc 720

accaagctgg agatcaag 738

<210> 153

<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 153
gaagtccagc tcgtggagtc cggcggaggc cttgtgaagc ctggaggttc gctgagactg 60

tcctgcgccg cctccggctt caccttctcc gactactaca tgtcctggat cagacaggcc 120

ccgggaaagg gcctggaatg ggtgtcctac atctcgtcat cgggcagcac tatctactac 180

gcggactcag tgaaggggcg gttcaccatt tcccgggata acgcgaagaa ctcgctgtat 240

ctgcaaatga actcactgag ggccgaggac accgccgtgt actactgcgc ccgcgatctc 300

cgcggggcat ttgacatctg gggacaggga accatggtca cagtgtccag cggaggggga 360

ggatcgggtg gcggaggttc cgggggtgga ggctcctcct acgtgctgac tcagagccca 420

agcgtcagcg ctgcgcccgg ttacacggca accatctcct gtggcggaaa caacattggg 480

accaagtctg tgcactggta tcagcagaag ccgggccaag ctcccctgtt ggtgatccgc 540

gatgactccg tgcggcctag caaaattccg ggacggttct ccggctccaa cagcggcaat 600

atggccactc tcaccatctc gggagtgcag gccggagatg aagccgactt ctactgccaa 660

gtctgggact cagactccga gcatgtggtg ttcgggggcg gaaccaagct gactgtgctc 720

<210> 154
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 154
caagtgcagc tggtgcagag cggggccgaa gtcaagaagc cgggagcctc cgtgaaagtg 60

tcctgcaagc cttcgggata caccgtgacc tcccactaca ttcattgggt ccgccgcgcc 120

cccggccaag gactcgagtg gatgggcatg atcaacccta gcggcggagt gaccgcgtac 180

agccagacgc tgcagggacg cgtgactatg acctcggata cctcctcctc caccgtctat 240

atggaactgt ccagcctgcg gtccgaggat accgccatgt actactgcgc ccgggaagga 300

tcaggctccg ggtggtattt cgacttctgg ggaagaggca ccctcgtgac tgtgtcatct 360

gggggagggg gttccggtgg tggcggatcg ggaggaggcg gttcatccta cgtgctgacc 420

cagccaccct ccgtgtccgt gagccccggc cagactgcat cgattacatg tagcggcgac 480

ggcctctcca agaaatacgt gtcgtggtac cagcagaagg ccggacagag cccggtggtg 540

ctgatctcaa gagataagga gcggcctagc ggaatcccgg acaggttctc gggttccaac 600

tccgcggaca ctgctactct gaccatctcg gggacccagg ctatggacga agccgattac 660

tactgccaag cctgggacga cactactgtc gtgtttggag ggggcaccaa gttgaccgtc 720

ctt 723

<210> 155
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 155
caagtgcagc ttcaggagag cggcccggga ctcgtgaagc cgtcccagac cctgtccctg 60

acttgcaccg tgtcgggagg aagcatctcg agcggaggct actattggtc gtggattcgg 120

cagcaccctg gaaagggcct ggaatggatc ggctacatct actactccgg ctcgacctac 180

tacaacccat cgctgaagtc cagagtgaca atctcagtgg acacgtccaa gaatcagttc 240

agcctgaagc tctcttccgt gactgcggcc gacaccgccg tgtactactg cgcacgcgct 300

ggaattgccg cccggctgag gggtgccttc gacatttggg gacagggcac catggtcacc 360

gtgtcctccg gcggcggagg ttccgggggt ggaggctcag gaggaggggg gtccgacatc 420

gtcatgactc agtcgccctc aagcgtcagc gcgtccgtcg gggacagagt gatcatcacc 480

tgtcgggcgt cccagggaat tcgcaactgg ctggcctggt atcagcagaa gcccggaaag 540

gcccccaacc tgttgatcta cgccgcctca aacctccaat ccggggtgcc gagccgcttc 600

agcggctccg gttcgggtgc cgatttcact ctgaccatct cctccctgca acctgaagat 660

gtggctacct actactgcca aaagtacaac tccgcacctt ttactttcgg accggggacc 720

aaagtggaca ttaag 735

<210> 156
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 156
caagtgcagc tggtccagtc gggcgccgag gtcaagaagc ccgggagctc tgtgaaagtg 60

tcctgcaagg cctccggggg cacctttagc tcctacgcca tctcctgggt ccgccaagca 120

ccgggtcaag gcctggagtg gatgggggga attatcccta tcttcggcac tgccaactac 180

gcccagaagt tccagggacg cgtgaccatt accgcggacg aatccacctc caccgcttat 240

atggagctgt ccagcttgcg ctcggaagat accgccgtgt actactgcgc ccggaggggt 300

ggataccagc tgctgagatg ggacgtgggc ctcctgcggt cggcgttcga catctggggc 360

cagggcacta tggtcactgt gtccagcgga ggaggcggat cgggaggcgg cggatcaggg 420

ggaggcggtt ccagctacgt gcttactcaa ccccccttcgg tgtccgtggc cccgggacag 480

accgccagaa tcacttgcgg aggaaacaac attgggtcca agagcgtgca ttggtaccag 540

cagaagccag gacaggcccc tgtgctggtg ctctacggga agaacaatcg gcccagcgga 600

gtgccggaca ggttctcggg ttcacgctcc ggtacaaccg cttcactgac tatcaccggg 660

gcccaggcag aggatgaagc ggactactac tgttcctccc gggattcatc cggcgaccac 720

ctccgggtgt tcggaaccgg aacgaaggtc accgtgctg 759

<210> 157
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 157
gaagtgcagc tccaacagtc aggaccgggg ctcgtgaagc catcccagac cctgtccctg 60

acttgtgcca tctcgggaga tagcgtgtca tcgaactccg ccgcctggaa ctggattcgg 120

cagagcccgt cccgcggact ggagtggctt ggaaggacct actaccggtc caagtggtac 180

tctttctacg cgatctcgct gaagtcccgc attatcatta accctgatac ctccaagaat 240

cagttctccc tccaactgaa atccgtcacc cccgaggaca cagcagtgta ttactgcgca 300

cggagcagcc ccgaaggact gttcctgtat tggtttgacc cctggggcca ggggactctt 360

gtgaccgtgt cgagcggcgg agatgggtcc ggtggcggtg gttcgggggg cggcggatca 420

tcatccgaac tgacccagga cccggctgtg tccgtggcgc tgggacaaac catccgcatt 480

acgtgccagg gagactccct gggcaactac tacgccactt ggtaccagca gaagccgggc 540

caagcccctg tgttggtcat ctacgggacc aacaacagac cttccggcat ccccgaccgg 600

ttcagcgctt cgtcctccgg caacactgcc agcctgacca tcactggagc gcaggccgaa 660

gatgaggccg actactactg caacagcaga gactcctcgg gtcatcacct cttgttcgga 720

actggaacca aggtcaccgt gctg 744

<210> 158
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 158
gaagtgcagc tcgtggagtc aggaggcggc ctggtccagc cgggagggtc ccttagactg 60

tcatgcgccg caagcggatt cactttctcc tcctatgcca tgagctgggt ccgccaagcc 120

cccggaaagg gactggaatg ggtgtccgcc atctcggggt ctggaggctc aacttactac 180

gctgactccg tgaagggacg gttcaccatt agccgcgaca actccaagaa caccctctac 240

ctccaaatga actccctgcg ggccgaggat accgccgtct actactgcgc caaagtggaa 300

ggttcaggat cgctggacta ctggggacag ggtactctcg tgaccgtgtc atcgggcgga 360

ggaggttccg gcggtggcgg ctccggcggc ggagggtcgg agatcgtgat gacccagagc 420

cctggtactc tgagcctttc gccgggagaa agggccaccc tgtcctgccg cgcttcccaa 480

tccgtgtcct ccgcgtactt ggcgtggtac cagcagaagc cgggacagcc ccctcggctg 540

ctgatcagcg gggccagcac ccgggcaacc ggaatcccag acagattcgg gggttccggc 600

agcggcacag atttcaccct gactatttcg aggttggagc ccgaggactt tgcggtgtat 660

tactgtcagc actacgggtc gtcctttaat ggctccagcc tgttcacgtt cggacagggg 720

acccgcctgg aaatcaag 738

<210> 159
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 159
gaagtgcaac tggtggaaac cggtggcggc ctggtgcagc ctggaggatc attgaggctg 60

tcatgcgcgg ccagcggtat taccttctcc cggtacccca tgtcctgggt cagacaggcc 120

ccggggaaag ggcttgaatg ggtgtccggg atctcggact ccggtgtcag cacttactac 180

gccgactccg ccaagggacg cttcaccatt tcccgggaca actcgaagaa caccctgttc 240

ctccaaatga gctccctccg ggacgaggat actgcagtgt actactgcgt gacccgcgcc 300

gggtccgagg cgtctgacat ttggggacag ggcactatgg tcaccgtgtc gtccggcgga 360

gggggctcgg gaggcggtgg cagcggagga ggagggtccg agatcgtgct gacccaatcc 420

ccggccaccc tctcgctgag ccctggagaa agggcaacct tgtcctgtcg cgcgagccag 480

tccgtgagca actccctggc ctggtaccag cagaagcccg gacaggctcc gagacttctg 540

atctacgacg cttcgagccg ggccactgga atccccgacc gcttttcggg gtccggctca 600

ggaaccgatt tcaccctgac aatctcacgg ctggagccag aggatttcgc catctattac 660

tgccagcagt tcggtacttc ctccggcctg actttcggag gcggcacgaa gctcgaaatc 720

aag 723

<210> 160
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 160
caagtgcagc tcgtggaatc gggtggcgga ctggtgcagc cgggggctc acttagactg 60

tcctgcgcgg ccagcggatt cactttctcc tcctacgcca tgtcctgggt cagacaggcc 120

cctggaaagg gcctggaatg ggtgtccgca atcagcggca gcggcggctc gacctattac 180

gcggattcag tgaagggcag attcaccatt tcccgggaca acgccaagaa ctccttgtac 240

cttcaaatga actccctccg cgcggaagat accgcaatct actactgcgc tcgggccact 300

tacaagaggg aactgcgcta ctactacggg atggacgtct ggggccaggg aaccatggtc 360

accgtgtcca gcggaggagg aggatcggga ggaggcggta gcgggggtgg agggtcggag 420

atcgtgatga cccagtcccc cggcactgtg tcgctgtccc ccggcgaacg ggccaccctg 480

tcatgtcggg ccagccagtc agtgtcgtca agcttcctcg cctggtacca gcagaaaccg 540

ggacaagctc cccgcctgct gatctacgga gccagcagcc gggccaccgg tattcctgac 600

cggttctccg gttcggggtc cgggaccgac tttactctga ctatctctcg cctcgagcca 660

gaggactccg ccgtgtatta ctgccagcag taccactcct ccccgtcctg gacgttcgga 720

cagggcacaa ggctggagat taag 744

<210> 161
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 161
gaggtgcagc ttgtggaaac cggtggcgga ctggtgcagc ccggaggaag cctcaggctg 60

tcctgcgccg cgtccggctt caccttctcc tcgtacgcca tgtcctgggt ccgccaggcc 120

cccggaaagg gcctggaatg ggtgtccgcc atctctggaa gcggaggttc cacgtactac 180

gcggacagcg tcaagggaag gttcacaatc tcccgcgata attcgaagaa cactctgtac 240

cttcaaatga acaccctgaa ggccgaggac actgctgtgt actactgcgc acgggccacc 300

tacaagagag agctccggta ctactacgga atggacgtct ggggccaggg aactactgtg 360

accgtgtcct cgggaggggg tggctccggg gggggcggct ccggcggagg cggttccgag 420

attgtgctga cccagtcacc ttcaactctg tcgctgtccc cgggagagag cgctactctg 480

agctgccggg ccagccagtc cgtgtccacc accttcctcg cctggtatca gcagaagccg 540

gggcaggcac cacggctctt gatctacggg tcaagcaaca gagcgaccgg aattcctgac 600

cgcttctcgg ggagcggttc aggcaccgac ttcaccctga ctatccggcg cctggaaccc 660

gaagatttcg ccgtgtatta ctgtcaacag taccactcct cgccgtcctg gacctttggc 720

caaggaacca aagtggaaat caag 744

<210> 162
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 162
gaagtgcagc tcgtggaaac tggaggtgga ctcgtgcagc ctggacggtc gctgcggctg 60

agctgcgctg catccggctt caccttcgac gattatgcca tgcactgggt cagacaggcg 120

ccagggaagg gacttgagtg ggtgtccggt atcagctgga atagcggctc aatcggatac 180

gcggactccg tgaagggaag gttcaccatt tcccgcgaca acgccaagaa ctccctgtac 240

ttgcaaatga acagcctccg ggatgaggac actgccgtgt actactgcgc ccgcgtcgga 300

aaagctgtgc ccgacgtctg gggccaggga accactgtga ccgtgtccag cggcgggggt 360

ggatcgggcg gtggagggtc cggtggaggg ggctcagata ttgtgatgac ccagaccccc 420

tcgtccctgt ccgcctcggt cggcgaccgc gtgactatca catgtagagc ctcgcagagc 480

atctccagct acctgaactg gtatcagcag aagccgggga aggccccgaa gctcctgatc 540

tacgcggcat catcactgca atcgggagtg ccgagccggt tttccgggtc cggctccggc 600

accgacttca cgctgaccat ttcttccctg caacccgagg acttcgccac ttactactgc 660

cagcagtcct actccacccc ttactccttc ggccaaggaa ccaggctgga aatcaag 717

<210> 163
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 163
gaagtgcagc tcgtggagag cgggggagga ttggtgcagc ccggaaggtc cctgcggctc 60

tcctgcactg cgtctggctt caccttcgac gactacgcga tgcactgggt cagacagcgc 120

ccgggaaagg gcctggaatg ggtcgcctca atcaactgga agggaaactc cctggcctat 180

ggcgacagcg tgaagggccg cttcgccatt tcgcgcgaca acgccaagaa caccgtgttt 240

ctgcaaatga attccctgcg gaccgaggat accgctgtgt actactgcgc cagccaccag 300

ggcgtggcat actataacta cgccatggac gtgtggggaa gagggacgct cgtcaccgtg 360

tcctccgggg gcggtggatc gggtggagga ggaagcggtg gcgggggcag cgaaatcgtg 420

ctgactcaga gcccgggaac tctttcactg tccccgggag aacgggccac tctctcgtgc 480

cgggccaccc agtccatcgg ctcctccttc cttgcctggt accagcagag gccaggacag 540

gcgccccgcc tgctgatcta cggtgcttcc caacgcgcca ctggcattcc tgaccggttc 600

agcggcagag ggtcgggaac cgatttcaca ctgaccattt cccgggtgga gcccgaagat 660

tcggcagtct actactgtca gcattacgag tcctcccctt catggacctt cggtcaaggg 720

accaaagtgg agatcaag 738

<210> 164
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 164
gaggtgcagt tggtcgaaag cgggggcggg cttgtgcagc ctggcggatc actgcggctg 60

tcctgcgcgg catcaggctt cacgttttct tcctacgcca tgtcctgggt gcgccaggcc 120

cctggaaagg gactggaatg ggtgtccgcg atttcggggt ccggcgggag cacctactac 180

gccgattccg tgaagggccg cttcactatc tcgcgggaca actccaagaa caccctctac 240

ctccaaatga atagcctgcg ggccgaggat accgccgtct actattgcgc taaggtcgtg 300

cgcgacggaa tggacgtgtg gggacagggt accaccgtga cagtgtcctc gggggggaggc 360

ggtagcggcg gaggaggaag cggtggtgga ggttccgaga ttgtgctgac tcaatcaccc 420

gcgaccctga gcctgtcccc cggcgaaagg gccactctgt cctgtcgggc cagccaatca 480

gtctcctcct cgtacctggc ctggtaccag cagaagccag gacaggctcc gagactcctt 540

atctatggcg catcctcccg cgccaccgga atcccggata ggttctcggg aaacggatcg 600

gggaccgact tcactctcac catctcccgg ctggaaccgg aggacttcgc cgtgtactac 660

tgccagcagt acggcagccc gcctagattc actttcggcc ccggcaccaa agtggacatc 720

aag 723

<210> 165
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 165
gaagtgcagc tgctggagtc cggcggtgga ttggtgcaac cgggggggatc gctcagactg 60

tcctgtgcgg cgtcaggctt caccttctcg agctacgcca tgtcatgggt cagacaggcc 120

cctggaaagg gtctggaatg ggtgtccgcc atttccggga gcgggggatc tacatactac 180

gccgatagcg tgaagggccg cttcaccatt tcccgggaca actccaagaa cactctctat 240

ctgcaaatga actccctccg cgctgaggac actgccgtgt actactgcgc caaaatccct 300

cagaccggca ccttcgacta ctggggacag gggactctgg tcaccgtcag cagcggtggc 360

ggaggttcgg ggggaggagg aagcggcggc ggagggtccg agattgtgct gacccagtca 420

cccggcactt tgtccctgtc gcctggagaa agggccaccc tttcctgccg ggcatcccaa 480

tccgtgtcct cctcgtacct ggcctggtac cagcagaggc ccggacaggc cccacggctt 540

ctgatctacg gagcaagcag ccgcgcgacc ggtatcccgg accggttttc gggctcgggc 600

tcaggaactg acttcaccct caccatctcc cgcctggaac ccgaagattt cgctgtgtat 660

tactgccagc actacggcag ctccccgtcc tggacgttcg gccagggaac tcggctggag 720

atcaag 726

<210> 166
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 166
gaagtgcaac tggtggaaac cggtggagga ctcgtgcagc ctggcggcag cctccggctg 60

agctgcgccg cttcgggatt cacctttcc tcctacgcga tgtcttgggt cagacaggcc 120

cccggaaagg ggctggaatg ggtgtcagcc atctccggct ccggcggatc aacgtactac 180

gccgactccg tgaaaggccg gttcaccatg tcgcgcgaga atgacaagaa ctccgtgttc 240

ctgcaaatga actccctgag ggtggaggac accggagtgt actattgtgc gcgcgccaac 300

tacaagagag agctgcggta ctactacgga atggacgtct ggggacaggg aactatggtg 360

accgtgtcat ccggtggagg gggaagcggc ggtggaggca gcgggggcgg gggttcagaa 420

attgtcatga cccagtcccc gggaactctt tccctctccc ccggggaatc cgcgactttg 480

tcctgccggg ccagccagcg cgtggcctcg aactacctcg catggtacca gcataagcca 540

ggccaagccc cttccctgct gatttccggg gctagcagcc gcgccactgg cgtgccggat 600

aggttctcgg gaagcggctc gggtaccgat ttcaccctgg caatctcgcg gctggaaccg 660

gaggattcgg ccgtgtacta ctgccagcac tatgactcat ccccctcctg gacattcgga 720

cagggcacca aggtcgagat caag 744

<210> 167

<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 167
gaagtgcagc tgctcgaaac cggtggaggg ctggtgcagc cagggggctc cctgaggctt 60

tcatgcgccg ctagcggatt ctccttctcc tcttacgcca tgtcgtgggt ccgccaagcc 120

cctggaaaag gcctggaatg ggtgtccgcg atttccggga gcggaggttc gacctattac 180

gccgactccg tgaagggccg ctttaccatc tcccgggata actccaagaa cactctgtac 240

ctccaaatga actcgctgag agccgaggac accgccgtgt attactgcgc gaaggcgctg 300

gtcggcgcga ctggggcatt cgacatctgg ggacagggaa ctcttgtgac cgtgtcgagc 360

ggaggcggcg gctccggcgg aggagggagc gggggcggtg gttccgaaat cgtgttgact 420

cagtccccgg gaaccctgag cttgtcaccc ggggagcggg ccactctctc ctgtcgcgcc 480

tcccaatcgc tctcatccaa tttcctggcc tggtaccagc agaagcccgg acaggccccg 540

ggcctgctca tctacggcgc ttcaaactgg gcaacgggaa cccctgatcg gttcagcgga 600

agcggatcgg gtactgactt taccctgacc atcaccagac tggaaccgga ggacttcgcc 660

gtgtactact gccagtacta cggcacctcc cccatgtaca cattcggaca gggtaccaag 720

gtcgagatta ag 732

<210> 168
<211> 733
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 168

gaagtgcagc tgcttgagag cggtggaggt ctggtgcagc ccgggggatc actgcgcctg 60

tcctgtgccg cgtccggttt cactttctcc tcgtacgcca tgtcgtgggt cagacaggca 120

ccgggaaagg gactggaatg ggtgtcagcc atttcgggtt cgggggggcag cacctactac 180

gctgactccg tgaagggccg gttcaccatt tcccgcgaca actccaagaa caccttgtac 240

ctccaaatga actccctgcg ggccgaagat accgccgtgt attactgcgt gctgtggttc 300

ggagagggat tcgacccgtg gggacaagga acactcgtga ctgtgtcatc cggcggaggc 360

ggcagcggtg gcggcggttc cggcggcggc ggatctgaca tcgtgttgac ccagtcccct 420

ctgagcctgc cggtcactcc tggcgaacca gccagcatct cctgccggtc gagccagtcc 480

ctcctgcact ccaatgggta caactacctc gattggtatc tgcaaaagcc gggccagagc 540

ccccagctgc tgatctacct tgggtcaaac cgcgcttccg gggtgcctga tagattctcc 600

gggtccggga gcggaaccga ctttaccctg aaaatctcga gggtggaggc cgaggacgtc 660

ggagtgtact actgcatgca ggcgctccag actcccctga ccttcggagg aggaacgaag 720

gtcgacatca aga 733

<210> 169
<211> 753
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 169
caagtgcagc tcgtggagtc aggcggagga ctggtgcagc ccgggggctc cctgagactt 60

tcctgcgcgg catcgggttt taccttctcc tcctatgcta tgtcctgggt gcgccaggcc 120

ccgggaaagg gactggaatg ggtgtccgca atcagcggta gcgggggctc aacatactac 180

gccgactccg tcaagggtcg cttcactatt tcccgggaca actccaagaa taccctgtac 240

ctccaaatga acagcctcag ggccgaggat actgccgtgt actactgcgc caaagtcgga 300

tacgatagct ccggttacta ccgggactac tacggaatgg acgtgtgggg acagggcacc 360

accgtgaccg tgtcaagcgg cggaggcggt tcaggagggg gaggctccgg cggtggaggg 420

tccgaaatcg tcctgactca gtcgcctggc actctgtcgt tgtccccggg ggagcgcgct 480

accctgtcgt gtcgggcgtc gcagtccgtg tcgagctcct acctcgcgtg gtaccagcag 540

aagcccggac aggcccctag acttctgatc tacggcactt cttcacgcgc caccgggatc 600

agcgacaggt tcagcggctc cggctccggg accgacttca ccctgaccat tagccggctg 660

gagcctgaag atttcgccgt gtattactgc caacactacg gaaactcgcc gccaaagttc 720

acgttcggac ccggaaccaa gctggaaatc aag 753

<210> 170
<211> 739
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 170
gaagtccaac tggtggagtc cgggggaggg ctcgtgcagc ccggaggcag ccttcggctg 60

tcgtgcgccg cctccgggtt cacgttctca tcctacgcga tgtcgtgggt cagacaggca 120

ccaggaaagg gactggaatg ggtgtccgcc attagcggct ccggcggtag cacctactat 180

gccgactcag tgaagggaag gttcactatc tcccgcgaca acagcaagaa caccctgtac 240

ctccaaatga actctctgcg ggccgaggat accgcggtgt actattgcgc caagatgggt 300

tggtccagcg gatacttggg agccttcgac atttggggac agggcactac tgtgaccgtg 360

tcctccgggg gtggcggatc gggaggcggc ggctcgggtg gaggggttc cgaaatcgtg 420

ttgacccagt caccgggaac cctctcgctg tccccgggag aacgggctac actgtcatgt 480

agagcgtccc agtccgtggc ttcctcgttc ctggcctggt accagcagaa gccgggacag 540

gcaccccgcc tgctcatcta cggagccagc ggccgggcga ccggcatccc tgaccgcttc 600

tccggttccg gctcgggcac cgactttact ctgaccatta gcaggcttga gcccgaggat 660

tttgccgtgt actactgcca acactacggg gggagccctc gcctgacctt cggaggcgga 720

actaaggtcg atatcaaaa 739

<210> 171
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 171
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 172
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 172
Gln Val Asn Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Arg Thr Ser
20 25 30

Gly Met Cys Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

Trp Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys Phe Tyr Ser Thr Ser
50 55 60

Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Asp Asn Gln Val
65 70 75 80

Val Leu Arg Met Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile
100 105 110

Trp Gly Pro Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 173
<211> 119
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 173
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 174
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 174
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Arg Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser
115

<210> 175
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 175
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

```
Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr Thr Val Thr Ser His
            20                  25                  30


Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ser Ser Thr Val Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe Trp Gly Arg
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 176
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 176
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
            20                  25                  30
```

```
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
        35                  40                  45


Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
    50                  55                  60


Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80


Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95


Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
            100                 105                 110


Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210> 177
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 177
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu
            100                 105                 110

Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
        115                 120                 125

Ser
```

<210> 178
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 178

```
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
            20                  25                  30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala
```

50 55 60

Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe
100 105 110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 179
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 179
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210> 180
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 180
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Ser Arg Tyr
            20                  25                  30


Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr Tyr Ala Asp Ser Ala
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80


Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser
        115


<210> 181
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 181
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95


Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110
```

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 182
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 182
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Thr Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100   105   110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 183

<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 183
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 184
<211> 122
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 184
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Arg Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala Tyr Gly Asp Ser Val
50 55 60

Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val Trp
100 105 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 185
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 185

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Val Val Arg Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 186
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 186
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
```

20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 187
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 187
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Met Ser Arg Glu Asn Asp Lys Asn Ser Val Phe
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110


Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210> 188
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 188
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 189
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 189
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
```

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 190
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 190
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly

100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 191
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 191
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 192
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 192
Glu Thr Thr Leu Thr Gln Ser Pro Ala Phe Met Ser Ala Thr Pro Gly
1 5 10 15

Asp Lys Val Ile Ile Ser Cys Lys Ala Ser Gln Asp Ile Asp Asp Ala
20 25 30

Met Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Leu Phe Ile Ile
35 40 45

Gln Ser Ala Thr Ser Pro Val Pro Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

Ser Gly Phe Gly Thr Asp Phe Ser Leu Thr Ile Asn Asn Ile Glu Ser
65 70 75 80

Glu Asp Ala Ala Tyr Tyr Phe Cys Leu Gln His Asp Asn Phe Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 193
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 193
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Tyr Asn Asn
20 25 30

Leu Ala Trp Phe Gln Leu Lys Pro Gly Ser Ala Pro Arg Ser Leu Met
35 40 45

Tyr Ala Ala Asn Lys Ser Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Ala Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Tyr Tyr Arg Phe Pro Tyr
85 90 95

Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 194
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 194
Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Glu
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser

20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 195
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 195
Ser Tyr Val Leu Thr Gln Ser Pro Ser Val Ser Ala Ala Pro Gly Tyr
1 5 10 15

Thr Ala Thr Ile Ser Cys Gly Gly Asn Asn Ile Gly Thr Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Arg
35 40 45

Asp Asp Ser Val Arg Pro Ser Lys Ile Pro Gly Arg Phe Ser Gly Ser
50 55 60

```
Asn Ser Gly Asn Met Ala Thr Leu Thr Ile Ser Gly Val Gln Ala Gly
65                  70                  75                  80


Asp Glu Ala Asp Phe Tyr Cys Gln Val Trp Asp Ser Asp Ser Glu His
                85                  90                  95


Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
            100                 105


<210> 196
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 196
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1               5                   10                  15


Thr Ala Ser Ile Thr Cys Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val
            20                  25                  30


Ser Trp Tyr Gln Gln Lys Ala Gly Gln Ser Pro Val Val Leu Ile Ser
        35                  40                  45


Arg Asp Lys Glu Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50                  55                  60


Asn Ser Ala Asp Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65                  70                  75                  80


Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Asp Thr Thr Val Val
                85                  90                  95
```

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 197
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 197
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 198
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 198
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Leu Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
50 55 60

Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Ser Ser Gly Asp His
85 90 95

Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105

<210> 199
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 199
Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

```
Thr Ile Arg Ile Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala
            20                  25                  30


Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45


Gly Thr Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala Ser
    50                  55                  60


Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80


Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His His
                85                  90                  95


Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu
            100                 105


<210> 200
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 200
Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
        35                  40                  45
```

Ile Ser Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Gly
    50   55   60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Ser Ser Phe
                85   90   95

Asn Gly Ser Ser Leu Phe Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
            100   105   110

Lys

<210> 201
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 201
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Asn Ser
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Phe Gly Thr Ser Ser Gly
85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 202
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 202
Glu Ile Val Met Thr Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys

100 105

<210> 203
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 203
Glu Ile Val Leu Thr Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ser Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 204
<211> 107
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 204
Asp Ile Val Met Thr Gln Thr Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Tyr
85 90 95

Ser Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 205
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 205
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Gln Ser Ile Gly Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gln Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Arg Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Val Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Glu Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 206
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 206
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser

50 55 60

Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Pro Pro
85 90 95

Arg Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 207
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 207
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Ser Ser Pro
85 90 95

```
Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105


<210> 208
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 208
Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu
        35                  40                  45


Ile Ser Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro
                85                  90                  95


Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 209
<211> 109
<212> PRT
```

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 209
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Ser Ser Asn
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Gly Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Asn Trp Ala Thr Gly Thr Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Tyr Tyr Gly Thr Ser Pro
85 90 95

Met Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 210
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 210
Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly

1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 211
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 211
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

```
Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn Ser Pro
                85                  90                  95


Pro Lys Phe Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210> 212
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 212
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ala Ser Ser
            20                  25                  30


Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
```

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro
85 90 95

Arg Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 213
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 213
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly
35 40 45

Ser Ile Ser Ser Ser Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro
50 55 60

Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala
65 70 75 80

Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr
85 90 95

Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp
100 105 110

```
Thr Ala Val Tyr Tyr Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Thr Thr
145                 150                 155                 160

Leu Thr Gln Ser Pro Ala Phe Met Ser Ala Thr Pro Gly Asp Lys Val
                165                 170                 175

Ile Ile Ser Cys Lys Ala Ser Gln Asp Ile Asp Asp Ala Met Asn Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Glu Ala Pro Leu Phe Ile Ile Gln Ser Ala
        195                 200                 205

Thr Ser Pro Val Pro Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Phe
    210                 215                 220

Gly Thr Asp Phe Ser Leu Thr Ile Asn Asn Ile Glu Ser Glu Asp Ala
225                 230                 235                 240

Ala Tyr Tyr Phe Cys Leu Gln His Asp Asn Phe Pro Leu Thr Phe Gly
                245                 250                 255

Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300
```

```
Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320


Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335


Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
            340                 345                 350


Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
        355                 360                 365


Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
    370                 375                 380


Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385                 390                 395                 400


Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
                405                 410                 415


Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
            420                 425                 430


Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
        435                 440                 445


Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
    450                 455                 460


Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465                 470                 475                 480


Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 214
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 214

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Gln Val Asn Leu Arg Glu Ser Gly Pro Ala Leu
            20                  25                  30


Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe
        35                  40                  45


Ser Leu Arg Thr Ser Gly Met Cys Val Ser Trp Ile Arg Gln Pro Pro
    50                  55                  60


Gly Lys Ala Leu Glu Trp Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys
65                  70                  75                  80


Phe Tyr Ser Thr Ser Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr
                85                  90                  95


Ser Asp Asn Gln Val Val Leu Arg Met Thr Asn Met Asp Pro Ala Asp
            100                 105                 110


Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala
        115                 120                 125


Thr Ala Phe Asp Ile Trp Gly Pro Gly Thr Met Val Thr Val Ser Ser
    130                 135                 140


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
```

```
145                 150                 155                 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                165                 170                 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Tyr Asn Asn Leu
            180                 185                 190

Ala Trp Phe Gln Leu Lys Pro Gly Ser Ala Pro Arg Ser Leu Met Tyr
        195                 200                 205

Ala Ala Asn Lys Ser Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220

Ala Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225                 230                 235                 240

Asp Phe Ala Thr Tyr Tyr Cys Gln His Tyr Tyr Arg Phe Pro Tyr Ser
                245                 250                 255

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305                 310                 315                 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
                325                 330                 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
```

```
            340                 345                 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
        355                 360                 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
    370                 375                 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385                 390                 395                 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
                405                 410                 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
            420                 425                 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
        435                 440                 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
    450                 455                 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465                 470                 475                 480

Leu His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 215
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 215
```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp
        115                 120                 125

Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
145                 150                 155                 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Glu Glu Pro Ala Ser Ile
                165                 170                 175

Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
            180                 185                 190
```

```
Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
        195                 200                 205

Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr
                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380
```

```
Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400


Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415


Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430


Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445


Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460


Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480


Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 216
<211> 484
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 216
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30
```

```
Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Leu Arg Gly Ala Phe Asp Ile Trp
        115                 120                 125

Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Ser Val Ser Ala Ala Pro Gly Tyr Thr Ala Thr Ile Ser Cys Gly
                165                 170                 175

Gly Asn Asn Ile Gly Thr Lys Ser Val His Trp Tyr Gln Gln Lys Pro
            180                 185                 190

Gly Gln Ala Pro Leu Leu Val Ile Arg Asp Asp Ser Val Arg Pro Ser
        195                 200                 205

Lys Ile Pro Gly Arg Phe Ser Gly Ser Asn Ser Gly Asn Met Ala Thr
    210                 215                 220
```

```
Leu Thr Ile Ser Gly Val Gln Ala Gly Asp Glu Ala Asp Phe Tyr Cys
225                 230                 235                 240


Gln Val Trp Asp Ser Asp Ser Glu His Val Val Phe Gly Gly Gly Thr
                245                 250                 255


Lys Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
            260                 265                 270


Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
        275                 280                 285


Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
    290                 295                 300


Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu
305                 310                 315                 320


Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys
                325                 330                 335


Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
            340                 345                 350


Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
        355                 360                 365


Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
    370                 375                 380


Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
385                 390                 395                 400


Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
                405                 410                 415
```

```
Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
            420                 425                 430


Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
        435                 440                 445


Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
    450                 455                 460


Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
465                 470                 475                 480


Leu Pro Pro Arg



<210> 217
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 217
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr
        35                  40                  45


Thr Val Thr Ser His Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln
    50                  55                  60
```

```
Gly Leu Glu Trp Met Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala
65                  70                  75                  80


Tyr Ser Gln Thr Leu Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser
                85                  90                  95


Ser Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110


Ala Met Tyr Tyr Cys Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe
        115                 120                 125


Asp Phe Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140


Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Tyr Val Leu
145                 150                 155                 160


Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile
                165                 170                 175


Thr Cys Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val Ser Trp Tyr Gln
            180                 185                 190


Gln Lys Ala Gly Gln Ser Pro Val Val Leu Ile Ser Arg Asp Lys Glu
        195                 200                 205


Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Asn Ser Ala Asp
    210                 215                 220


Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp
225                 230                 235                 240


Tyr Tyr Cys Gln Ala Trp Asp Asp Thr Thr Val Val Phe Gly Gly Gly
                245                 250                 255
```

```
Thr Lys Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385                 390                 395                 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
                405                 410                 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
            420                 425                 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
        435                 440                 445
```

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 218
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 218
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly
35 40 45

Ser Ile Ser Ser Gly Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro
50 55 60

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr
65 70 75 80

Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr
85 90 95

Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp

```
            100                 105                 110

Thr Ala Val Tyr Tyr Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg
        115                 120                 125

Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp
                165                 170                 175

Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr
        195                 200                 205

Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225                 230                 235                 240

Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe Thr
                245                 250                 255

Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
```

```
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305                 310                 315                 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
                325                 330                 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
            340                 345                 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
        355                 360                 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
    370                 375                 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385                 390                 395                 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
                405                 410                 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
            420                 425                 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
        435                 440                 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
    450                 455                 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465                 470                 475                 480

Leu His Met Gln Ala Leu Pro Pro Arg
```

485

<210> 219
<211> 497
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 219
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly
35 40 45

Thr Phe Ser Ser Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Arg Gly Gly Tyr Gln Leu Leu Arg Trp
115 120 125

Asp Val Gly Leu Leu Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr
130 135 140

```
Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Gly Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser
                165                 170                 175

Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile
            180                 185                 190

Gly Ser Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
        195                 200                 205

Val Leu Val Leu Tyr Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp
    210                 215                 220

Arg Phe Ser Gly Ser Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr
225                 230                 235                 240

Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp
                245                 250                 255

Ser Ser Gly Asp His Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr
            260                 265                 270

Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
        275                 280                 285

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
    290                 295                 300

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
305                 310                 315                 320

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
                325                 330                 335
```

```
Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
            340                 345                 350

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
        355                 360                 365

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
    370                 375                 380

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
385                 390                 395                 400

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
                405                 410                 415

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
            420                 425                 430

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
        435                 440                 445

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
    450                 455                 460

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
465                 470                 475                 480

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
                485                 490                 495

Arg
```

<210> 220
<211> 492

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 220

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu
            20                  25                  30


Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp
        35                  40                  45


Ser Val Ser Ser Asn Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro
    50                  55                  60


Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp
65                  70                  75                  80


Tyr Ser Phe Tyr Ala Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro
                85                  90                  95


Asp Thr Ser Lys Asn Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro
            100                 105                 110


Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu
        115                 120                 125


Phe Leu Tyr Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val
    130                 135                 140


Ser Ser Gly Gly Asp Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160
```

```
Ser Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly
                165                 170                 175

Gln Thr Ile Arg Ile Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr
            180                 185                 190

Ala Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile
        195                 200                 205

Tyr Gly Thr Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala
    210                 215                 220

Ser Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala
225                 230                 235                 240

Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His
                245                 250                 255

His Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350
```

```
Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365


Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380


Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400


Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415


Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430


Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445


Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460


Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480


Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 221
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 221
```

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45


Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80


Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95


Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr
        115                 120                 125


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln
145                 150                 155                 160


Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
                165                 170                 175


Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Tyr Leu Ala Trp Tyr Gln
            180                 185                 190
```

```
Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu Ile Ser Gly Ala Ser Thr
        195                 200                 205

Arg Ala Thr Gly Ile Pro Asp Arg Phe Gly Gly Ser Gly Ser Gly Thr
    210                 215                 220

Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val
225                 230                 235                 240

Tyr Tyr Cys Gln His Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe
                245                 250                 255

Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380
```

```
Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400


Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415


Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430


Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445


Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460


Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480


Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 222
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 222
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile
```

```
        35                  40                  45

Thr Phe Ser Arg Tyr Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Ala Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Phe Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile
        115                 120                 125

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
145                 150                 155                 160

Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
                165                 170                 175

Cys Arg Ala Ser Gln Ser Val Ser Asn Ser Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Ser Arg
        195                 200                 205

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Ile Tyr
```

```
225                 230                 235                 240

Tyr Cys Gln Gln Phe Gly Thr Ser Ser Gly Leu Thr Phe Gly Gly Gly
                245                 250                 255

Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385                 390                 395                 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
                405                 410                 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
```

420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 223
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 223
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

```
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Ile Tyr Tyr Cys Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr
        115                 120                 125

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Glu Ile Val Met Thr Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly
                165                 170                 175

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            180                 185                 190

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
225                 230                 235                 240

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
                245                 250                 255

Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270
```

```
Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460
```

```
Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480


Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 224
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 224
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45


Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80


Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95


Lys Asn Thr Leu Tyr Leu Gln Met Asn Thr Leu Lys Ala Glu Asp Thr
            100                 105                 110
```

```
Ala Val Tyr Tyr Cys Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr
        115                 120                 125

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Glu Ile Val Leu Thr Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly
                165                 170                 175

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr
            180                 185                 190

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr Gly Ser Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
                245                 250                 255

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300
```

```
His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 225
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 225
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp
115 120 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
145                 150                 155                 160


Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175


Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
            180                 185                 190


Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
        195                 200                 205


Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220


Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
225                 230                 235                 240


Cys Gln Gln Ser Tyr Ser Thr Pro Tyr Ser Phe Gly Gln Gly Thr Arg
                245                 250                 255


Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270


Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285


Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300


Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320


Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335
```

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
340 345 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
355 360 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
370 375 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385 390 395 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
405 410 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
420 425 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
435 440 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
450 455 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465 470 475 480

Pro Pro Arg

<210> 226
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 226

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe
        35                  40                  45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Arg Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala
65                  70                  75                  80

Tyr Gly Asp Ser Val Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Thr Val Phe Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr
        115                 120                 125

Ala Met Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Leu Ser Cys Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu
```

```
            180                 185                 190

Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        195                 200                 205

Gly Ala Ser Gln Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Arg
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Val Glu Pro Glu
225                 230                 235                 240

Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Glu Ser Ser Pro Ser Trp
                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
```

370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 227
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 227
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

```
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Val Val Arg Asp Gly Met Asp Val Trp
        115                 120                 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg
        195                 200                 205

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp
    210                 215                 220
```

```
Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Gly Ser Pro Pro Arg Phe Thr Phe Gly Pro Gly
                245                 250                 255

Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385                 390                 395                 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
                405                 410                 415
```

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 228
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 228
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

```
Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
145                 150                 155                 160

Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
                165                 170                 175

Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln
            180                 185                 190

Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser
        195                 200                 205

Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
    210                 215                 220

Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val
225                 230                 235                 240

Tyr Tyr Cys Gln His Tyr Gly Ser Ser Pro Ser Trp Thr Phe Gly Gln
                245                 250                 255
```

```
Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445
```

```
Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460


Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480


Gln Ala Leu Pro Pro Arg
                485


<210> 229
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 229
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45


Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80


Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Met Ser Arg Glu Asn Asp
                85                  90                  95
```

```
Lys Asn Ser Val Phe Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr
            100                 105                 110


Gly Val Tyr Tyr Cys Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr
        115                 120                 125


Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser
    130                 135                 140


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160


Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
                165                 170                 175


Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn
            180                 185                 190


Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu
        195                 200                 205


Ile Ser Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser
    210                 215                 220


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu
225                 230                 235                 240


Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro
                245                 250                 255


Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270


Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285
```

```
Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480
```

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 230
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 230
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Ser Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe
115 120 125

Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly

```
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
145                 150                 155                 160

Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Gly Leu Leu Ile Tyr Gly Ala
        195                 200                 205

Ser Asn Trp Ala Thr Gly Thr Pro Asp Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu Pro Glu Asp Phe
225                 230                 235                 240

Ala Val Tyr Tyr Cys Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr Phe
                245                 250                 255

Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
```

325 330 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
340 345 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
355 360 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
370 375 380

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385 390 395 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
405 410 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
420 425 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
435 440 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
450 455 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465 470 475 480

His Met Gln Ala Leu Pro Pro Arg
485

<210> 231
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 231

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45


Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80


Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95


Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp
        115                 120                 125


Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser
145                 150                 155                 160


Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
                165                 170                 175
```

```
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
            180                 185                 190

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
        195                 200                 205

Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
    210                 215                 220

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
225                 230                 235                 240

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe
                245                 250                 255

Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365
```

```
Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
        435                 440                 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
    450                 455                 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465                 470                 475                 480

His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 232
<211> 495
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 232

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr
        115                 120                 125

Arg Asp Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr
    130                 135                 140

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser
                165                 170                 175

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
            180                 185                 190

Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205
```

```
Leu Leu Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg
225                 230                 235                 240

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn
                245                 250                 255

Ser Pro Pro Lys Phe Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
            260                 265                 270

Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
        275                 280                 285

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
    290                 295                 300

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
305                 310                 315                 320

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
                325                 330                 335

Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
            340                 345                 350

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
        355                 360                 365

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
    370                 375                 380

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
385                 390                 395                 400
```

```
Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
                405                 410                 415


Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
            420                 425                 430


Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
        435                 440                 445


Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
    450                 455                 460


Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
465                 470                 475                 480


Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490                 495


<210> 233
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 233
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45
```

```
Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly
        115                 120                 125

Ala Phe Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        195                 200                 205

Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
225                 230                 235                 240
```

```
Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro Arg Leu
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430
```

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435   440   445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450   455   460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465   470   475   480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485   490

<210> 234
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 234
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg   60

ccccaagtgc agcttcagga aagcggaccg ggcctggtca agccatccga aactctctcc   120

ctgacttgca ctgtgtctgg cggttccatc tcatcgtcgt actactactg gggctggatt   180

aggcagccgc ccggaaaggg actggagtgg atcggaagca tctactattc cggctcggcg   240

tactacaacc ctagcctcaa gtcgagagtg accatctccg tggatacctc caagaaccag   300

ttttccctgc gcctgagctc cgtgaccgcc gctgacaccg ccgtgtacta ctgtgctcgg   360

cattggcagg aatggcccga tgccttcgac atttggggcc agggcactat ggtcactgtg   420

tcatccgggg gtggaggcag cgggggagga gggtccgggg ggggaggttc agagacaacc   480

ttgacccagt cacccgcatt catgtccgcc actccgggag acaaggtcat catctcgtgc   540

aaagcgtccc aggatatcga cgatgccatg aattggtacc agcagaagcc tggcgaagcg   600

ccgctgttca ttatccaatc cgcaacctcg cccgtgcctg gaatcccacc gcggttcagc   660

ggcagcggtt tcggaaccga cttttccctg accattaaca acattgagtc cgaggacgcc 720

gcctactact tctgcctgca acacgacaac ttccctctca cgttcggcca gggaaccaag 780

ctggaaatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 235
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 235
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtca atctgcgcga atccggcccc gccttggtca agcctaccca gaccctcact 120

ctgacctgta ctttctccgg cttctccctg cggacttccg ggatgtgcgt gtcctggatc 180

agacagcctc cgggaaaggc cctggagtgg ctcgctcgca ttgactggga tgaggacaag 240

ttctactcca cctcactcaa gaccaggctg accatcagca aagatacctc tgacaaccaa 300

gtggtgctcc gcatgaccaa catggaccca gccgacactg ccacttacta ctgcgcgagg 360

agcggagcgg gcggaacctc cgccaccgcc ttcgatattt ggggcccggg taccatggtc 420

accgtgtcaa gcggaggagg ggggtccggg ggcggcggtt ccgggggagg cggatcggac 480

attcagatga ctcagtcacc atcgtccctg agcgctagcg tgggcgacag agtgacaatc 540

acttgccggg catcccagga catctataac aaccttgcgt ggttccagct gaagcctggt 600

tccgcaccgc ggtcacttat gtacgccgcc aacaagagcc agtcgggagt gccgtcccgg 660

ttttccggtt cggcctcggg aactgacttc accctgacga tctccagcct gcaacccgag 720

gatttcgcca cctactactg ccagcactac taccgctttc cctactcgtt cggacaggga 780

accaagctgg aaatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 236
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 236
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agcttgtcga atccgggggg ggactggtca agccgggcgg atcactgaga 120

ctgtcctgcg ccgcgagcgg cttcacgttc tcctcctact ccatgaactg ggtccgccaa 180

gcccccggga agggactgga atgggtgtcc tctatctcct cgtcgtcgtc ctacatctac 240

tacgccgact ccgtgaaggg aagattcacc atttcccgcg acaacgcaaa gaactcactg 300

tacttgcaaa tgaactcact ccgggccgaa gatactgctg tgtactattg cgccaagact 360

attgccgccg tctacgcttt cgacatctgg ggccagggaa ccaccgtgac tgtgtcgtcc 420

ggtggtggtg gctcgggcgg aggaggaagc ggcggcgggg ggtccgagat tgtgctgacc 480

cagtcgccac tgagcctccc tgtgaccccc gaggaacccg ccagcatcag ctgccggtcc 540

agccagtccc tgctccactc caacggatac aattacctcg attggtacct tcagaagcct 600

ggacaaagcc cgcagctgct catctacttg ggatcaaacc gcgcgtcagg agtgcctgac 660

cggttctccg gctcgggcag cggtaccgat ttcaccctga aaatctccag ggtggaggca 720

gaggacgtgg gagtgtatta ctgtatgcag gcgctgcaga ctccgtacac atttgggcag 780

ggcaccaagc tggagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 237
<211> 1452
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 237
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtcc agctcgtgga gtccggcgga ggccttgtga agcctggagg ttcgctgaga 120

ctgtcctgcg ccgcctccgg cttcaccttc tccgactact acatgtcctg gatcagacag 180

gccccgggaa agggcctgga atgggtgtcc tacatctcgt catcgggcag cactatctac 240

tacgcggact cagtgaaggg gcggttcacc atttcccggg ataacgcgaa gaactcgctg 300

tatctgcaaa tgaactcact gagggccgag gacaccgccg tgtactactg cgcccgcgat 360

ctccgcgggg catttgacat ctggggacag ggaaccatgg tcacagtgtc cagcggaggg 420

ggaggatcgg gtggcggagg ttccgggggt ggaggctcct cctacgtgct gactcagagc 480

ccaagcgtca gcgctgcgcc cggttacacg gcaaccatct cctgtggcgg aaacaacatt 540

gggaccaagt ctgtgcactg gtatcagcag aagccgggcc aagctcccct gttggtgatc 600

cgcgatgact ccgtgcggcc tagcaaaatt ccgggacggt tctccggctc caacagcggc 660

aatatggcca ctctcaccat ctcgggagtg caggccggag atgaagccga cttctactgc 720

caagtctggg actcagactc cgagcatgtg gtgttcgggg gcggaaccaa gctgactgtg 780

ctcaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 840

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 900

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 960

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1020

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1080

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1140

gatgctccag cctacaagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1200

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 1260

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 1320

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 1380

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 1440

ctgccgcctc gg 1452

<210> 238
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 238
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtgca gagcggggcc gaagtcaaga agccgggagc ctccgtgaaa 120

gtgtcctgca agccttcggg atacaccgtg acctcccact acattcattg ggtccgccgc 180

gcccccggcc aaggactcga gtggatgggc atgatcaacc ctagcggcgg agtgaccgcg 240

tacagccaga cgctgcaggg acgcgtgact atgacctcgg atacctcctc ctccaccgtc 300

tatatggaac tgtccagcct gcggtccgag gataccgcca tgtactactg cgcccgggaa 360

ggatcaggct ccgggtggta tttcgacttc tggggaagag gcaccctcgt gactgtgtca 420

tctgggggag ggggttccgg tggtggcgga tcgggaggag gcggttcatc ctacgtgctg 480

acccagccac cctccgtgtc cgtgagcccc ggccagactg catcgattac atgtagcggc 540

gacggcctct ccaagaaata cgtgtcgtgg taccagcaga aggccggaca gagcccggtg 600

gtgctgatct caagagataa ggagcggcct agcggaatcc cggacaggtt ctcgggttcc 660

aactccgcgg acactgctac tctgaccatc tcggggaccc aggctatgga cgaagccgat 720

tactactgcc aagcctggga cgacactact gtcgtgtttg gagggggcac caagttgacc 780

gtccttacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 239
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 239

atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agcttcagga gagcggcccg ggactcgtga agccgtccca gaccctgtcc 120

ctgacttgca ccgtgtcggg aggaagcatc tcgagcggag gctactattg gtcgtggatt 180

cggcagcacc ctggaaaggg cctggaatgg atcggctaca tctactactc cggctcgacc 240

tactacaacc catcgctgaa gtccagagtg acaatctcag tggacacgtc caagaatcag 300

ttcagcctga agctctcttc cgtgactgcg gccgacaccg ccgtgtacta ctgcgcacgc 360

gctggaattg ccgcccggct gaggggtgcc ttcgacattt ggggacaggg caccatggtc 420

accgtgtcct ccggcggcgg aggttccggg ggtggaggct caggaggagg ggggtccgac 480

atcgtcatga ctcagtcgcc ctcaagcgtc agcgcgtccg tcggggacag agtgatcatc 540

acctgtcggg cgtcccaggg aattcgcaac tggctggcct ggtatcagca gaagcccgga 600

aaggccccca acctgttgat ctacgccgcc tcaaacctcc aatccggggt gccgagccgc 660

ttcagcggct ccggttcggg tgccgatttc actctgacca tctcctccct gcaacctgaa 720

gatgtggcta cctactactg ccaaaagtac aactccgcac cttttacttt cggaccgggg 780

accaaagtgg acattaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 240
<211> 1491
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 240
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtcca gtcgggcgcc gaggtcaaga agcccgggag ctctgtgaaa 120

gtgtcctgca aggcctccgg gggcaccttt agctcctacg ccatctcctg ggtccgccaa 180

gcaccgggtc aaggcctgga gtggatgggg ggaattatcc ctatcttcgg cactgccaac 240

tacgcccaga agttccaggg acgcgtgacc attaccgcgg acgaatccac ctccaccgct 300

tatatggagc tgtccagctt gcgctcggaa gataccgccg tgtactactg cgcccggagg 360

ggtggatacc agctgctgag atgggacgtg ggcctcctgc ggtcggcgtt cgacatctgg 420

ggccagggca ctatggtcac tgtgtccagc ggaggaggcg gatcgggagg cggcggatca 480

gggggaggcg gttccagcta cgtgcttact caacccccct cggtgtccgt ggccccggga 540

cagaccgcca gaatcacttg cggaggaaac aacattgggt ccaagagcgt gcattggtac 600

cagcagaagc caggacaggc ccctgtgctg gtgctctacg ggaagaacaa tcggcccagc 660

ggagtgccgg acaggttctc gggttcacgc tccggtacaa ccgcttcact gactatcacc 720

ggggcccagg cagaggatga agcggactac tactgttcct cccgggattc atccggcgac 780

cacctccggg tgttcggaac cggaacgaag gtcaccgtgc tgaccactac cccagcaccg 840

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 900

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 960

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 1020

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1080

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1140

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctacaagcag 1200

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1260

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1320

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1380

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1440

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1491

<210> 241
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 241
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctccaaca gtcaggaccg gggctcgtga agccatccca gaccctgtcc 120

ctgacttgtg ccatctcggg agatagcgtg tcatcgaact ccgccgcctg gaactggatt 180

cggcagagcc cgtcccgcgg actggagtgg cttggaagga cctactaccg gtccaagtgg 240

tactctttct acgcgatctc gctgaagtcc cgcattatca ttaaccctga tacctccaag 300

aatcagttct ccctccaact gaaatccgtc acccccgagg acacagcagt gtattactgc 360

gcacggagca gccccgaagg actgttcctg tattggtttg acccctgggg ccaggggact 420

cttgtgaccg tgtcgagcgg cggagatggg tccggtggcg gtggttcggg gggcggcgga 480

tcatcatccg aactgaccca ggacccggct gtgtccgtgg cgctgggaca aaccatccgc 540

attacgtgcc agggagactc cctgggcaac tactacgcca cttggtacca gcagaagccg 600

ggccaagccc ctgtgttggt catctacggg accaacaaca gaccttccgg catccccgac 660

cggttcagcg cttcgtcctc cggcaacact gccagcctga ccatcactgg agcgcaggcc 720

gaagatgagg ccgactacta ctgcaacagc agagactcct cgggtcatca cctcttgttc 780

ggaactggaa ccaaggtcac cgtgctgacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 242
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 242
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtgga gtcaggaggc ggcctggtcc agccgggagg gtcccttaga 120

ctgtcatgcg ccgcaagcgg attcactttc tcctcctatg ccatgagctg ggtccgccaa 180

gcccccggaa agggactgga atgggtgtcc gccatctcgg ggtctggagg ctcaacttac 240

tacgctgact ccgtgaaggg acggttcacc attagccgcg acaactccaa gaacaccctc 300

tacctccaaa tgaactccct gcgggccgag gataccgccg tctactactg cgccaaagtg 360

gaaggttcag gatcgctgga ctactgggga cagggtactc tcgtgaccgt gtcatcgggc 420

ggaggaggtt ccggcggtgg cggctccggc ggcggagggt cggagatcgt gatgacccag 480

agccctggta ctctgagcct ttcgccggga gaaagggcca ccctgtcctg ccgcgcttcc 540

caatccgtgt cctccgcgta cttggcgtgg taccagcaga agccgggaca gccccctcgg 600

ctgctgatca gcggggccag cacccgggca accggaatcc cagacagatt cgggggttcc 660

ggcagcggca cagatttcac cctgactatt tcgaggttgg agcccgagga ctttgcggtg 720

tattactgtc agcactacgg gtcgtccttt aatggctcca gcctgttcac gttcggacag 780

gggacccgcc tggaaatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 243
<211> 1455

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 243
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactggtgga aaccggtggc ggcctggtgc agcctggagg atcattgagg 120

ctgtcatgcg cggccagcgg tattaccttc tcccggtacc ccatgtcctg ggtcagacag 180

gccccgggga aagggcttga atgggtgtcc gggatctcgg actccggtgt cagcacttac 240

tacgccgact ccgccaaggg acgcttcacc atttcccggg acaactcgaa gaacaccctg 300

ttcctccaaa tgagctccct ccgggacgag gatactgcag tgtactactg cgtgacccgc 360

gccgggtccg aggcgtctga catttgggga cagggcacta tggtcaccgt gtcgtccggc 420

ggaggggct cgggaggcgg tggcagcgga ggaggagggt ccgagatcgt gctgacccaa 480

tccccggcca ccctctcgct gagccctgga gaaagggcaa ccttgtcctg tcgcgcgagc 540

cagtccgtga gcaactccct ggcctggtac cagcagaagc ccggacaggc tccgagactt 600

ctgatctacg acgcttcgag ccgggccact ggaatccccg accgcttttc ggggtccggc 660

tcaggaaccg atttcaccct gacaatctca cggctggagc cagaggattt cgccatctat 720

tactgccagc agttcggtac ttcctccggc ctgactttcg gaggcggcac gaagctcgaa 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 244
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 244
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtgga atcgggtggc ggactggtgc agccgggggg ctcacttaga 120

ctgtcctgcg cggccagcgg attcactttc tcctcctacg ccatgtcctg ggtcagacag 180

gcccctggaa agggcctgga atgggtgtcc gcaatcagcg gcagcggcgg ctcgacctat 240

tacgcggatt cagtgaaggg cagattcacc atttcccggg acaacgccaa gaactccttg 300

taccttcaaa tgaactccct ccgcgcggaa gataccgcaa tctactactg cgctcgggcc 360

acttacaaga gggaactgcg ctactactac gggatggacg tctggggcca gggaaccatg 420

gtcaccgtgt ccagcggagg aggaggatcg ggaggaggcg gtagcggggg tggagggtcg 480

gagatcgtga tgacccagtc ccccggcact gtgtcgctgt ccccccggcga acgggccacc 540

ctgtcatgtc gggccagcca gtcagtgtcg tcaagcttcc tcgcctggta ccagcagaaa 600

ccgggacaag ctccccgcct gctgatctac ggagccagca gccgggccac cggtattcct 660

gaccggttct ccggttcggg gtccgggacc gactttactc tgactatctc tcgcctcgag 720

ccagaggact ccgccgtgta ttactgccag cagtaccact cctccccgtc ctggacgttc 780

ggacagggca caaggctgga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 245
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 245
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agcttgtgga aaccggtggc ggactggtgc agcccggagg aagcctcagg 120

ctgtcctgcg ccgcgtccgg cttcaccttc tcctcgtacg ccatgtcctg ggtccgccag 180

gcccccggaa agggcctgga atgggtgtcc gccatctctg gaagcggagg ttccacgtac 240

tacgcggaca gcgtcaaggg aaggttcaca atctcccgcg ataattcgaa gaacactctg 300

taccttcaaa tgaacaccct gaaggccgag gacactgctg tgtactactg cgcacgggcc 360

acctacaaga gagagctccg gtactactac ggaatggacg tctggggcca gggaactact 420

gtgaccgtgt cctcgggagg gggtggctcc gggggggggcg gctccggcgg aggcggttcc 480

gagattgtgc tgacccagtc accttcaact ctgtcgctgt ccccgggaga gagcgctact 540

ctgagctgcc gggccagcca gtccgtgtcc accaccttcc tcgcctggta tcagcagaag 600

ccggggcagg caccacggct cttgatctac gggtcaagca acagagcgac cggaattcct 660

gaccgcttct cggggagcgg ttcaggcacc gacttcaccc tgactatccg gcgcctggaa 720

cccgaagatt tcgccgtgta ttactgtcaa cagtaccact cctcgccgtc ctggaccttt 780

ggccaaggaa ccaaagtgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 246
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 246
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtgga aactggaggt ggactcgtgc agcctggacg gtcgctgcgg 120

ctgagctgcg ctgcatccgg cttcaccttc gacgattatg ccatgcactg ggtcagacag 180

gcgccaggga agggacttga gtgggtgtcc ggtatcagct ggaatagcgg ctcaatcgga 240

tacgcggact ccgtgaaggg aaggttcacc atttcccgcg acaacgccaa gaactccctg 300

tacttgcaaa tgaacagcct ccgggatgag gacactgccg tgtactactg cgcccgcgtc 360

ggaaaagctg tgcccgacgt ctggggccag ggaaccactg tgaccgtgtc cagcggcggg 420

ggtggatcgg gcggtggagg gtccggtgga gggggctcag atattgtgat gacccagacc 480

ccctcgtccc tgtccgcctc ggtcggcgac cgcgtgacta tcacatgtag agcctcgcag 540

agcatctcca gctacctgaa ctggtatcag cagaagccgg ggaaggcccc gaagctcctg 600

atctacgcgg catcatcact gcaatcggga gtgccgagcc ggttttccgg gtccggctcc 660

ggcaccgact tcacgctgac catttcttcc ctgcaacccg aggacttcgc cacttactac 720

tgccagcagt cctactccac cccttactcc ttcggccaag gaaccaggct ggaaatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 247
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 247
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtgga gagcggggga ggattggtgc agcccggaag gtccctgcgg 120

ctctcctgca ctgcgtctgg cttcaccttc gacgactacg cgatgcactg ggtcagacag 180

cgcccgggaa agggcctgga atgggtcgcc tcaatcaact ggaagggaaa ctccctggcc 240

tatggcgaca gcgtgaaggg ccgcttcgcc atttcgcgcg acaacgccaa gaacaccgtg 300

tttctgcaaa tgaattccct gcggaccgag gataccgctg tgtactactg cgccagccac 360

cagggcgtgg catactataa ctacgccatg gacgtgtggg gaagagggac gctcgtcacc 420

gtgtcctccg ggggcggtgg atcgggtgga ggaggaagcg gtggcggggg cagcgaaatc 480

gtgctgactc agagcccggg aactctttca ctgtccccgg gagaacgggc cactctctcg 540

tgccgggcca cccagtccat cggctcctcc ttccttgcct ggtaccagca gaggccagga 600

caggcgcccc gcctgctgat ctacggtgct tcccaacgcg ccactggcat tcctgaccgg 660

ttcagcggca gagggtcggg aaccgatttc acactgacca tttcccgggt ggagcccgaa 720

gattcggcag tctactactg tcagcattac gagtcctccc cttcatggac cttcggtcaa 780

gggaccaaag tggagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 248
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 248
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agttggtcga aagcgggggc gggcttgtgc agcctggcgg atcactgcgg 120

ctgtcctgcg cggcatcagg cttcacgttt tcttcctacg ccatgtcctg ggtgcgccag 180

gcccctggaa agggactgga atgggtgtcc gcgatttcgg ggtccggcgg gagcacctac 240

tacgccgatt ccgtgaaggg ccgcttcact atctcgcggg acaactccaa gaacaccctc 300

tacctccaaa tgaatagcct gcgggccgag gataccgccg tctactattg cgctaaggtc 360

gtgcgcgacg gaatggacgt gtggggacag ggtaccaccg tgacagtgtc ctcgggggga 420

ggcggtagcg gcggaggagg aagcggtggt ggaggttccg agattgtgct gactcaatca 480

cccgcgaccc tgagcctgtc ccccggcgaa agggccactc tgtcctgtcg ggccagccaa 540

tcagtctcct cctcgtacct ggcctggtac cagcagaagc caggacaggc tccgagactc 600

cttatctatg gcgcatcctc ccgcgccacc ggaatcccgg ataggttctc gggaaacgga 660

tcggggaccg acttcactct caccatctcc cggctggaac cggaggactt cgccgtgtac 720

tactgccagc agtacggcag cccgcctaga ttcactttcg gccccggcac caaagtggac 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 249
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 249
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctgctgga gtccggcggt ggattggtgc aaccgggggg atcgctcaga 120

ctgtcctgtg cggcgtcagg cttcaccttc tcgagctacg ccatgtcatg ggtcagacag 180

gcccctggaa agggtctgga atgggtgtcc gccatttccg ggagcggggg atctacatac 240

tacgccgata gcgtgaaggg ccgcttcacc atttcccggg acaactccaa gaacactctc 300

tatctgcaaa tgaactccct ccgcgctgag gacactgccg tgtactactg cgccaaaatc 360

cctcagaccg gcaccttcga ctactgggga caggggactc tggtcaccgt cagcagcggt 420

ggcggaggtt cgggggggagg aggaagcggc ggcggagggt ccgagattgt gctgacccag 480

tcacccggca ctttgtccct gtcgcctgga gaaagggcca ccctttcctg ccgggcatcc 540

caatccgtgt cctcctcgta cctggcctgg taccagcaga ggcccggaca ggccccacgg 600

cttctgatct acggagcaag cagccgcgcg accggtatcc cggaccggtt ttcgggctcg 660

ggctcaggaa ctgacttcac cctcaccatc tcccgcctgg aacccgaaga tttcgctgtg 720

tattactgcc agcactacgg cagctccccg tcctggacgt tcggccaggg aactcggctg 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 250
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 250
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactggtgga aaccggtgga ggactcgtgc agcctggcgg cagcctccgg 120

ctgagctgcg ccgcttcggg attcaccttt tcctcctacg cgatgtcttg ggtcagacag 180

gcccccggaa aggggctgga atgggtgtca gccatctccg gctccggcgg atcaacgtac 240

tacgccgact ccgtgaaagg ccggttcacc atgtcgcgcg agaatgacaa gaactccgtg 300

ttcctgcaaa tgaactccct gagggtggag gacaccggag tgtactattg tgcgcgcgcc 360

aactacaaga gagagctgcg gtactactac ggaatggacg tctggggaca gggaactatg 420

gtgaccgtgt catccggtgg agggggaagc ggcggtggag gcagcggggg cgggggttca 480

gaaattgtca tgacccagtc cccgggaact ctttccctct cccccgggga atccgcgact 540

ttgtcctgcc gggccagcca gcgcgtggcc tcgaactacc tcgcatggta ccagcataag 600

ccaggccaag ccccttccct gctgatttcc ggggctagca gccgcgccac tggcgtgccg 660

gataggttct cgggaagcgg ctcgggtacc gatttcaccc tggcaatctc gcggctggaa 720

ccggaggatt cggccgtgta ctactgccag cactatgact catccccctc ctggacattc 780

ggacagggca ccaaggtcga gatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 251
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 251
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctgctcga aaccggtgga gggctggtgc agccaggggg ctccctgagg 120

ctttcatgcg ccgctagcgg attctccttc tcctcttacg ccatgtcgtg ggtccgccaa 180

gcccctggaa aaggcctgga atgggtgtcc gcgatttccg ggagcggagg ttcgacctat 240

tacgccgact ccgtgaaggg ccgctttacc atctcccggg ataactccaa gaacactctg 300

tacctccaaa tgaactcgct gagagccgag gacaccgccg tgtattactg cgcgaaggcg 360

ctggtcggcg cgactggggc attcgacatc tggggacagg gaactcttgt gaccgtgtcg 420

agcggaggcg gcggctccgg cggaggaggg agcgggggcg gtggttccga aatcgtgttg 480

actcagtccc cgggaaccct gagcttgtca cccggggagc gggccactct ctcctgtcgc 540

gcctcccaat cgctctcatc caatttcctg gcctggtacc agcagaagcc cggacaggcc 600

ccgggcctgc tcatctacgg cgcttcaaac tgggcaacgg gaacccctga tcggttcagc 660

ggaagcggat cgggtactga ctttaccctg accatcacca gactggaacc ggaggacttc 720

gccgtgtact actgccagta ctacggcacc tcccccatgt acacattcgg acagggtacc 780

aaggtcgaga ttaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 252
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 252
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctgcttga gagcggtgga ggtctggtgc agcccggggg atcactgcgc 120

ctgtcctgtg ccgcgtccgg tttcactttc tcctcgtacg ccatgtcgtg ggtcagacag 180

gcaccgggaa agggactgga atgggtgtca gccatttcgg gttcgggggg cagcacctac 240

tacgctgact ccgtgaaggg ccggttcacc atttcccgcg acaactccaa gaacaccttg 300

tacctccaaa tgaactccct gcgggccgaa gataccgccg tgtattactg cgtgctgtgg 360

ttcggagagg gattcgaccc gtggggacaa ggaacactcg tgactgtgtc atccggcgga 420

ggcggcagcg gtggcggcgg ttccggcggc ggcggatctg acatcgtgtt gacccagtcc 480

cctctgagcc tgccggtcac tcctggcgaa ccagccagca tctcctgccg gtcgagccag 540

tccctcctgc actccaatgg gtacaactac ctcgattggt atctgcaaaa gccgggccag 600

agcccccagc tgctgatcta ccttgggtca aaccgcgctt ccggggtgcc tgatagattc 660

tccgggtccg ggagcggaac cgactttacc ctgaaaatct cgagggtgga ggccgaggac 720

gtcggagtgt actactgcat gcaggcgctc cagactcccc tgaccttcgg aggaggaacg 780

aaggtcgaca tcaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 253
<211> 1485
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 253
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtgga gtcaggcgga ggactggtgc agcccggggg ctccctgaga 120

ctttcctgcg cggcatcggg ttttaccttc tcctcctatg ctatgtcctg ggtgcgccag 180

gccccgggaa agggactgga atgggtgtcc gcaatcagcg gtagcggggg ctcaacatac 240

tacgccgact ccgtcaaggg tcgcttcact atttcccggg acaactccaa gaataccctg 300

tacctccaaa tgaacagcct cagggccgag gatactgccg tgtactactg cgccaaagtc 360

ggatacgata gctccggtta ctaccgggac tactacggaa tggacgtgtg gggacagggc 420

accaccgtga ccgtgtcaag cggcggaggc ggttcaggag ggggaggctc cggcggtgga 480

gggtccgaaa tcgtcctgac tcagtcgcct ggcactctgt cgttgtcccc gggggagcgc 540

gctaccctgt cgtgtcgggc gtcgcagtcc gtgtcgagct cctacctcgc gtggtaccag 600

cagaagcccg gacaggcccc tagacttctg atctacggca cttcttcacg cgccaccggg 660

atcagcgaca ggttcagcgg ctccggctcc gggaccgact tcaccctgac cattagccgg 720

ctggagcctg aagatttcgc cgtgtattac tgccaacact acggaaactc gccgccaaag 780

ttcacgttcg gacccggaac caagctggaa atcaagacca ctaccccagc accgaggcca 840

cccaccccgg ctcctaccat cgcctcccag cctctgtccc tgcgtccgga ggcatgtaga 900

cccgcagctg gtggggccgt gcatacccgg ggtcttgact tcgcctgcga tatctacatt 960

tgggcccctc tggctggtac ttgcggggtc ctgctgcttt cactcgtgat cactctttac 1020

tgtaagcgcg gtcggaagaa gctgctgtac atctttaagc aacccttcat gaggcctgtg 1080

cagactactc aagaggagga cggctgttca tgccggttcc cagaggagga ggaaggcggc 1140

tgcgaactgc gcgtgaaatt cagccgcagc gcagatgctc agcctacaa gcaggggcag 1200

aaccagctct acaacgaact caatcttggt cggagagagg agtacgacgt gctggacaag 1260

cggagaggac gggacccaga aatgggcggg aagccgcgca gaaagaatcc ccaagagggc 1320

ctgtacaacg agctccaaaa ggataagatg gcagaagcct atagcgagat tggtatgaaa 1380

ggggaacgca gaagaggcaa aggccacgac ggactgtacc agggactcag caccgccacc 1440

aaggacacct atgacgctct tcacatgcag gccctgccgc ctcgg 1485

<210> 254
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 254
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtcc aactggtgga gtccggggga gggctcgtgc agcccggagg cagccttcgg 120

ctgtcgtgcg ccgcctccgg gttcacgttc tcatcctacg cgatgtcgtg ggtcagacag 180

gcaccaggaa agggactgga atgggtgtcc gccattagcg gctccggcgg tagcacctac 240

tatgccgact cagtgaaggg aaggttcact atctcccgcg acaacagcaa gaacaccctg 300

tacctccaaa tgaactctct gcgggccgag gataccgcgg tgtactattg cgccaagatg 360

ggttggtcca gcggatactt gggagccttc gacatttggg gacagggcac tactgtgacc 420

gtgtcctccg ggggtggcgg atcgggaggc ggcggctcgg gtggaggggg ttccgaaatc 480

gtgttgaccc agtcaccggg aaccctctcg ctgtccccgg gagaacgggc tacactgtca 540

tgtagagcgt cccagtccgt ggcttcctcg ttcctggcct ggtaccagca gaagccggga 600

caggcacccc gcctgctcat ctacggagcc agcggccggg cgaccggcat ccctgaccgc 660

ttctccggtt ccggctcggg caccgacttt actctgacca ttagcaggct tgagcccgag 720

gattttgccg tgtactactg ccaacactac ggggggagcc ctcgcctgac cttcggaggc 780

ggaactaagg tcgatatcaa aaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 255
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 255
Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
50 55 60

```
Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65                  70                  75                  80


Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
                85                  90                  95


Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Leu Val Thr Val Ser Ala
        115                 120


<210> 256
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 256
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15


Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45


Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
    50                  55                  60


Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80
```

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 257
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 257
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala

100 105 110

Leu Thr Val Ser Ser
115

<210> 258
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 258
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 259
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 259
Asp Val Val Met Thr Gln Ser His Arg Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Phe Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Asp Ile Lys
100 105

<210> 260
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 260
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Ser Val Ile
20 25 30

Gly Ala His Leu Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Thr Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp
65 70 75 80

Pro Val Glu Glu Asp Asp Val Ala Ile Tyr Ser Cys Leu Gln Ser Arg
85 90 95

Ile Phe Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 261
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 261
Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Thr Ile Leu

20 25 30

Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
65 70 75 80

Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys Leu Gln Ser Arg
85 90 95

Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 262
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 262
Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Thr Ile Leu
20 25 30

Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr Gly Val Pro Ala
50 55 60

```
Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
65                  70                  75                  80


Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys Leu Gln Ser Arg
                85                  90                  95


Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210> 263
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 263
Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1               5                   10                  15


Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
            20                  25                  30


Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
        35                  40                  45


Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
    50                  55                  60


Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65                  70                  75                  80


Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
                85                  90                  95
```

```
Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Leu Val Thr Val Ser Ala Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser
    130                 135                 140


His Arg Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys
145                 150                 155                 160


Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser Trp Tyr Gln Gln Lys
                165                 170                 175


Pro Gly Gln Ser Pro Lys Leu Leu Ile Phe Ser Ala Ser Tyr Arg Tyr
            180                 185                 190


Thr Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Ala Asp Phe
        195                 200                 205


Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
    210                 215                 220


Cys Gln Gln His Tyr Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240


Leu Asp Ile Lys
```

<210> 264
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 264
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
50 55 60

Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys
130 135 140

Lys Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr
145 150 155 160

Phe Thr Asp Tyr Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly
165 170 175

Leu Lys Trp Met Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr
180 185 190

Ala Tyr Asp Phe Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala
195 200 205

Ser Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala
210 215 220

Thr Tyr Phe Cys Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly
225 230 235 240

Gln Gly Thr Ser Val Thr Val Ser Ser
245

<210> 265
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 265
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr

65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
100 105 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
130 135 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145 150 155 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
195 200 205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
210 215 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 266

<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 266
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
130 135 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145 150 155 160

```
Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180                 185                 190


Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195                 200                 205


Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210                 215                 220


Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240


Glu Ile Lys



<210> 267
<211> 467
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 267
Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1               5                   10                  15


Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
            20                  25                  30


Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
        35                  40                  45
```

```
Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
    50                  55                  60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
                85                  90                  95

Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ala Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser
    130                 135                 140

His Arg Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Gln Ser Pro Lys Leu Leu Ile Phe Ser Ala Ser Tyr Arg Tyr
            180                 185                 190

Thr Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Ala Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
    210                 215                 220

Cys Gln Gln His Tyr Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240
```

```
Leu Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
                245                 250                 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
            260                 265                 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
        275                 280                 285

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
    290                 295                 300

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
        355                 360                 365

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
    370                 375                 380

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
385                 390                 395                 400

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
                405                 410                 415

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
            420                 425                 430
```

```
Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
        435                 440                 445


Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
    450                 455                 460


Pro Pro Arg
465


<210> 268
<211> 472
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 268
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15


Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45


Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
    50                  55                  60


Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
                85                  90                  95
```

```
Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys
    130                 135                 140

Lys Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr
145                 150                 155                 160

Phe Thr Asp Tyr Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly
                165                 170                 175

Leu Lys Trp Met Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr
            180                 185                 190

Ala Tyr Asp Phe Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala
        195                 200                 205

Ser Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala
    210                 215                 220

Thr Tyr Phe Cys Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly
225                 230                 235                 240

Gln Gly Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg
                245                 250                 255

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
            260                 265                 270

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
        275                 280                 285
```

```
Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
    290                 295                 300

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
305                 310                 315                 320

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
                325                 330                 335

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
            340                 345                 350

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
        355                 360                 365

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
    370                 375                 380

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
385                 390                 395                 400

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
                405                 410                 415

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
            420                 425                 430

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
        435                 440                 445

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
    450                 455                 460

His Met Gln Ala Leu Pro Pro Arg
465                 470
```

<210> 269
<211> 466
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 269

```
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15


Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
            20                  25                  30


Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45


Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
    50                  55                  60


Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80


Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
                85                  90                  95


Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
            100                 105                 110


Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
    130                 135                 140


Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
```

```
145                 150                 155                 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180                 185                 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210                 215                 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    290                 295                 300

Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu
305                 310                 315                 320

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
                325                 330                 335

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
```

340 345 350

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
355 360 365

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
370 375 380

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
385 390 395 400

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
405 410 415

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
420 425 430

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
435 440 445

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
450 455 460

Pro Arg
465

<210> 270
<211> 466
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 270
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

```
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
            20                  25                  30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
    50                  55                  60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
                85                  90                  95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
            100                 105                 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
    130                 135                 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145                 150                 155                 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180                 185                 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195                 200                 205
```

```
Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210                 215                 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    290                 295                 300

Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu
305                 310                 315                 320

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
                325                 330                 335

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
            340                 345                 350

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
        355                 360                 365

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
    370                 375                 380

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
385                 390                 395                 400
```

```
Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
                405                 410                 415


Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
            420                 425                 430


Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
        435                 440                 445


Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
    450                 455                 460


Pro Arg
465
```

<210> 271

<400> 271
000

<210> 272

<400> 272
000

<210> 273

<400> 273
000

<210> 274

<400> 274
000

<210> 275

<400> 275
000

<210> 276

<400> 276
000

<210> 277

<400> 277
000

<210> 278

<400> 278
000

<210> 279

<400> 279
000

<210> 280

<400> 280
000

<210> 281

<400> 281
000

<210> 282

<400> 282
000

<210> 283

<400> 283
000

<210> 284

<400> 284
000

<210> 285

<400> 285
000

<210> 286

<400> 286
000

<210> 287

<400> 287
000

<210> 288

<400> 288
000

<210> 289

<400> 289
000

<210> 290

<400> 290
000

<210> 291

<400> 291
000

<210> 292

<400> 292
000

<210> 293

<400> 293
000

<210> 294

<400> 294
000

<210> 295

<400> 295
000

<210> 296

<400> 296
000

<210> 297

<400> 297
000

<210> 298

<400> 298
000

<210> 299

<400> 299
000

<210> 300

<400> 300
000

<210> 301

<400> 301
000

<210> 302

<400> 302
000

<210> 303

<400> 303
000

<210> 304

<400> 304
000

<210> 305

<400> 305
000

<210> 306

<400> 306
000

<210> 307

<400> 307
000

<210> 308

<400> 308
000

<210> 309

<400> 309
000

<210> 310

<400> 310
000

<210> 311

<400> 311
000

<210> 312

<400> 312
000

<210> 313

<400> 313
000

<210> 314

<400> 314
000

<210> 315

<400> 315
000

<210> 316

<400> 316
000

<210> 317

<400> 317
000

<210> 318

<400> 318
000

<210> 319

<400> 319
000

<210> 320

<400> 320
000

<210> 321

<400> 321
000

<210> 322

<400> 322
000

<210> 323

<400> 323
000

<210> 324

<400> 324
000

<210> 325

<400> 325
000

<210> 326

<400> 326
000

<210> 327

<400> 327
000

<210> 328

<400> 328
000

<210> 329

<400> 329
000

<210> 330

<400> 330
000

<210> 331

<400> 331
000

<210> 332

<400> 332
000

<210> 333

<400> 333
000

<210> 334

<400> 334
000

<210> 335

<400> 335
000

<210> 336

<400> 336
000

<210> 337

<400> 337
000

<210> 338

<400> 338
000

<210> 339

<400> 339
000

<210> 340

<400> 340
000

<210> 341

<400> 341
000

<210> 342

<400> 342
000

<210> 343

<400> 343
000

<210> 344

<400> 344
000

<210> 345

<400> 345
000

<210> 346

<400> 346
000

<210> 347

<400> 347
000

<210> 348

<400> 348
000

<210> 349

<400> 349
000

<210> 350

<400> 350
000

<210> 351

<400> 351
000

<210> 352

<400> 352
000

<210> 353

<400> 353
000

<210> 354

<400> 354
000

<210> 355

<400> 355
000

<210> 356

<400> 356
000

<210> 357

<400> 357
000

<210> 358

<400> 358
000

<210> 359

<400> 359
000

<210> 360

<400> 360
000

<210> 361

<400> 361
000

<210> 362

<400> 362
000

<210> 363

<400> 363
000

<210> 364

<400> 364
000

<210> 365

<400> 365
000

<210> 366

<400> 366
000

<210> 367

<400> 367
000

<210> 368

<400> 368
000

<210> 369

<400> 369
000

<210> 370

<400> 370
000

<210> 371

<400> 371
000

<210> 372

<400> 372
000

<210> 373

<400> 373
000

<210> 374

<400> 374
000

<210> 375

<400> 375
000

<210> 376

<400> 376
000

<210> 377

<400> 377
000

<210> 378

<400> 378
000

<210> 379

<400> 379
000

<210> 380

<400> 380
000

<210> 381

<400> 381
000

<210> 382

<400> 382
000

<210> 383

<400> 383
000

<210> 384

<400> 384
000

<210> 385

<400> 385
000

<210> 386

<400> 386
000

<210> 387

<400> 387
000

<210> 388

<400> 388
000

<210> 389

<400> 389
000

<210> 390

<400> 390
000

<210> 391

<400> 391
000

<210> 392
<211> 462
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 392
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val

```
        35                  40                  45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
    210                 215                 220

Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr
```

```
225                 230                 235                 240

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
                245                 250                 255

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
            260                 265                 270

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
        275                 280                 285

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
    290                 295                 300

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
305                 310                 315                 320

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
                325                 330                 335

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
            340                 345                 350

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
        355                 360                 365

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
    370                 375                 380

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
385                 390                 395                 400

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
                405                 410                 415

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
```

420 425 430

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
435 440 445

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
450 455 460

<210> 393
<211> 445
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 393
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

```
Val Ser Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala
        115                 120                 125

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
    130                 135                 140

Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
145                 150                 155                 160

Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg
                165                 170                 175

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
            180                 185                 190

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser
        195                 200                 205

Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr
    210                 215                 220

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
225                 230                 235                 240

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
                245                 250                 255

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
            260                 265                 270

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
        275                 280                 285

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
    290                 295                 300
```

```
Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
305                 310                 315                 320

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
                325                 330                 335

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
            340                 345                 350

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
        355                 360                 365

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
    370                 375                 380

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
385                 390                 395                 400

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
                405                 410                 415

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
            420                 425                 430

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
        435                 440                 445


<210> 394

<400> 394
000


<210> 395

<400> 395
000
```

<210> 396

<400> 396
000

<210> 397

<400> 397
000

<210> 398

<400> 398
000

<210> 399

<400> 399
000

<210> 400

<400> 400
000

<210> 401

<400> 401
000

<210> 402

<400> 402
000

<210> 403

<400> 403
000

<210> 404

<400> 404
000

<210> 405

<400> 405
000

<210> 406

<400> 406
000

<210> 407

<400> 407
000

<210> 408

<400> 408
000

<210> 409

<400> 409
000

<210> 410

<400> 410
000

<210> 411

<400> 411
000

<210> 412

<400> 412
000

<210> 413

<400> 413
000

<210> 414

<400> 414
000

<210> 415

<400> 415
000

<210> 416

<400> 416
000

<210> 417

<400> 417
000

<210> 418

<400> 418
000

<210> 419

<400> 419
000

<210> 420

<400> 420
000

<210> 421

<400> 421
000

<210> 422

<400> 422
000

<210> 423

<400> 423
000

<210> 424

<400> 424
000

<210> 425

<400> 425
000

<210> 426

<400> 426
000

<210> 427

<400> 427
000

<210> 428

<400> 428
000

<210> 429

<400> 429
000

<210> 430

<400> 430
000

<210> 431

<400> 431
000

<210> 432

<400> 432
000

<210> 433

<400> 433
000

<210> 434

<400> 434
000

<210> 435

<400> 435
000

<210> 436

<400> 436
000

<210> 437

<400> 437
000

<210> 438

<400> 438
000

<210> 439

<400> 439
000

<210> 440

<400> 440
000

<210> 441

<400> 441
000

<210> 442

<400> 442
000

<210> 443

<400> 443
000

<210> 444

<400> 444
000

<210> 445

<400> 445
000

<210> 446

<400> 446
000

<210> 447

<400> 447
000

<210> 448

<400> 448
000

<210> 449

<400> 449
000

<210> 450

<400> 450
000

<210> 451

<400> 451
000

<210> 452

<400> 452
000

<210> 453

<400> 453
000

<210> 454

<400> 454
000

<210> 455

<400> 455
000

<210> 456

<400> 456
000

<210> 457

<400> 457
000

<210> 458

<400> 458
000

<210> 459

<400> 459
000

<210> 460

<400> 460
000

<210> 461

<400> 461
000

<210> 462

<400> 462
000

<210> 463

<400> 463
000

<210> 464

<400> 464
000

<210> 465

<400> 465
000

<210> 466

<400> 466
000

<210> 467

<400> 467
000

<210> 468

<400> 468
000

<210> 469

<400> 469
000

<210> 470

<400> 470
000

<210> 471

<400> 471
000

<210> 472

<400> 472
000

<210> 473

<400> 473
000

<210> 474

<400> 474
000

<210> 475

<400> 475
000

<210> 476

<400> 476
000

<210> 477

<400> 477
000

<210> 478

<400> 478
000

<210> 479

<400> 479
000

<210> 480

<400> 480
000

<210> 481

<400> 481
000

<210> 482

<400> 482
000

<210> 483

<400> 483
000

<210> 484

<400> 484
000

<210> 485

<400> 485
000

<210> 486

<400> 486
000

<210> 487

<400> 487
000

<210> 488

<400> 488
000

<210> 489

<400> 489
000

<210> 490

<400> 490
000

<210> 491

<400> 491
000

<210> 492

<400> 492
000

<210> 493

<400> 493
000

<210> 494

<400> 494
000

<210> 495

<400> 495
000

<210> 496

<400> 496
000

<210> 497

<400> 497
000

<210> 498

<400> 498
000

<210> 499

<400> 499
000

<210> 500

<400> 500
000

<210> 501
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 501
Thr Tyr Trp Met His
1 5

<210> 502
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 502
Asn Ile Tyr Pro Gly Thr Gly Gly Ser Asn Phe Asp Glu Lys Phe Lys
1 5 10 15

Asn

<210> 503
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 503
Trp Thr Thr Gly Thr Gly Ala Tyr
1 5

<210> 504
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 504
Gly Tyr Thr Phe Thr Thr Tyr
1 5

<210> 505
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 505
Tyr Pro Gly Thr Gly Gly
1 5

<210> 506
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 506
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1   5   10   15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Thr Tyr
            20   25   30

Trp Met His Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Asn Ile Tyr Pro Gly Thr Gly Gly Ser Asn Phe Asp Glu Lys Phe
    50   55   60

Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Thr Arg Trp Thr Thr Gly Thr Gly Ala Tyr Trp Gly Gln Gly Thr Thr
            100   105   110

Val Thr Val Ser Ser
        115

<210> 507
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 507
gaggtgcagc tggtgcagtc aggcgccgaa gtgaagaagc ccggcgagtc actgagaatt   60

agctgtaaag gttcaggcta caccttcact acctactgga tgcactgggt ccgccaggct   120

accggtcaag gcctcgagtg gatgggtaat atctaccccg gcaccggcgg ctctaacttc 180

gacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcac taggtggact 300

accggcacag gcgcctactg gggtcaaggc actaccgtga ccgtgtctag c 351

<210> 508
<211> 443
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 508

Glu	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Glu
1				5				10					15		
Ser	Leu	Arg	Ile	Ser	Cys	Lys	Gly	Ser	Gly	Tyr	Thr	Phe	Thr	Thr	Tyr
			20					25					30		
Trp	Met	His	Trp	Val	Arg	Gln	Ala	Thr	Gly	Gln	Gly	Leu	Glu	Trp	Met
		35					40					45			
Gly	Asn	Ile	Tyr	Pro	Gly	Thr	Gly	Gly	Ser	Asn	Phe	Asp	Glu	Lys	Phe
	50					55					60				
Lys	Asn	Arg	Val	Thr	Ile	Thr	Ala	Asp	Lys	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Thr	Arg	Trp	Thr	Thr	Gly	Thr	Gly	Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Thr
			100					105					110		

```
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125


Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
    130                 135                 140


Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160


Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175


Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190


Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
        195                 200                 205


Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
    210                 215                 220


Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
225                 230                 235                 240


Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
                245                 250                 255


Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
            260                 265                 270


Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
        275                 280                 285


Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
    290                 295                 300
```

```
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305                 310                 315                 320


Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
                325                 330                 335


Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
            340                 345                 350


Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
        355                 360                 365


Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
    370                 375                 380


Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
385                 390                 395                 400


Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
                405                 410                 415


Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
            420                 425                 430


Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440


<210> 509
<211> 1329
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 509
```

gaggtgcagc tggtgcagtc aggcgccgaa gtgaagaagc ccggcgagtc actgagaatt 60

agctgtaaag gttcaggcta caccttcact acctactgga tgcactgggt ccgccaggct 120

accggtcaag gcctcgagtg gatgggtaat atctaccccg gcaccggcgg ctctaacttc 180

gacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcac taggtggact 300

accggcacag gcgcctactg gggtcaaggc actaccgtga ccgtgtctag cgctagcact 360

aagggcccgt ccgtgttccc cctggcacct tgtagccgga gcactagcga atccaccgct 420

gccctcggct gcctggtcaa ggattacttc ccggagcccg tgaccgtgtc ctggaacagc 480

ggagccctga cctccggagt gcacaccttc cccgctgtgc tgcagagctc cgggctgtac 540

tcgctgtcgt cggtggtcac ggtgccttca tctagcctgg gtaccaagac ctacacttgc 600

aacgtggacc acaagccttc caacactaag gtggacaagc gcgtcgaatc gaagtacggc 660

ccaccgtgcc cgccttgtcc cgcgccggag ttcctcggcg gtccctcggt ctttctgttc 720

ccaccgaagc ccaaggacac tttgatgatt tcccgcaccc ctgaagtgac atgcgtggtc 780

gtggacgtgt cacaggaaga tccggaggtg cagttcaatt ggtacgtgga tggcgtcgag 840

gtgcacaacg ccaaaaccaa gccgagggag gagcagttca actccactta ccgcgtcgtg 900

tccgtgctga cggtgctgca tcaggactgg ctgaacggga aggagtacaa gtgcaaagtg 960

tccaacaagg gacttcctag ctcaatcgaa aagaccatct cgaaagccaa gggacagccc 1020

cgggaacccc aagtgtatac cctgccaccg agccaggaag aaatgactaa gaaccaagtc 1080

tcattgactt gccttgtgaa gggcttctac ccatcggata tcgccgtgga atgggagtcc 1140

aacggccagc cggaaaacaa ctacaagacc acccctccgg tgctggactc agacggatcc 1200

ttcttcctct actcgcggct gaccgtggat aagagcagat ggcaggaggg aaatgtgttc 1260

agctgttctg tgatgcatga agccctgcac aaccactaca ctcagaagtc cctgtccctc 1320

tccctggga 1329

<210> 510

<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 510
Lys Ser Ser Gln Ser Leu Leu Asp Ser Gly Asn Gln Lys Asn Phe Leu
1 5 10 15

Thr

<210> 511
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 511
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 512
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 512
Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr
1 5

<210> 513
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 513
Ser Gln Ser Leu Leu Asp Ser Gly Asn Gln Lys Asn Phe
1 5 10

<210> 514
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 514
Trp Ala Ser
1

<210> 515
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 515
Asp Tyr Ser Tyr Pro Tyr
1 5

<210> 516
<211> 113
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 516
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Lys
35 40 45

Ala Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65 70 75 80

Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 517
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 517
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg taaagcccct aagctgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tgcagcccga ggatatcgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaag 339

<210> 518
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 518
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Lys
35 40 45

Ala Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65 70 75 80

Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Asn

85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145 150 155 160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
165 170 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 519
<211> 660
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 519
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg taaagcccct aagctgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tgcagcccga ggatatcgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaagc gtacggtggc cgctcccagc 360

gtgttcatct tccccccag cgacgagcag ctgaagagcg gcaccgccag cgtggtgtgc 420

ctgctgaaca acttctaccc ccgggaggcc aaggtgcagt ggaaggtgga caacgccctg 480

cagagcggca acagccagga gagcgtcacc gagcaggaca gcaaggactc cacctacagc 540

ctgagcagca ccctgaccct gagcaaggcc gactacgaga agcataaggt gtacgcctgc 600

gaggtgaccc accagggcct gtccagcccc gtgaccaaga gcttcaacag gggcgagtgc 660

<210> 520
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 520
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ala Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65 70 75 80

Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 521
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 521
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg tcaagccccct agactgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tggaagccga ggacgccgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaag 339

<210> 522
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 522

```
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20                  25                  30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45

Ala Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65                  70                  75                  80

Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Asn
                85                  90                  95

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145                 150                 155                 160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
```

180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 523
<211> 660
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 523
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg tcaagcccct agactgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tggaagccga ggacgccgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaagc gtacggtggc cgctcccagc 360

gtgttcatct tccccccag cgacgagcag ctgaagagcg gcaccgccag cgtggtgtgc 420

ctgctgaaca acttctaccc ccgggaggcc aaggtgcagt ggaaggtgga caacgccctg 480

cagagcggca acagccagga gagcgtcacc gagcaggaca gcaaggactc cacctacagc 540

ctgagcagca ccctgaccct gagcaaggcc gactacgaga agcataaggt gtacgcctgc 600

gaggtgaccc accagggcct gtccagcccc gtgaccaaga gcttcaacag gggcgagtgc 660

<210> 524
<211> 15
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 524
acctactgga tgcac 15

<210> 525
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 525
aatatctacc ccggcaccgg cggctctaac ttcgacgaga agtttaagaa t 51

<210> 526
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 526
tggactaccg gcacaggcgc ctac 24

<210> 527
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 527
ggctacacct tcactaccta c 21

<210> 528
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 528
taccccggca ccggcggc 18

<210> 529
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 529
aaatctagtc agtcactgct ggatagcggt aatcagaaga acttcctgac c 51

<210> 530
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 530
tgggcctcta ctagagaatc a 21

<210> 531

<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 531
cagaacgact atagctaccc ctacacc 27

<210> 532
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 532
agtcagtcac tgctggatag cggtaatcag aagaacttc 39

<210> 533
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 533
tgggcctct 9

<210> 534
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 534
gactatagct acccctac 18

<210> 535
<211> 440
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 535
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
115 120 125

```
Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys
            180                 185                 190

Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala
    210                 215                 220

Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
225                 230                 235                 240

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
                245                 250                 255

Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val
            260                 265                 270

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
        275                 280                 285

Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
    290                 295                 300

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
305                 310                 315                 320
```

```
Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
                325                 330                 335

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr
            340                 345                 350

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
        355                 360                 365

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
    370                 375                 380

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
385                 390                 395                 400

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
                405                 410                 415

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
            420                 425                 430

Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440


<210> 536
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 536
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15
```

```
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
```

```
Phe Asn Arg Gly Glu Cys
    210


<210> 537
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 537
Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30


Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
    50                  55                  60


Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125
```

```
Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320
```

```
Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335


Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350


Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365


Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380


Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400


Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440                 445


<210> 538
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 538
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
```

```
            20                  25                  30

Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
        35                  40                  45

Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg
                85                  90                  95

Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
```

210 215

<210> 539
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 539
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Gln Trp Met
35 40 45

Gly Trp Ile Asn Thr Asp Ser Gly Glu Ser Thr Tyr Ala Glu Glu Phe
50 55 60

Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Asn Thr Ala Tyr
65 70 75 80

Leu Gln Ile Thr Ser Leu Thr Ala Glu Asp Thr Gly Met Tyr Phe Cys
85 90 95

Val Arg Val Gly Tyr Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140

```
Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335
```

```
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350


Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365


Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380


Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400


Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> 540
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 540
Glu Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Ser Ala Arg Ser Ser Val Ser Tyr Met
            20                  25                  30
```

```
His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr
        35                  40                  45

Arg Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60

Gly Ser Gly Thr Ser Tyr Cys Leu Thr Ile Asn Ser Leu Gln Pro Glu
65                  70                  75                  80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Phe Pro Leu Thr
                85                  90                  95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205

Asn Arg Gly Glu Cys
    210
```

<210> 541
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 541
Gly Tyr Thr Phe Thr Thr Tyr Trp Met His
1 5 10

<210> 542

<400> 542
000

<210> 543

<400> 543
000

<210> 544

<400> 544
000

<210> 545

<400> 545
000

<210> 546

<400> 546
000

<210> 547

<400> 547
000

<210> 548

<400> 548
000

<210> 549

<400> 549
000

<210> 550

<400> 550
000

<210> 551

<400> 551
000

<210> 552

<400> 552
000

<210> 553

<400> 553
000

<210> 554

<400> 554
000

<210> 555

<400> 555
000

<210> 556

<400> 556
000

<210> 557

<400> 557
000

<210> 558

<400> 558
000

<210> 559

<400> 559
000

<210> 560

<400> 560
000

<210> 561

<400> 561
000

<210> 562

<400> 562
000

<210> 563

<400> 563
000

<210> 564

<400> 564
000

<210> 565

<400> 565
000

<210> 566

<400> 566
000

<210> 567

<400> 567
000

<210> 568

<400> 568
000

<210> 569

<400> 569
000

<210> 570

<400> 570
000

<210> 571

<400> 571
000

<210> 572

<400> 572
000

<210> 573

<400> 573
000

<210> 574

<400> 574
000

<210> 575

<400> 575
000

<210> 576

<400> 576
000

<210> 577

<400> 577
000

<210> 578

<400> 578
000

<210> 579

<400> 579
000

<210> 580

<400> 580
000

<210> 581

<400> 581
000

<210> 582

<400> 582
000

<210> 583

<400> 583
000

<210> 584

<400> 584
000

<210> 585

<400> 585
000

<210> 586

<400> 586
000

<210> 587

<400> 587
000

<210> 588

<400> 588
000

<210> 589

<400> 589
000

<210> 590

<400> 590
000

<210> 591

<400> 591
000

<210> 592

<400> 592
000

<210> 593

<400> 593
000

<210> 594

<400> 594
000

<210> 595

<400> 595
000

<210> 596

<400> 596
000

<210> 597

<400> 597
000

<210> 598

<400> 598
000

<210> 599

<400> 599
000

<210> 600

<400> 600
000

<210> 601
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 601
Ser Tyr Trp Met Tyr
1 5

<210> 602
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 602
Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe Lys
1 5 10 15

Asn

<210> 603
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 603
Asp Tyr Arg Lys Gly Leu Tyr Ala Met Asp Tyr
1 5 10

<210> 604
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 604
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 605
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 605
Asp Pro Asn Ser Gly Ser
1 5

<210> 606
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 606
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Tyr Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
35 40 45

Gly Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Asn Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Arg Lys Gly Leu Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 607
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 607
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

agagggcaaa gactggagtg gatcggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag gttcactatt agtagggata actctaagaa caccctgtac 240

ctgcagatga atagcctgag agccgaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

<210> 608
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 608
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

```
1               5                   10                  15

Thr Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Tyr Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Asn Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Tyr Arg Lys Gly Leu Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
```

```
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
```

385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
435 440 445

<210> 609
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 609
Lys Ala Ser Gln Asp Val Gly Thr Ala Val Ala
1 5 10

<210> 610
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 610
Trp Ala Ser Thr Arg His Thr
1 5

<210> 611
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 611
Gln Gln Tyr Asn Ser Tyr Pro Leu Thr
1 5

<210> 612
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 612
Ser Gln Asp Val Gly Thr Ala
1 5

<210> 613
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 613
Trp Ala Ser
1

<210> 614
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 614
Tyr Asn Ser Tyr Pro Leu
1 5

<210> 615
<211> 1338
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 615
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

agagggcaaa gactggagtg gatcggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag gttcactatt agtagggata actctaagaa caccctgtac 240

ctgcagatga atagcctgag agccgaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

gctagcacta agggcccgtc cgtgttcccc ctggcacctt gtagccggag cactagcgaa 420

tccaccgctg ccctcggctg cctggtcaag gattacttcc cggagcccgt gaccgtgtcc 480

tggaacagcg gagccctgac ctccggagtg cacaccttcc ccgctgtgct gcagagctcc 540

gggctgtact cgctgtcgtc ggtggtcacg gtgccttcat ctagcctggg taccaagacc 600

tacacttgca acgtggacca caagccttcc aacactaagg tggacaagcg cgtcgaatcg 660

aagtacggcc caccgtgccc gccttgtccc gcgccggagt tcctcggcgg tccctcggtc 720

tttctgttcc caccgaagcc caaggacact ttgatgattt cccgcacccc tgaagtgaca 780

tgcgtggtcg tggacgtgtc acaggaagat ccggaggtgc agttcaattg gtacgtggat 840

ggcgtcgagg tgcacaacgc caaaaccaag ccgagggagg agcagttcaa ctccacttac 900

cgcgtcgtgt ccgtgctgac ggtgctgcat caggactggc tgaacgggaa ggagtacaag 960

tgcaaagtgt ccaacaaggg acttcctagc tcaatcgaaa agaccatctc gaaagccaag 1020

ggacagcccc gggaacccca agtgtatacc ctgccaccga gccaggaaga aatgactaag 1080

aaccaagtct cattgacttg ccttgtgaag ggcttctacc catcggatat cgccgtggaa 1140

tgggagtcca acggccagcc ggaaaacaac tacaagacca cccctccggt gctggactca 1200

gacggatcct tcttcctcta ctcgcggctg accgtggata agagcagatg gcaggaggga 1260

aatgtgttca gctgttctgt gatgcatgaa gccctgcaca accactacac tcagaagtcc 1320

ctgtccctct ccctggga 1338

<210> 616
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 616
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
20 25 30

Val Ala Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 617
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 617
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta aagcctctca ggacgtgggc accgccgtgg cctggtatct gcagaagcct 120

ggtcaatcac ctcagctgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgac ttcaccttca ctatctcttc actggaagcc 240

gaggacgccg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 618
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 618
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

```
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
            20                  25                  30

Val Ala Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65                  70                  75                  80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
```

Phe Asn Arg Gly Glu Cys
210

<210> 619
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 619
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta aagcctctca ggacgtgggc accgccgtgg cctggtatct gcagaagcct 120

ggtcaatcac ctcagctgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgac ttcaccttca ctatctcttc actggaagcc 240

gaggacgccg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 620
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 620
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Thr Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Trp Met Tyr Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe
    50   55   60

Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Asp Tyr Arg Lys Gly Leu Tyr Ala Met Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 621
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 621
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

accggtcaag gcctggagtg gatgggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

<210> 622
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 622
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Tyr Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Arg Lys Gly Leu Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

```
Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300
```

```
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320


Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335


Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350


Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365


Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380


Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400


Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440                 445


<210> 623
<211> 1338
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 623
```

gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

accggtcaag gcctggagtg gatgggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

gctagcacta agggcccgtc cgtgttcccc ctggcacctt gtagccggag cactagcgaa 420

tccaccgctg ccctcggctg cctggtcaag gattacttcc cggagcccgt gaccgtgtcc 480

tggaacagcg gagccctgac ctccggagtg cacaccttcc ccgctgtgct gcagagctcc 540

gggctgtact cgctgtcgtc ggtggtcacg gtgccttcat ctagcctggg taccaagacc 600

tacacttgca acgtggacca caagccttcc aacactaagg tggacaagcg cgtcgaatcg 660

aagtacggcc caccgtgccc gccttgtccc gcgccggagt tcctcggcgg tccctcggtc 720

tttctgttcc caccgaagcc caaggacact ttgatgattt cccgcacccc tgaagtgaca 780

tgcgtggtcg tggacgtgtc acaggaagat ccggaggtgc agttcaattg gtacgtggat 840

ggcgtcgagg tgcacaacgc caaaaccaag ccgagggagg agcagttcaa ctccacttac 900

cgcgtcgtgt ccgtgctgac ggtgctgcat caggactggc tgaacgggaa ggagtacaag 960

tgcaaagtgt ccaacaaggg acttcctagc tcaatcgaaa agaccatctc gaaagccaag 1020

ggacagcccc gggaacccca agtgtatacc ctgccaccga gccaggaaga aatgactaag 1080

aaccaagtct cattgacttg ccttgtgaag ggcttctacc catcggatat cgccgtggaa 1140

tgggagtcca acggccagcc ggaaaacaac tacaagacca cccctccggt gctggactca 1200

gacggatcct tcttcctcta ctcgcggctg accgtggata agagcagatg gcaggaggga 1260

aatgtgttca gctgttctgt gatgcatgaa gccctgcaca accactacac tcagaagtcc 1320

ctgtccctct ccctggga 1338

<210> 624

<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 624
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 625
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 625
gacgtcgtga tgactcagtc acccctgagc ctgcccgtga ccctggggca gcccgcctct 60

attagctgta aagcctctca ggacgtgggc accgccgtgg cctggtatca gcagaagcca 120

gggcaagccc ctagactgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctcttc actgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 626
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 626
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
85 90 95

```
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160


Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175


Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190


Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205


Phe Asn Arg Gly Glu Cys
    210


<210> 627
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 627
gacgtcgtga tgactcagtc acccctgagc ctgcccgtga ccctggggca gcccgcctct       60

attagctgta aagcctctca ggacgtgggc accgccgtgg cctggtatca gcagaagcca      120
```

gggcaagccc ctagactgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctcttc actgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 628
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 628
agctactgga tgtac 15

<210> 629
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 629
agaatcgacc ctaatagcgg ctctactaag tataacgaga agtttaagaa t 51

<210> 630

<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 630
gactatagaa agggcctgta cgctatggac tac 33

<210> 631
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 631
ggctacacct tcactagcta c 21

<210> 632
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 632
gaccctaata gcggctct 18

<210> 633
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 633
aaagcctctc aggacgtggg caccgccgtg gcc 33

<210> 634
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 634
tgggcctcta ctagacacac c 21

<210> 635
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 635
cagcagtata atagctaccc cctgacc 27

<210> 636
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 636
tctcaggacg tgggcaccgc c 21

<210> 637
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 637
tgggcctct 9

<210> 638
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 638
tataatagct acccctg 18

<210> 639
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 639
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Ser
20 25 30

```
Trp Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Trp Ile Ser Pro Tyr Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg His Trp Pro Gly Gly Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220
```

```
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240


Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255


Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270


Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285


Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val
    290                 295                 300


Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320


Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335


Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350


Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365


Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380


Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400


Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
```

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 640
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 640
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Leu Tyr His Pro Ala
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly

115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 641
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 641
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ile Met Met Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Ser Ile Tyr Pro Ser Gly Gly Ile Thr Phe Tyr Ala Asp Thr Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ile Lys Leu Gly Thr Val Thr Thr Val Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240
```

```
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430
```

```
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445


Gly Lys
    450


<210> 642
<211> 216
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 642
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15


Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20                  25                  30


Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45


Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60


Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80


Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95


Ser Thr Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Gln
            100                 105                 110
```

```
Pro Lys Ala Asn Pro Thr Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
        115                 120                 125


Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
    130                 135                 140


Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Gly Ser Pro Val Lys
145                 150                 155                 160


Ala Gly Val Glu Thr Thr Lys Pro Ser Lys Gln Ser Asn Asn Lys Tyr
                165                 170                 175


Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
            180                 185                 190


Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
        195                 200                 205


Thr Val Ala Pro Thr Glu Cys Ser
    210                 215


<210> 643
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 643
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
            20                  25                  30
```

```
Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Gly Gly Trp Phe Gly Glu Leu Ala Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
    210                 215                 220
```

```
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly
225                 230                 235                 240


Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255


Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270


Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285


His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300


Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320


Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile
                325                 330                 335


Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350


Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365


Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380


Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400


Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415
```

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 644
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 644
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Leu Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala

100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 645
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 645
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Thr Ser Gly Asp Thr Phe Ser Thr Tyr
20 25 30

```
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Gly Ile Ile Pro Ile Phe Gly Lys Ala His Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95

Ala Arg Lys Phe His Phe Val Ser Gly Ser Pro Phe Gly Met Asp Val
            100                 105                 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 646
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 646
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45
```

```
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Thr
                85                  90                  95


Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 647
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 647
Gly Tyr Thr Phe Thr Ser Tyr Trp Met Tyr
1               5                   10


<210> 648

<400> 648
000


<210> 649

<400> 649
000


<210> 650

<400> 650
000
```

<210> 651

<400> 651
000

<210> 652

<400> 652
000

<210> 653

<400> 653
000

<210> 654

<400> 654
000

<210> 655

<400> 655
000

<210> 656

<400> 656
000

<210> 657

<400> 657
000

<210> 658

<400> 658
000

<210> 659

<400> 659
000

<210> 660

<400> 660
000

<210> 661

<400> 661
000

<210> 662

<400> 662
000

<210> 663

<400> 663
000

<210> 664

<400> 664
000

<210> 665

<400> 665
000

<210> 666

<400> 666
000

<210> 667

<400> 667
000

<210> 668

<400> 668
000

<210> 669

<400> 669
000

<210> 670

<400> 670
000

<210> 671

<400> 671
000

<210> 672

<400> 672
000

<210> 673

<400> 673
000

<210> 674

<400> 674
000

<210> 675

<400> 675
000

<210> 676

<400> 676
000

<210> 677

<400> 677
000

<210> 678

<400> 678
000

<210> 679

<400> 679
000

<210> 680

<400> 680
000

<210> 681

<400> 681
000

<210> 682

<400> 682
000

<210> 683

<400> 683
000

<210> 684

<400> 684
000

<210> 685

<400> 685
000

<210> 686

<400> 686
000

<210> 687

<400> 687
000

<210> 688

<400> 688
000

<210> 689

<400> 689
000

<210> 690

<400> 690
000

<210> 691

<400> 691
000

<210> 692

<400> 692
000

<210> 693

<400> 693
000

<210> 694

<400> 694
000

<210> 695

<400> 695
000

<210> 696

<400> 696
000

<210> 697

<400> 697
000

<210> 698

<400> 698
000

<210> 699

<400> 699
000

<210> 700

<400> 700
000

<210> 701
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 701
Asn Tyr Gly Met Asn
1 5

<210> 702
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 702
Trp Ile Asn Thr Asp Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 703
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 703
Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met Asp Tyr
1 5 10 15

<210> 704
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 704
Gly Phe Thr Leu Thr Asn Tyr
1 5

<210> 705
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 705
Asn Thr Asp Thr Gly Glu
1 5

<210> 706
<211> 125
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 706
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Leu Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
35 40 45

Gly Trp Ile Asn Thr Asp Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 707
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 707
caagtgcagc tggtgcagtc gggagccgaa gtgaagaagc ctggagcctc ggtgaaggtg 60

tcgtgcaagg catccggatt caccctcacc aattacggga tgaactgggt cagacaggcc 120

cggggtcaac ggctggagtg gatcggatgg attaacaccg acaccgggga gcctacctac 180

gcggacgatt tcaagggacg gttcgtgttc tccctcgaca cctccgtgtc caccgcctac 240

ctccaaatct cctcactgaa agcggaggac accgccgtgt actattgcgc gaggaacccg 300

ccctactact acggaaccaa caacgccgaa gccatggact actggggcca gggcaccact 360

gtgactgtgt ccagc 375

<210> 708
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 708
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

aggggccagc ggctggaatg gatcggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctct 375

<210> 709
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 709
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Leu Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
35 40 45

Gly Trp Ile Asn Thr Asp Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
115 120 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
130 135 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145 150 155 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His

```
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys
        195                 200                 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser
                325                 330                 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
```

```
        355                 360                 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr
                405                 410                 415

Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Leu Gly
    450


<210> 710
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 710
Ser Ser Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1               5                   10


<210> 711
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
```

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 711
Tyr Thr Ser Thr Leu His Leu
1 5

<210> 712
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 712
Gln Gln Tyr Tyr Asn Leu Pro Trp Thr
1 5

<210> 713
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 713
Ser Gln Asp Ile Ser Asn Tyr
1 5

<210> 714
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 714
Tyr Thr Ser
1

<210> 715
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 715
Tyr Tyr Asn Leu Pro Trp
1 5

<210> 716
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 716
caagtgcagc tggtgcagtc gggagccgaa gtgaagaagc ctggagcctc ggtgaaggtg 60

tcgtgcaagg catccggatt caccctcacc aattacggga tgaactgggt cagacaggcc 120

cggggtcaac ggctggagtg gatcggatgg attaacaccg acaccgggga gcctacctac 180

gcggacgatt tcaagggacg gttcgtgttc tccctcgaca cctccgtgtc caccgcctac 240

ctccaaatct cctcactgaa agcggaggac accgccgtgt actattgcgc gaggaacccg 300

ccctactact acggaaccaa caacgccgaa gccatggact actggggcca gggcaccact 360

gtgactgtgt ccagcgcgtc cactaagggc ccgtccgtgt tccccctggc accttgtagc 420

cggagcacta gcgaatccac cgctgccctc ggctgcctgg tcaaggatta cttcccggag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgacctccg gagtgcacac cttccccgct 540

gtgctgcaga gctccgggct gtactcgctg tcgtcggtgg tcacggtgcc ttcatctagc 600

ctgggtacca agacctacac ttgcaacgtg gaccacaagc cttccaacac taaggtggac 660

aagcgcgtcg aatcgaagta cggcccaccg tgcccgcctt gtcccgcgcc ggagttcctc 720

ggcggtccct cggtctttct gttcccaccg aagcccaagg acactttgat gatttcccgc 780

acccctgaag tgacatgcgt ggtcgtggac gtgtcacagg aagatccgga ggtgcagttc 840

aattggtacg tggatggcgt cgaggtgcac aacgccaaaa ccaagccgag ggaggagcag 900

ttcaactcca cttaccgcgt cgtgtccgtg ctgacggtgc tgcatcagga ctggctgaac 960

gggaaggagt acaagtgcaa agtgtccaac aagggacttc ctagctcaat cgaaaagacc 1020

atctcgaaag ccaagggaca gccccgggaa ccccaagtgt ataccctgcc accgagccag 1080

gaagaaatga ctaagaacca agtctcattg acttgccttg tgaagggctt ctacccatcg 1140

gatatcgccg tggaatggga gtccaacggc cagccggaaa acaactacaa gaccacccct 1200

ccggtgctgg actcagacgg atccttcttc ctctactcgc ggctgaccgt ggataagagc 1260

agatggcagg agggaaatgt gttcagctgt tctgtgatgc atgaagccct gcacaaccac 1320

tacactcaga agtccctgtc cctctccctg gga 1353

<210> 717
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 717
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

aggggccagc ggctggaatg gatcggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctctgcttc taccaagggg cccagcgtgt tccccctggc cccctgctcc 420

agaagcacca gcgagagcac agccgccctg ggctgcctgg tgaaggacta cttccccgag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgaccagcg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgaccgtgcc cagcagcagc 600

ctgggcacca agacctacac ctgtaacgtg gaccacaagc ccagcaacac caaggtggac 660

aagagggtgg agagcaagta cggcccaccc tgccccccct gcccagcccc cgagttcctg 720

ggcggaccca gcgtgttcct gttccccccc aagcccaagg acaccctgat gatcagcaga 780

acccccgagg tgacctgtgt ggtggtggac gtgtcccagg aggaccccga ggtccagttc 840

aactggtacg tggacggcgt ggaggtgcac aacgccaaga ccaagcccag agaggagcag 900

tttaacagca cctaccgggt ggtgtccgtg ctgaccgtgc tgcaccagga ctggctgaac 960

ggcaaagagt acaagtgtaa ggtctccaac aagggcctgc caagcagcat cgaaaagacc 1020

atcagcaagg ccaagggcca gcctagagag ccccaggtct acaccctgcc acccagccaa 1080

gaggagatga ccaagaacca ggtgtccctg acctgtctgg tgaagggctt ctacccaagc 1140

gacatcgccg tggagtggga gagcaacggc cagcccgaga acaactacaa gaccaccccc 1200

ccagtgctgg acagcgacgg cagcttcttc ctgtacagca ggctgaccgt ggacaagtcc 1260

agatggcagg agggcaacgt ctttagctgc tccgtgatgc acgaggccct gcacaaccac 1320

tacacccaga agagcctgag cctgtccctg ggc 1353

<210> 718
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 718
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 719
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 719
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gctctagtca ggatatctct aactacctga actggtatct gcagaagccc 120

ggtcaatcac ctcagctgct gatctactac actagcaccc tgcacctggg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctctag cctgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 720
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 720
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatct gcagaagccc 120

ggccagtccc ctcagctgct gatctactac acctccaccc tgcacctggg cgtgccctcc 180

agattttccg gctctggctc tggcaccgag tttaccctga ccatcagctc cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa g 321

<210> 721
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 721
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr

```
            20                  25                  30

Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
```

210

<210> 722
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 722
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gctctagtca ggatatctct aactacctga actggtatct gcagaagccc 120

ggtcaatcac ctcagctgct gatctactac actagcaccc tgcacctggg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctctag cctgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 723
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 723

gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatct gcagaagccc 120

ggccagtccc ctcagctgct gatctactac acctccaccc tgcacctggg cgtgccctcc 180

agattttccg gctctggctc tggcaccgag tttaccctga ccatcagctc cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa gcgtacggtg gccgctccca gcgtgttcat cttcccccca 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gtctgctgaa caacttctac 420

cccagggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gtgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 724
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 724
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Leu Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Asp Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 725
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 725
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtc 60

agctgtaaag ctagtggctt caccctgact aactacggga tgaactgggt ccgccaggcc 120

ccaggtcaag gcctcgagtg gatgggctgg attaacaccg acaccggcga gcctacctac 180

gccgacgact ttaagggcag attcgtgttt agcctggaca ctagtgtgtc taccgcctac 240

ctgcagatct ctagcctgaa ggccgaggac accgccgtct actactgcgc tagaaacccc 300

ccctactact acggcactaa caacgccgag gctatggact actggggtca aggcactacc 360

gtgaccgtgt ctagc 375

<210> 726
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 726
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

cctggacagg gcctggaatg gatgggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctct 375

<210> 727
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 727
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Leu Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Asp Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

```
Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
            100                 105                 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
    130                 135                 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys
        195                 200                 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
```

```
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser
                325                 330                 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr
                405                 410                 415

Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
```

Ser Leu Gly
    450

<210> 728
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 728
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtc 60

agctgtaaag ctagtggctt caccctgact aactacggga tgaactgggt ccgccaggcc 120

ccaggtcaag gcctcgagtg gatgggctgg attaacaccg acaccggcga gcctacctac 180

gccgacgact ttaagggcag attcgtgttt agcctggaca ctagtgtgtc taccgcctac 240

ctgcagatct ctagcctgaa ggccgaggac accgccgtct actactgcgc tagaaacccc 300

ccctactact acggcactaa caacgccgag gctatggact actggggtca aggcactacc 360

gtgaccgtgt ctagcgctag cactaagggc ccgtccgtgt tccccctggc accttgtagc 420

cggagcacta gcgaatccac cgctgccctc ggctgcctgg tcaaggatta cttcccggag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgacctccg gagtgcacac cttccccgct 540

gtgctgcaga gctccgggct gtactcgctg tcgtcggtgg tcacggtgcc ttcatctagc 600

ctgggtacca agacctacac ttgcaacgtg gaccacaagc cttccaacac taaggtggac 660

aagcgcgtcg aatcgaagta cggcccaccg tgcccgcctt gtcccgcgcc ggagttcctc 720

ggcggtccct cggtctttct gttcccaccg aagcccaagg acactttgat gatttcccgc 780

acccctgaag tgacatgcgt ggtcgtggac gtgtcacagg aagatccgga ggtgcagttc 840

aattggtacg tggatggcgt cgaggtgcac aacgccaaaa ccaagccgag ggaggagcag 900

ttcaactcca cttaccgcgt cgtgtccgtg ctgacggtgc tgcatcagga ctggctgaac 960

gggaaggagt acaagtgcaa agtgtccaac aagggacttc ctagctcaat cgaaaagacc 1020

atctcgaaag ccaagggaca gccccgggaa ccccaagtgt ataccctgcc accgagccag 1080

gaagaaatga ctaagaacca agtctcattg acttgccttg tgaagggctt ctacccatcg 1140

gatatcgccg tggaatggga gtccaacggc cagccggaaa acaactacaa gaccacccct 1200

ccggtgctgg actcagacgg atccttcttc ctctactcgc ggctgaccgt ggataagagc 1260

agatggcagg agggaaatgt gttcagctgt tctgtgatgc atgaagccct gcacaaccac 1320

tacactcaga agtccctgtc cctctccctg gga 1353

<210> 729
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 729
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

cctggacagg gcctggaatg gatgggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctctgcttc taccaagggg cccagcgtgt tccccctggc cccctgctcc 420

agaagcacca gcgagagcac agccgccctg ggctgcctgg tgaaggacta cttccccgag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgaccagcg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgaccgtgcc cagcagcagc 600

ctgggcacca agacctacac ctgtaacgtg gaccacaagc ccagcaacac caaggtggac 660

aagagggtgg agagcaagta cggcccaccc tgccccccct gcccagcccc cgagttcctg 720

ggcggaccca gcgtgttcct gttccccccc aagcccaagg acaccctgat gatcagcaga 780

acccccgagg tgacctgtgt ggtggtggac gtgtcccagg aggaccccga ggtccagttc 840

aactggtacg tggacggcgt ggaggtgcac aacgccaaga ccaagcccag agaggagcag 900

tttaacagca cctaccgggt ggtgtccgtg ctgaccgtgc tgcaccagga ctggctgaac 960

ggcaaagagt acaagtgtaa ggtctccaac aagggcctgc caagcagcat cgaaaagacc 1020

atcagcaagg ccaagggcca gcctagagag ccccaggtct acaccctgcc acccagccaa 1080

gaggagatga ccaagaacca ggtgtccctg acctgtctgg tgaagggctt ctacccaagc 1140

gacatcgccg tggagtggga gagcaacggc cagcccgaga acaactacaa gaccaccccc 1200

ccagtgctgg acagcgacgg cagcttcttc ctgtacagca ggctgaccgt ggacaagtcc 1260

agatggcagg agggcaacgt ctttagctgc tccgtgatgc acgaggccct gcacaaccac 1320

tacacccaga agagcctgag cctgtccctg ggc 1353

<210> 730
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 730
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Asn Asn Ile Glu Ser
65 70 75 80

Glu Asp Ala Ala Tyr Tyr Phe Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 731
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 731
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gctctagtca ggatatctct aactacctga actggtatca gcagaagccc 120

ggtaaagccc ctaagctgct gatctactac actagcaccc tgcacctggg aatcccccct 180

aggtttagcg gtagcggcta cggcaccgac ttcaccctga ctattaacaa tatcgagtca 240

gaggacgccg cctactactt ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 732
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 732
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatca gcagaagccc 120

ggcaaggccc ccaagctgct gatctactac acctccaccc tgcacctggg catcccccct 180

agattctccg gctctggcta cggcaccgac ttcaccctga ccatcaacaa catcgagtcc 240

gaggacgccg cctactactt ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa g 321

<210> 733
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 733
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Asn Asn Ile Glu Ser
65 70 75 80

Glu Asp Ala Ala Tyr Tyr Phe Cys Gln Gln Tyr Tyr Asn Leu Pro Trp

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 734
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 734
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gctctagtca ggatatctct aactacctga actggtatca gcagaagccc 120

ggtaaagccc ctaagctgct gatctactac actagcaccc tgcacctggg aatcccccct 180

aggtttagcg gtagcggcta cggcaccgac ttcaccctga ctattaacaa tatcgagtca 240

gaggacgccg cctactactt ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 735
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 735
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatca gcagaagccc 120

ggcaaggccc ccaagctgct gatctactac acctccaccc tgcacctggg catccccct 180

agattctccg gctctggcta cggcaccgac ttcaccctga ccatcaacaa catcgagtcc 240

gaggacgccg cctactactt ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa gcgtacggtg gccgctccca gcgtgttcat cttccccca 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gtctgctgaa caacttctac 420

cccagggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gtgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 736
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 736
aattacggga tgaac 15

<210> 737
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 737
aactacggca tgaac 15

<210> 738
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 738
tggattaaca ccgacaccgg ggagcctacc tacgcggacg atttcaaggg a 51

<210> 739
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 739
tggatcaaca ccgacaccgg cgagcctacc tacgccgacg acttcaaggg c 51

<210> 740
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 740
aacccgccct actactacgg aaccaacaac gccgaagcca tggactac 48

<210> 741
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 741
aacccccctt actactacgg caccaacaac gccgaggcca tggactat 48

<210> 742
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 742
ggattcaccc tcaccaatta c 21

<210> 743
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 743
ggcttcaccc tgaccaacta c 21

<210> 744
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 744
aacaccgaca ccggggag 18

<210> 745
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 745

aacaccgaca ccggcgag 18

<210> 746
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 746
agctctagtc aggatatctc taactacctg aac 33

<210> 747
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 747
tcctccagcc aggacatctc caactacctg aac 33

<210> 748
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 748
tacactagca ccctgcacct g 21

<210> 749
<211> 21
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 749
tacacctcca ccctgcacct g 21

<210> 750
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 750
cagcagtact ataacctgcc ctggacc 27

<210> 751
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 751
cagcagtact acaacctgcc ctggacc 27

<210> 752
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 752
agtcaggata tctctaacta c 21

<210> 753
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 753
agccaggaca tctccaacta c 21

<210> 754
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 754
tacactagc 9

<210> 755
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 755
tacacctcc 9

<210> 756

<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 756
tactataacc tgccctgg 18

<210> 757
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 757
tactacaacc tgccctgg 18

<210> 758
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 758
aactacggga tgaac 15

<210> 759
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 759
tggattaaca ccgacaccgg cgagcctacc tacgccgacg actttaaggg c 51

<210> 760
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 760
aacccccct actactacgg cactaacaac gccgaggcta tggactac 48

<210> 761
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 761
ggcttcaccc tgactaacta c 21

<210> 762
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 762
Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

```
Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Asp Tyr
            20                  25                  30

Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Glu Ile Asn His Arg Gly Ser Thr Asn Ser Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Leu Ser Leu Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Phe Gly Tyr Ser Asp Tyr Glu Tyr Asn Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205
```

```
Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400
```

```
Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440                 445


<210> 763
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 763
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu
                85                  90                  95
```

```
Thr Phe Gly Gln Gly Thr Asn Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160


Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175


Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190


Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205


Phe Asn Arg Gly Glu Cys
    210


<210> 764
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 764
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1               5                   10                  15
```

```
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ala Tyr
            20                  25                  30

Gly Val Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
        35                  40                  45

Gly Met Ile Trp Asp Asp Gly Ser Thr Asp Tyr Asn Ser Ala Leu Lys
    50                  55                  60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65                  70                  75                  80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Arg Tyr Tyr Cys Ala
                85                  90                  95

Arg Glu Gly Asp Val Ala Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205
```

```
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400
```

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
405 410 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
420 425 430

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 765
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 765
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Val Gly
1 5 10 15

Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Gly
20 25 30

Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Val Tyr Phe Ala Ser Thr Arg Asp Ser Gly Val
50 55 60

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr Phe Cys Leu Gln
85 90 95

His Phe Gly Thr Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile

100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145 150 155 160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
165 170 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 766
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 766
Gly Phe Thr Leu Thr Asn Tyr Gly Met Asn
1 5 10

<210> 767

<400> 767
000

<210> 768

<400> 768
000

<210> 769

<400> 769
000

<210> 770

<400> 770
000

<210> 771

<400> 771
000

<210> 772

<400> 772
000

<210> 773

<400> 773
000

<210> 774

<400> 774
000

<210> 775

<400> 775
000

<210> 776

<400> 776
000

<210> 777

<400> 777
000

<210> 778

<400> 778
000

<210> 779

<400> 779
000

<210> 780

<400> 780
000

<210> 781

<400> 781
000

<210> 782

<400> 782
000

<210> 783

<400> 783
000

<210> 784

<400> 784
000

<210> 785

<400> 785
000

<210> 786

<400> 786
000

<210> 787

<400> 787
000

<210> 788

<400> 788
000

<210> 789

<400> 789
000

<210> 790

<400> 790
000

<210> 791

<400> 791
000

<210> 792

<400> 792
000

<210> 793

<400> 793
000

<210> 794

<400> 794
000

<210> 795

<400> 795
000

<210> 796

<400> 796
000

<210> 797

<400> 797
000

<210> 798

<400> 798
000

<210> 799

<400> 799
000

<210> 800

<400> 800
000

<210> 801
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 801
Ser Tyr Asn Met His
1 5

<210> 802
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 802
Asp Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 803
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 803
Val Gly Gly Ala Phe Pro Met Asp Tyr
1 5

<210> 804
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 804
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 805
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 805
Tyr Pro Gly Asn Gly Asp
1 5

<210> 806
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 806
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Asp Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 807
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 807
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggctctag cgtgaaagtt 60

tcttgtaaag ctagtggcta caccttcact agctataata tgcactgggt tcgccaggcc 120

ccagggcaag gcctcgagtg gatgggcgat atctaccccg ggaacggcga cactagttat 180

aatcagaagt ttaagggtag agtcactatc accgccgata agtctactag caccgtctat 240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc ctatggacta ctggggtcaa ggcactaccg tgaccgtgtc tagc 354

<210> 808
<211> 444
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 808
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Asp Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr

```
            100                 105                 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
```

```
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440
```

<210> 809
<211> 1332
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 809
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggctctag cgtgaaagtt 60

tcttgtaaag ctagtggcta caccttcact agctataata tgcactgggt tcgccaggcc 120

ccagggcaag gcctcgagtg gatgggcgat atctaccccg ggaacggcga cactagttat 180

aatcagaagt ttaagggtag agtcactatc accgccgata agtctactag caccgtctat 240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc ctatggacta ctggggtcaa ggcactaccg tgaccgtgtc tagcgctagc 360

actaagggcc cgtccgtgtt ccccctggca ccttgtagcc ggagcactag cgaatccacc 420

gctgccctcg gctgcctggt caaggattac ttcccggagc ccgtgaccgt gtcctggaac 480

agcggagccc tgacctccgg agtgcacacc ttccccgctg tgctgcagag ctccgggctg 540

tactcgctgt cgtcggtggt cacggtgcct tcatctagcc tgggtaccaa gacctacact 600

tgcaacgtgg accacaagcc ttccaacact aaggtggaca agcgcgtcga atcgaagtac 660

ggcccaccgt gcccgccttg tcccgcgccg gagttcctcg gcggtccctc ggtctttctg 720

ttcccaccga agcccaagga cactttgatg atttcccgca cccctgaagt gacatgcgtg 780

gtcgtggacg tgtcacagga agatccggag gtgcagttca attggtacgt ggatggcgtc 840

gaggtgcaca acgccaaaac caagccgagg gaggagcagt tcaactccac ttaccgcgtc 900

gtgtccgtgc tgacggtgct gcatcaggac tggctgaacg ggaaggagta caagtgcaaa 960

gtgtccaaca agggacttcc tagctcaatc gaaaagacca tctcgaaagc caagggacag 1020

ccccgggaac cccaagtgta taccctgcca ccgagccagg aagaaatgac taagaaccaa 1080

gtctcattga cttgccttgt gaagggcttc tacccatcgg atatcgccgt ggaatgggag 1140

tccaacggcc agccggaaaa caactacaag accacccctc cggtgctgga ctcagacgga 1200

tccttcttcc tctactcgcg gctgaccgtg gataagagca gatggcagga gggaaatgtg 1260

ttcagctgtt ctgtgatgca tgaagccctg cacaaccact acactcagaa gtccctgtcc 1320

ctctccctgg ga 1332

<210> 810
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 810
Arg Ala Ser Glu Ser Val Glu Tyr Tyr Gly Thr Ser Leu Met Gln
1 5 10 15

<210> 811
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 811
Ala Ala Ser Asn Val Glu Ser
1 5

<210> 812
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 812
Gln Gln Ser Arg Lys Asp Pro Ser Thr
1 5

<210> 813
<211> 11

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 813
Ser Glu Ser Val Glu Tyr Tyr Gly Thr Ser Leu
1 5 10

<210> 814
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 814
Ala Ala Ser
1

<210> 815
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 815
Ser Arg Lys Asp Pro Ser
1 5

<210> 816
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 816
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
20 25 30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Ser
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Ser Arg
85 90 95

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 817
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 817
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat 120

cagcagaagc ccgggaaagc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca 180

ggcgtgccct ctaggtttag cggtagcggt agtggcaccg acttcaccct gactatctct 240

agcctgcagc ccgaggactt cgctacctac ttctgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aag 333

<210> 818
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 818
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
20 25 30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Ser
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Ser Arg
85 90 95

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

```
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125


Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140


Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175


Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190


His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 819
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 819
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact       60

atcacctgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat      120

cagcagaagc ccgggaaagc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca      180

ggcgtgccct ctaggtttag cggtagcggt agtggcaccg acttcaccct gactatctct      240
```

agcctgcagc ccgaggactt cgctacctac ttctgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aagcgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 820
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 820
Asp Ile Tyr Pro Gly Gln Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 821
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 821
Tyr Pro Gly Gln Gly Asp
1 5

<210> 822
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 822
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asp Ile Tyr Pro Gly Gln Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Ala Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 823
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 823
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtt 60

agctgtaaag ctagtggcta tactttcact tcttataata tgcactgggt ccgccaggcc 120

ccaggtcaag gcctcgagtg gatcggcgat atctaccccg gtcaaggcga cacttcctat 180

aatcagaagt ttaagggtag agctactatg accgccgata agtctacttc taccgtctat 240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc caatggacta ctggggtcaa ggcaccctgg tcaccgtgtc tagc 354

<210> 824
<211> 444
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 824
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asp Ile Tyr Pro Gly Gln Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Ala Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Val Tyr

```
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
```

260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
435 440

<210> 825

<211> 1332
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 825
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtt 60

agctgtaaag ctagtggcta tactttcact tcttataata tgcactgggt ccgccaggcc 120

ccaggtcaag gcctcgagtg gatcggcgat atctaccccg gtcaaggcga cacttcctat 180

aatcagaagt ttaagggtag agctactatg accgccgata agtctacttc taccgtctat 240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc caatggacta ctggggtcaa ggcaccctgg tcaccgtgtc tagcgctagc 360

actaagggcc cgtccgtgtt ccccctggca ccttgtagcc ggagcactag cgaatccacc 420

gctgccctcg gctgcctggt caaggattac ttcccggagc ccgtgaccgt gtcctggaac 480

agcggagccc tgacctccgg agtgcacacc ttccccgctg tgctgcagag ctccgggctg 540

tactcgctgt cgtcggtggt cacggtgcct tcatctagcc tgggtaccaa gacctacact 600

tgcaacgtgg accacaagcc ttccaacact aaggtggaca agcgcgtcga atcgaagtac 660

ggcccaccgt gcccgccttg tcccgcgccg gagttcctcg gcggtccctc ggtctttctg 720

ttcccaccga agcccaagga cactttgatg atttcccgca cccctgaagt gacatgcgtg 780

gtcgtggacg tgtcacagga agatccggag gtgcagttca attggtacgt ggatggcgtc 840

gaggtgcaca acgccaaaac caagccgagg gaggagcagt tcaactccac ttaccgcgtc 900

gtgtccgtgc tgacggtgct gcatcaggac tggctgaacg ggaaggagta caagtgcaaa 960

gtgtccaaca agggacttcc tagctcaatc gaaaagacca tctcgaaagc caagggacag 1020

ccccgggaac cccaagtgta taccctgcca ccgagccagg aagaaatgac taagaaccaa 1080

gtctcattga cttgccttgt gaagggcttc tacccatcgg atatcgccgt ggaatgggag 1140

tccaacggcc agccggaaaa caactacaag accacccctc cggtgctgga ctcagacgga 1200

tccttcttcc tctactcgcg gctgaccgtg gataagagca gatggcagga gggaaatgtg 1260

ttcagctgtt ctgtgatgca tgaagccctg cacaaccact acactcagaa gtccctgtcc 1320

ctctccctgg ga 1332

<210> 826
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 826
Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
20 25 30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Arg
85 90 95

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 827
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 827
gatatcgtcc tgactcagtc acccgatagc ctggccgtca gcctgggcga gcgggctact 60

attaactgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat 120

cagcagaagc ccggtcaacc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca 180

ggcgtgcccg ataggtttag cggtagcggt agtggcaccg acttcaccct gactattagt 240

agcctgcagg ccgaggacgt ggccgtctac tactgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aag 333

<210> 828
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 828
Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
20 25 30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Asp

```
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Arg
                85                  90                  95

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
```

<210> 829
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 829
gatatcgtcc tgactcagtc acccgatagc ctggccgtca gcctgggcga gcgggctact 60

attaactgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat 120

cagcagaagc ccggtcaacc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca 180

ggcgtgcccg ataggtttag cggtagcggt agtggcaccg acttcaccct gactattagt 240

agcctgcagg ccgaggacgt ggccgtctac tactgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aagcgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 830
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 830
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ala Ser Gly Phe Thr Phe Ser Ser
20 25 30

Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp
35 40 45

Val Ser Thr Ile Ser Gly Gly Gly Thr Tyr Thr Tyr Tyr Gln Asp Ser
50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Ser Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
100 105 110

Ser Ala

<210> 831
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 831
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Arg Tyr
20 25 30

Leu Asn Trp Tyr His Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser His Ser Ala Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 832
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 832
Glu Val Gln Val Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Tyr Cys Val Ala Ser Gly Phe Thr Phe Ser Gly Ser
20 25 30

Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
35 40 45

Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser
50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
85 90 95

```
Cys Ala Lys Lys Tyr Tyr Val Gly Pro Ala Asp Tyr Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser Gly
        115                 120


<210> 833
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 833
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
            20                  25                  30


Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln
        35                  40                  45


Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                85                  90                  95


Tyr Tyr Ser Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Ile Glu Val
            100                 105                 110
```

Lys

<210> 834

<400> 834
000

<210> 835

<400> 835
000

<210> 836

<400> 836
000

<210> 837

<400> 837
000

<210> 838

<400> 838
000

<210> 839

<400> 839
000

<210> 840

<400> 840
000

<210> 841

<400> 841
000

<210> 842

<400> 842
000

<210> 843

<400> 843
000

<210> 844

<400> 844
000

<210> 845

<400> 845
000

<210> 846

<400> 846
000

<210> 847

<400> 847
000

<210> 848

<400> 848
000

<210> 849

<400> 849
000

<210> 850

<400> 850
000

<210> 851

<400> 851
000

<210> 852

<400> 852
000

<210> 853

<400> 853
000

<210> 854

<400> 854
000

<210> 855

<400> 855
000

<210> 856

<400> 856
000

<210> 857

<400> 857
000

<210> 858

<400> 858
000

<210> 859

<400> 859
000

<210> 860

<400> 860
000

<210> 861

<400> 861
000

<210> 862

<400> 862
000

<210> 863

<400> 863
000

<210> 864

<400> 864
000

<210> 865

<400> 865
000

<210> 866

<400> 866
000

<210> 867

<400> 867
000

<210> 868

<400> 868
000

<210> 869

<400> 869
000

<210> 870

<400> 870
000

<210> 871

<400> 871
000

<210> 872

<400> 872
000

<210> 873

<400> 873
000

<210> 874

<400> 874
000

<210> 875

<400> 875
000

<210> 876

<400> 876
000

<210> 877

<400> 877
000

<210> 878

<400> 878
000

<210> 879

<400> 879
000

<210> 880

<400> 880
000

<210> 881

<400> 881
000

<210> 882

<400> 882
000

<210> 883

<400> 883
000

<210> 884

<400> 884
000

<210> 885

<400> 885
000

<210> 886

<400> 886
000

<210> 887

<400> 887
000

<210> 888

<400> 888
000

<210> 889

<400> 889
000

<210> 890

<400> 890
000

<210> 891

<400> 891
000

<210> 892

<400> 892
000

<210> 893

<400> 893
000

<210> 894

<400> 894
000

<210> 895

<400> 895
000

<210> 896

<400> 896
000

<210> 897

<400> 897
000

<210> 898

<400> 898
000

<210> 899

<400> 899
000

<210> 900

<400> 900
000

<210> 901

<400> 901
000

<210> 902

<400> 902
000

<210> 903

<400> 903
000

<210> 904

<400> 904
000

<210> 905

<400> 905
000

<210> 906

<400> 906
000

<210> 907

<400> 907
000

<210> 908

<400> 908
000

<210> 909

<400> 909
000

<210> 910

<400> 910
000

<210> 911

<400> 911
000

<210> 912

<400> 912
000

<210> 913

<400> 913
000

<210> 914

<400> 914
000

<210> 915

<400> 915
000

<210> 916

<400> 916
000

<210> 917

<400> 917
000

<210> 918

<400> 918
000

<210> 919

<400> 919
000

<210> 920

<400> 920
000

<210> 921

<400> 921
000

<210> 922

<400> 922
000

<210> 923

<400> 923
000

<210> 924

<400> 924
000

<210> 925

<400> 925
000

<210> 926

<400> 926
000

<210> 927

<400> 927
000

<210> 928

<400> 928
000

<210> 929

<400> 929
000

<210> 930

<400> 930
000

<210> 931

<400> 931
000

<210> 932

<400> 932
000

<210> 933

<400> 933
000

<210> 934

<400> 934
000

<210> 935

<400> 935
000

<210> 936

<400> 936
000

<210> 937

<400> 937
000

<210> 938

<400> 938
000

<210> 939

<400> 939
000

<210> 940

<400> 940
000

<210> 941

<400> 941
000

<210> 942

<400> 942
000

<210> 943

<400> 943
000

<210> 944

<400> 944
000

<210> 945

<400> 945
000

<210> 946

<400> 946
000

<210> 947

<400> 947
000

<210> 948

<400> 948
000

<210> 949

<400> 949
000

<210> 950

<400> 950
000

<210> 951

<400> 951
000

<210> 952

<400> 952
000

<210> 953

<400> 953
000

<210> 954

<400> 954
000

<210> 955

<400> 955
000

<210> 956

<400> 956
000

<210> 957

<400> 957
000

<210> 958

<400> 958
000

<210> 959

<400> 959
000

<210> 960

<400> 960
000

<210> 961

<400> 961
000

<210> 962

<400> 962
000

<210> 963

<400> 963
000

<210> 964

<400> 964
000

<210> 965

<400> 965
000

<210> 966

<400> 966
000

<210> 967

<400> 967
000

<210> 968

<400> 968
000

<210> 969

<400> 969
000

<210> 970

<400> 970
000

<210> 971

<400> 971
000

<210> 972

<400> 972
000

<210> 973

<400> 973
000

<210> 974

<400> 974
000

<210> 975

<400> 975
000

<210> 976

<400> 976
000

<210> 977

<400> 977
000

<210> 978

<400> 978
000

<210> 979

<400> 979
000

<210> 980

<400> 980
000

<210> 981

<400> 981
000

<210> 982

<400> 982
000

<210> 983

<400> 983
000

<210> 984

<400> 984
000

<210> 985

<400> 985
000

<210> 986

<400> 986
000

<210> 987

<400> 987
000

<210> 988

<400> 988
000

<210> 989

<400> 989
000

<210> 990

<400> 990
000

<210> 991

<400> 991
000

<210> 992

<400> 992
000

<210> 993

<400> 993
000

<210> 994

<400> 994
000

<210> 995

<400> 995
000

<210> 996

<400> 996
000

<210> 997

<400> 997
000

<210> 998

<400> 998
000

<210> 999

<400> 999
000

<210> 1000

<400> 1000
000

<210> 1001

<211> 114
<212> PRT
<213> Homo sapiens

<400> 1001
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
1 5 10 15

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
            20 25 30

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
        35 40 45

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
    50 55 60

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
65 70 75 80

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
                85 90 95

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
            100 105 110

Thr Ser

<210> 1002
<211> 170
<212> PRT
<213> Homo sapiens

<400> 1002
Ile Thr Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val
1 5 10 15

Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly

```
            20                  25                  30

Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn
        35                  40                  45

Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile
    50                  55                  60

Arg Asp Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro Ser Thr Val
65                  70                  75                  80

Thr Thr Ala Gly Val Thr Pro Gln Pro Glu Ser Leu Ser Pro Ser Gly
                85                  90                  95

Lys Glu Pro Ala Ala Ser Ser Pro Ser Ser Asn Asn Thr Ala Ala Thr
            100                 105                 110

Thr Ala Ala Ile Val Pro Gly Ser Gln Leu Met Pro Ser Lys Ser Pro
        115                 120                 125

Ser Thr Gly Thr Thr Glu Ile Ser Ser His Glu Ser Ser His Gly Thr
    130                 135                 140

Pro Ser Gln Thr Thr Ala Lys Asn Trp Glu Leu Thr Ala Ser Ala Ser
145                 150                 155                 160

His Gln Pro Pro Gly Val Tyr Pro Gln Gly
                165                 170


<210> 1003
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
```

<400> 1003
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
1   5   10   15

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
            20   25   30

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
        35   40   45

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
    50   55   60

Asn Leu Ile Ile Leu Ala Asn Asp Ser Leu Ser Ser Asn Gly Asn Val
65   70   75   80

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
                85   90   95

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
            100   105   110

Thr Ser

<210> 1004
<211> 297
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1004
Ile Thr Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val
1   5   10   15

```
Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly
            20                  25                  30

Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn
        35                  40                  45

Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile
    50                  55                  60

Arg Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
65                  70                  75                  80

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
                85                  90                  95

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            100                 105                 110

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        115                 120                 125

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    130                 135                 140

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
145                 150                 155                 160

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                165                 170                 175

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            180                 185                 190

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        195                 200                 205
```

```
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    210                 215                 220


Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
225                 230                 235                 240


Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                245                 250                 255


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            260                 265                 270


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        275                 280                 285


Lys Ser Leu Ser Leu Ser Pro Gly Lys
    290                 295


<210> 1005
<211> 114
<212> PRT
<213> Homo sapiens


<220>
<221> VARIANT
<222> (93)..(93)
<223> /replace="Lys"

<220>
<221> SITE
<222> (1)..(114)
<223> /note="Variant residues given in the sequence have no
      preference with respect to those in the annotations
      for variant positions"

<400> 1005
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
1               5                   10                  15
```

```
Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
            20                  25                  30

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
        35                  40                  45

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
    50                  55                  60

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
65                  70                  75                  80

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
                85                  90                  95

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
            100                 105                 110

Thr Ser
```

<210> 1006
<211> 77
<212> PRT
<213> Homo sapiens

<400> 1006

```
Ile Thr Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val
1               5                   10                  15

Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly
            20                  25                  30

Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn
        35                  40                  45

Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile
    50                  55                  60
```

Arg Asp Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro
65 70 75

<210> 1007
<211> 1184
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1007
cgtgaggctc cggtgcccgt cagtgggcag agcgcacatc gcccacagtc cccgagaagt 60

tgggggggagg ggtcggcaat tgaaccggtg cctagagaag gtggcgcggg gtaaactggg 120

aaagtgatgt cgtgtactgg ctccgccttt ttcccgaggg tgggggagaa ccgtatataa 180

gtgcagtagt cgccgtgaac gttctttttc gcaacgggtt tgccgccaga acacaggtaa 240

gtgccgtgtg tggttcccgc gggcctggcc tctttacggg ttatggccct tgcgtgcctt 300

gaattacttc cacctggctg cagtacgtga ttcttgatcc cgagcttcgg gttggaagtg 360

ggtgggagag ttcgaggcct tgcgcttaag gagccccttc gcctcgtgct tgagttgagg 420

cctggcctgg gcgctggggc cgccgcgtgc gaatctggtg gcaccttcgc gcctgtctcg 480

ctgctttcga taagtctcta gccatttaaa atttttgatg acctgctgcg acgcttttt 540

tctggcaaga tagtcttgta aatgcgggcc aagatctgca cactggtatt tcggtttttg 600

gggccgcggg cggcgacggg gcccgtgcgt cccagcgcac atgttcggcg aggcggggcc 660

tgcgagcgcg gccaccgaga atcggacggg ggtagtctca agctggccgg cctgctctgg 720

tgcctggcct cgcgccgccg tgtatcgccc cgccctgggc ggcaaggctg gcccggtcgg 780

caccagttgc gtgagcggaa agatggccgc ttcccggccc tgctgcaggg agctcaaaat 840

ggaggacgcg gcgctcggga gagcgggcgg gtgagtcacc cacacaaagg aaaagggcct 900

ttccgtcctc agccgtcgct tcatgtgact ccacggagta ccgggcgccg tccaggcacc 960

tcgattagtt ctcgagcttt tggagtacgt cgtctttagg ttgggggggag gggttttatg 1020

cgatggagtt tccccacact gagtgggtgg agactgaagt taggccagct tggcacttga 1080

tgtaattctc cttggaattt gccctttttg agtttggatc ttggttcatt ctcaagcctc 1140

agacagtggt tcaaagtttt tttcttccat ttcaggtgtc gtga 1184

<210> 1008
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1008
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro
20

<210> 1009
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 1009
atggccctgc ctgtgacagc cctgctgctg cctctggctc tgctgctgca tgccgctaga 60

ccc 63

<210> 1010
<211> 63
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 1010
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccc 63

<210> 1011
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1011
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1 5 10 15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
20 25 30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
35 40 45

<210> 1012
<211> 135
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1012
accacgacgc cagcgccgcg accaccaaca ccggcgccca ccatcgcgtc gcagcccctg 60

tccctgcgcc cagaggcgtg ccggccagcg gcgggggcg cagtgcacac gagggggctg 120

gacttcgcct gtgat 135

<210> 1013
<211> 230
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1013
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe
1 5 10 15

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
20 25 30

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
35 40 45

Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
50 55 60

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
65 70 75 80

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
85 90 95

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser
100 105 110

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
115 120 125

Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln
130 135 140

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
145 150 155 160

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
165 170 175

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu
180 185 190

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser
195 200 205

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
210 215 220

Leu Ser Leu Gly Lys Met
225 230

<210> 1014
<211> 690
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1014
gagagcaagt acggccctcc ctgcccccct tgccctgccc ccgagttcct gggcggaccc 60

agcgtgttcc tgttcccccc caagcccaag gacaccctga tgatcagccg gacccccgag 120

gtgacctgtg tggtggtgga cgtgtcccag gaggaccccg aggtccagtt caactggtac 180

gtggacggcg tggaggtgca caacgccaag accaagcccc gggaggagca gttcaatagc 240

acctaccggg tggtgtccgt gctgaccgtg ctgcaccagg actggctgaa cggcaaggaa 300

tacaagtgta aggtgtccaa caagggcctg cccagcagca tcgagaaaac catcagcaag 360

gccaagggcc agcctcggga gccccaggtg tacaccctgc cccctagcca agaggagatg 420

accaagaacc aggtgtccct gacctgcctg gtgaagggct tctaccccag cgacatcgcc 480

gtggagtggg agagcaacgg ccagcccgag aacaactaca agaccacccc ccctgtgctg 540

gacagcgacg gcagcttctt cctgtacagc cggctgaccg tggacaagag ccggtggcag 600

gagggcaacg tctttagctg ctccgtgatg cacgaggccc tgcacaacca ctacacccag 660

aagagcctga gcctgtccct gggcaagatg 690

<210> 1015
<211> 282
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1015
Arg Trp Pro Glu Ser Pro Lys Ala Gln Ala Ser Ser Val Pro Thr Ala
1 5 10 15

Gln Pro Gln Ala Glu Gly Ser Leu Ala Lys Ala Thr Thr Ala Pro Ala
20 25 30

Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys
35 40 45

Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro
50 55 60

Ser His Thr Gln Pro Leu Gly Val Tyr Leu Leu Thr Pro Ala Val Gln
65 70 75 80

```
Asp Leu Trp Leu Arg Asp Lys Ala Thr Phe Thr Cys Phe Val Val Gly
                85                  90                  95

Ser Asp Leu Lys Asp Ala His Leu Thr Trp Glu Val Ala Gly Lys Val
            100                 105                 110

Pro Thr Gly Gly Val Glu Glu Gly Leu Leu Glu Arg His Ser Asn Gly
        115                 120                 125

Ser Gln Ser Gln His Ser Arg Leu Thr Leu Pro Arg Ser Leu Trp Asn
    130                 135                 140

Ala Gly Thr Ser Val Thr Cys Thr Leu Asn His Pro Ser Leu Pro Pro
145                 150                 155                 160

Gln Arg Leu Met Ala Leu Arg Glu Pro Ala Ala Gln Ala Pro Val Lys
                165                 170                 175

Leu Ser Leu Asn Leu Leu Ala Ser Ser Asp Pro Pro Glu Ala Ala Ser
            180                 185                 190

Trp Leu Leu Cys Glu Val Ser Gly Phe Ser Pro Pro Asn Ile Leu Leu
        195                 200                 205

Met Trp Leu Glu Asp Gln Arg Glu Val Asn Thr Ser Gly Phe Ala Pro
    210                 215                 220

Ala Arg Pro Pro Pro Gln Pro Gly Ser Thr Thr Phe Trp Ala Trp Ser
225                 230                 235                 240

Val Leu Arg Val Pro Ala Pro Pro Ser Pro Gln Pro Ala Thr Tyr Thr
                245                 250                 255

Cys Val Val Ser His Glu Asp Ser Arg Thr Leu Leu Asn Ala Ser Arg
            260                 265                 270
```

Ser Leu Glu Val Ser Tyr Val Thr Asp His
275 280

<210> 1016
<211> 847
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1016
aggtggcccg aaagtcccaa ggcccaggca tctagtgttc ctactgcaca gccccaggca 60

gaaggcagcc tagccaaagc tactactgca cctgccacta cgcgcaatac tggccgtggc 120

ggggaggaga agaaaaagga gaaagagaaa gaagaacagg aagagaggga gaccaagacc 180

cctgaatgtc catcccatac ccagccgctg ggcgtctatc tcttgactcc cgcagtacag 240

gacttgtggc ttagagataa ggccaccttt acatgtttcg tcgtgggctc tgacctgaag 300

gatgcccatt tgacttggga ggttgccgga aaggtaccca cagggggggt tgaggaaggg 360

ttgctggagc gccattccaa tggctctcag agccagcact caagactcac ccttccgaga 420

tccctgtgga acgccgggac ctctgtcaca tgtactctaa atcatcctag cctgccccca 480

cagcgtctga tggcccttag agagccagcc gcccaggcac cagttaagct tagcctgaat 540

ctgctcgcca gtagtgatcc cccagaggcc gccagctggc tcttatgcga agtgtccggc 600

tttagcccgc ccaacatctt gctcatgtgg ctggaggacc agcgagaagt gaacaccagc 660

ggcttcgctc cagcccggcc cccaccccag ccgggttcta ccacattctg ggcctggagt 720

gtcttaaggg tcccagcacc acctagcccc cagccagcca catacacctg tgttgtgtcc 780

catgaagata gcaggaccct gctaaatgct tctaggagtc tggaggtttc ctacgtgact 840

gaccatt 847

<210> 1017
<211> 10

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1017
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 1018
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 1018
ggtggcggag gttctggagg tggaggttcc 30

<210> 1019
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1019
Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys
20

<210> 1020
<211> 72

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 1020
atctacatct gggcgcccttggccgggact tgtggggtcc ttctcctgtc actggttatc 60

acccttttact gc 72

<210> 1021
<211> 72
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 1021
atctacattt gggcccctct ggctggtact tgcggggtcc tgctgctttc actcgtgatc 60

actctttact gt 72

<210> 1022
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1022
Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 1023
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1023
aaacggggca gaaagaaact cctgtatata ttcaaacaac catttatgag accagtacaa 60

actactcaag aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt 120

gaactg 126

<210> 1024
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1024
aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 60

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 120

gaactg 126

<210> 1025
<211> 48
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1025
Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu Pro
1 5 10 15

Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu Glu Gly Ser Thr
20 25 30

Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser Pro
35 40 45

<210> 1026
<211> 123
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1026
aggagtaaga ggagcaggct cctgcacagt gactacatga acatgactcc ccgccgcccc 60

gggcccaccc gcaagcatta ccagccctat gccccaccac gcgacttcgc agcctatcgc 120

tcc 123

<210> 1027
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1027
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            20   25   30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        35   40   45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    50   55   60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65   70   75   80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
                85   90   95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
            100   105   110

<210> 1028
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1028
agagtgaagt tcagcaggag cgcagacgcc cccgcgtaca agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc 120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat 180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc 240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc 300

tacgacgccc ttcacatgca ggccctgccc cctcgc   336

<210> 1029
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1029
cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 60

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 120

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 180

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 240

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 300

tatgacgctc ttcacatgca ggccctgccg cctcgg 336

<210> 1030
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1030
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 1031
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1031
agagtgaagt tcagcaggag cgcagacgcc cccgcgtacc agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc 120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat 180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc 240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc 300

tacgacgccc ttcacatgca ggccctgccc cctcgc 336

<210> 1032
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1032
Gly Gly Gly Gly Ser
1 5

<210> 1033
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 1033
ggtggcggag gttctggagg tggaggttcc 30

<210> 1034
<211> 150
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1034
Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Thr Leu Val
145 150

<210> 1035
<211> 450
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1035
cccggatggt ttctggactc tccggatcgc ccgtggaatc ccccaacctt ctcaccggca 60

ctcttggttg tgactgaggg cgataatgcg accttcacgt gctcgttctc caacacctcc 120

gaatcattcg tgctgaactg gtaccgcatg agcccgtcaa accagaccga caagctcgcc 180

gcgtttccgg aagatcggtc gcaaccggga caggattgtc ggttccgcgt gactcaactg 240

ccgaatggca gagacttcca catgagcgtg gtccgcgcta ggcgaaacga ctccgggacc 300

tacctgtgcg gagccatctc gctggcgcct aaggcccaaa tcaaagagag cttgagggcc 360

gaactgagag tgaccgagcg cagagctgag gtgccaactg cacatccatc cccatcgcct 420

cggcctgcgg ggcagtttca gaccctggtc 450

<210> 1036
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1036
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro
20 25 30

Trp Asn Pro Pro Thr Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly
35 40 45

Asp Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe
50 55 60

Val Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu
65 70 75 80

Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe
85 90 95

Arg Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val
100 105 110

Arg Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser
115 120 125

Leu Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg

```
    130                 135                 140

Val Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser
145                 150                 155                 160

Pro Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Thr Thr Thr Pro Ala
                165                 170                 175

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
            180                 185                 190

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
        195                 200                 205

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
    210                 215                 220

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
225                 230                 235                 240

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
                245                 250                 255

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            260                 265                 270

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
        275                 280                 285

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
    290                 295                 300

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
305                 310                 315                 320

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
```

325 330 335

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
340 345 350

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
355 360 365

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
370 375 380

Ala Leu His Met Gln Ala Leu Pro Pro Arg
385 390

<210> 1037
<211> 1182
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1037
atggccctcc ctgtcactgc cctgcttctc cccctcgcac tcctgctcca cgccgctaga 60

ccacccggat ggtttctgga ctctccggat cgcccgtgga atcccccaac cttctcaccg 120

gcactcttgg ttgtgactga gggcgataat gcgaccttca cgtgctcgtt ctccaacacc 180

tccgaatcat tcgtgctgaa ctggtaccgc atgagcccgt caaaccagac cgacaagctc 240

gccgcgtttc cggaagatcg gtcgcaaccg ggacaggatt gtcggttccg cgtgactcaa 300

ctgccgaatg gcagagactt ccacatgagc gtggtccgcg ctaggcgaaa cgactccggg 360

acctacctgt gcggagccat ctcgctggcg cctaaggccc aaatcaaaga gagcttgagg 420

gccgaactga gagtgaccga gcgcagagct gaggtgccaa ctgcacatcc atccccatcg 480

cctcggcctg cggggcagtt tcagaccctg gtcacgacca ctccggcgcc gcgcccaccg 540

actccggccc caactatcgc gagccagccc ctgtcgctga ggccggaagc atgccgccct 600

gccgccggag gtgctgtgca tacccgggga ttggacttcg catgcgacat ctacatttgg 660

gctcctctcg ccggaacttg tggcgtgctc cttctgtccc tggtcatcac cctgtactgc 720

aagcggggtc ggaaaaagct tctgtacatt ttcaagcagc ccttcatgag gcccgtgcaa 780

accacccagg aggaggacgg ttgctcctgc cggttccccg aagaggaaga aggaggttgc 840

gagctgcgcg tgaagttctc ccggagcgcc gacgcccccg cctataagca gggccagaac 900

cagctgtaca acgaactgaa cctgggacgg cgggaagagt acgatgtgct ggacaagcgg 960

cgcggccggg accccgaaat gggcgggaag cctagaagaa agaaccctca ggaaggcctg 1020

tataacgagc tgcagaagga caagatggcc gaggcctact ccgaaattgg gatgaaggga 1080

gagcggcgga ggggaaaggg gcacgacggc ctgtaccaag gactgtccac cgccaccaag 1140

gacacatacg atgccctgca catgcaggcc cttccccctc gc 1182

<210> 1038
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<220>
<221> SITE
<222> (1)..(40)
<223> /note="This sequence may encompass 1-10 'Gly Gly Gly Ser'
repeating units"

<400> 1038
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

Gly Gly Gly Ser Gly Gly Gly Ser
        35   40

<210> 1039
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1039
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 1040
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1040
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10   15

<210> 1041
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1041
Gly Gly Gly Ser
1

<210> 1042
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1042
Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly
1 5 10 15

Ser

<210> 1043
<211> 5000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> misc_feature
<222> (1)..(5000)
<223> /note="This sequence may encompass 50-5000 nucleotides"

<220>
<221> source
<223> /note="See specification as filed for detailed description of
substitutions and preferred embodiments"

<400> 1043
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 960

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1020

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1200

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1680

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2160

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2220

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2280

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2340

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2400

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2460

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2520

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2580

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2640

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2700

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2760

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2820

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2880

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2940

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3000

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3060

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3900

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3960

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4020

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4200

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4260

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4320

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4500

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4560

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4620

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4680

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4980

aaaaaaaaaa aaaaaaaaaa 5000

<210> 1044
<211> 373
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1044
Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu

```
    50                  55                  60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65                  70                  75                  80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
                85                  90                  95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
            100                 105                 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
        115                 120                 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
    130                 135                 140

Gln Phe Gln Thr Leu Val Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
145                 150                 155                 160

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
                165                 170                 175

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
            180                 185                 190

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
        195                 200                 205

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
    210                 215                 220

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
225                 230                 235                 240

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
```

245 250 255

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
260 265 270

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
275 280 285

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
290 295 300

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
305 310 315 320

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
325 330 335

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
340 345 350

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
355 360 365

Ala Leu Pro Pro Arg
370

<210> 1045
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1045
Thr Lys Lys Lys Tyr Ser Ser Ser Val His Asp Pro Asn Gly Glu Tyr
1 5 10 15

Met Phe Met Arg Ala Val Asn Thr Ala Lys Lys Ser Arg Leu Thr Asp
            20   25   30

Val Thr Leu
        35

<210> 1046
<211> 105
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1046
acaaaaaaga agtattcatc cagtgtgcac gaccctaacg gtgaatacat gttcatgaga 60

gcagtgaaca cagccaaaaa atccagactc acagatgtga cccta   105

<210> 1047
<211> 69
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1047
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1   5   10   15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
            20   25   30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Phe Trp Leu
        35   40   45

Pro Ile Gly Cys Ala Ala Phe Val Val Val Cys Ile Leu Gly Cys Ile
    50   55   60

Leu Ile Cys Trp Leu
65

<210> 1048
<211> 207
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1048
accacgacgc cagcgccgcg accaccaaca ccggcgccca ccatcgcgtc gcagcccctg 60

tccctgcgcc cagaggcgtg ccggccagcg gcgggggcg cagtgcacac gagggggctg 120

gacttcgcct gtgatttctg gttacccata ggatgtgcag cctttgttgt agtctgcatt 180

ttgggatgca tacttatttg ttggctt   207

<210> 1049
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1049
Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
1   5   10   15

Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
            20   25   30

Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 1050
<211> 123
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1050
aggagtaaga ggagcaggct cctgcacagt gactacatga acatgactcc ccgccgcccc 60

gggcccaccc gcaagcatta ccagccctat gccccaccac gcgacttcgc agcctatcgc 120

tcc 123

<210> 1051
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1051
Asn His Gly Met Ser
1 5

<210> 1052
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1052

Asn Tyr Ala Met Ser
1 5

<210> 1053
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1053
Asp Tyr Ala Met His
1 5

<210> 1054
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1054
Asn His Gly Met Ser
1 5

<210> 1055
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1055
Asn Phe Gly Ile Asn
1 5

<210> 1056
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1056
Ser Asp Ala Met Thr
1 5

<210> 1057
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1057
Asn Tyr Gly Ile Thr
1 5

<210> 1058
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1058
Asn His Gly Met Ser
1 5

<210> 1059
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1059
Asn His Gly Met Ser
1 5

<210> 1060
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1060
Asn His Gly Met Ser
1 5

<210> 1061
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1061
Asp Tyr Tyr Met Ser
1 5

<210> 1062
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1062
Asp Tyr Tyr Met Ser
1 5

<210> 1063
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1063
Asn His Gly Met Ser
1 5

<210> 1064
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1064
Asn His Gly Met Ser
1 5

<210> 1065
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1065
Asn His Gly Met Ser
1 5

<210> 1066
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1066
Ser Ser Tyr Tyr Tyr Trp Gly
1 5

<210> 1067
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1067
Thr Ser Gly Met Cys Val Ser
1 5

<210> 1068
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1068

Ser Tyr Ser Met Asn
1   5

<210> 1069
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1069
Asp Tyr Tyr Met Ser
1   5

<210> 1070
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1070
Ser His Tyr Ile His
1   5

<210> 1071
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1071
Ser Gly Gly Tyr Tyr Trp Ser
1   5

<210> 1072
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1072
Ser Tyr Ala Ile Ser
1 5

<210> 1073
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1073
Ser Asn Ser Ala Ala Trp Asn
1 5

<210> 1074
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1074
Ser Tyr Ala Met Ser
1 5

<210> 1075
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1075
Arg Tyr Pro Met Ser
1 5

<210> 1076
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1076
Ser Tyr Ala Met Ser
1 5

<210> 1077
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1077
Ser Tyr Ala Met Ser
1 5

<210> 1078
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1078
Asp Tyr Ala Met His
1 5

<210> 1079
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1079
Asp Tyr Ala Met His
1 5

<210> 1080
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1080
Ser Tyr Ala Met Ser
1 5

<210> 1081
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1081
Ser Tyr Ala Met Ser
1 5

<210> 1082
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1082
Ser Tyr Ala Met Ser
1 5

<210> 1083
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1083
Ser Tyr Ala Met Ser
1 5

<210> 1084
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1084

Ser Tyr Ala Met Ser
1   5

<210> 1085
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1085
Ser Tyr Ala Met Ser
1   5

<210> 1086
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1086
Ser Tyr Ala Met Ser
1   5

<210> 1087
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1087
Asn Phe Gly Met Asn
1   5

<210> 1088
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1088
Asp Tyr Ser Ile Asn
1 5

<210> 1089
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1089
His Tyr Ser Met Asn
1 5

<210> 1090
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1090
His Tyr Ser Met Asn
1 5

<210> 1091
<211> 16

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1091
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1092
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1092
Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1093
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1093
Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1094
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1094
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1095
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1095
Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1096
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1096

Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1097
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1097
Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1098
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1098
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1099
<211> 16
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1099
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1100
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1100
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1101
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1101
Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1102
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1102
Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1103
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1103
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1104
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1104
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1105
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1105
Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly
1 5 10 15

<210> 1106
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1106
Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 1107
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1107
Arg Ile Asp Trp Asp Glu Asp Lys Phe Tyr Ser Thr Ser Leu Lys Thr
1 5 10 15

<210> 1108
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1108
Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1109
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1109
Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1110
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1110
Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu Gln
1 5 10 15

Gly

<210> 1111
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1111
Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 1112
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1112
Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1113
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1113
Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala Ile Ser Leu

1 5 10 15

Lys Ser

<210> 1114
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1114
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1115
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1115
Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr Tyr Ala Asp Ser Ala Lys
1 5 10 15

Gly

<210> 1116
<211> 17
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1116
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1117
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1117
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1118
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1118
Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1119
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1119
Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala Tyr Gly Asp Ser Val Lys
1 5 10 15

Gly

<210> 1120
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1120
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1121
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1121
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1122
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1122
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1123
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1123
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1124
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1124
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1125
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1125
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1126
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1126
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1127
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1127
Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 1128
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1128
Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe Arg
1 5 10 15

Gly

<210> 1129
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1129
Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 1130
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1130
Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 1131
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1131
His Gly Gly Glu Ser Asp Val
1 5

<210> 1132
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1132
Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val
1 5 10

<210> 1133
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1133
His Ser Phe Leu Ala Tyr
1 5

<210> 1134
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1134
His Gly Gly Glu Ser Asp Val
1   5

<210> 1135
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1135
Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val
1   5   10

<210> 1136
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1136
Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
1   5   10

<210> 1137
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1137
Gly Pro Tyr Tyr Tyr Tyr Met Asp Val

1 5

<210> 1138
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1138
His Gly Gly Glu Ser Asp Val
1 5

<210> 1139
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1139
His Gly Gly Glu Ser Asp Val
1 5

<210> 1140
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1140
His Gly Gly Glu Ser Asp Val
1 5

<210> 1141
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1141
Glu Ser Gly Asp Gly Met Asp Val
1 5

<210> 1142
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1142
Ser Thr Met Val Arg Glu Asp Tyr
1 5

<210> 1143
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1143
His Gly Gly Glu Ser Asp Val
1 5

<210> 1144
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1144
His Gly Gly Glu Ser Asp Val
1   5

<210> 1145
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1145
His Gly Gly Glu Ser Asp Val
1   5

<210> 1146
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1146
His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile
1   5   10

<210> 1147
<211> 13
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1147
Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile
1 5 10

<210> 1148
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1148
Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile
1 5 10

<210> 1149
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1149
Asp Leu Arg Gly Ala Phe Asp Ile
1 5

<210> 1150
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1150
Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe
1 5 10

<210> 1151
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1151
Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
1 5 10

<210> 1152
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1152
Arg Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu Arg Ser
1 5 10 15

Ala Phe Asp Ile
20

<210> 1153
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1153
Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe Asp Pro
1   5   10

<210> 1154
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1154
Val Glu Gly Ser Gly Ser Leu Asp Tyr
1   5

<210> 1155
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1155
Arg Ala Gly Ser Glu Ala Ser Asp Ile
1   5

<210> 1156
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1156

Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 1157
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1157
Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 1158
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1158
Val Gly Lys Ala Val Pro Asp Val
1   5

<210> 1159
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1159
His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val
1   5   10

<210> 1160
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1160
Val Val Arg Asp Gly Met Asp Val
1 5

<210> 1161
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1161
Ile Pro Gln Thr Gly Thr Phe Asp Tyr
1 5

<210> 1162
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1162
Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 1163
<211> 11

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1163
Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile
1 5 10

<210> 1164
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1164
Trp Phe Gly Glu Gly Phe Asp Pro
1 5

<210> 1165
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1165
Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> 1166

<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1166
Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile
1 5 10

<210> 1167
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1167
Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr
1 5 10

<210> 1168
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1168
Asp Tyr Ser Tyr Ala Met Asp Tyr
1 5

<210> 1169
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1169
Asp Tyr Leu Tyr Ser Leu Asp Phe
1 5

<210> 1170
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1170
Asp Tyr Leu Tyr Ser Cys Asp Tyr
1 5

<210> 1171
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1171
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 1172
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1172
Arg Ala Ser Gln Ser Ile Ser Ser Ser Phe Leu Ala
1 5 10

<210> 1173
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1173
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 1174
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1174
Lys Ser Ser Gln Ser Leu Leu Arg Asn Asp Gly Lys Thr Pro Leu Tyr
1 5 10 15

<210> 1175
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1175
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asn
1 5 10 15

<210> 1176
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1176
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 1177
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1177
Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Val Asp
1 5 10 15

<210> 1178
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1178
Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
1 5 10

<210> 1179
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1179
Arg Ala Ser Gln Ser Val Ser Ser Lys Leu Ala
1 5 10

<210> 1180
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1180
Arg Ala Ser Gln Ser Val Gly Ser Thr Asn Leu Ala
1 5 10

<210> 1181
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1181
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 1182

<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1182
Lys Ser Ser Glu Ser Leu Val His Asn Ser Gly Lys Thr Tyr Leu Asn
1 5 10 15

<210> 1183
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1183
Gln Ala Ser Glu Asp Ile Asn Lys Phe Leu Asn
1 5 10

<210> 1184
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1184
Arg Ala Ser Gln Ser Val Gly Ser Asn Leu Ala
1 5 10

<210> 1185
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1185
Arg Ala Ser Gln Ser Ile Gly Ser Ser Ser Leu Ala
1 5 10

<210> 1186
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1186
Lys Ala Ser Gln Asp Ile Asp Asp Ala Met Asn
1 5 10

<210> 1187
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1187
Arg Ala Ser Gln Asp Ile Tyr Asn Asn Leu Ala
1 5 10

<210> 1188
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1188
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 1189
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1189
Gly Gly Asn Asn Ile Gly Thr Lys Ser Val His
1 5 10

<210> 1190
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1190
Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val Ser
1 5 10

<210> 1191
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1191
Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu Ala
1 5 10

<210> 1192
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1192
Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> 1193
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1193
Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala Thr
1 5 10

<210> 1194
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1194
Arg Ala Ser Gln Ser Val Ser Ser Ala Tyr Leu Ala
1 5 10

<210> 1195
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1195
Arg Ala Ser Gln Ser Val Ser Asn Ser Leu Ala
1 5 10

<210> 1196
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1196
Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala
1 5 10

<210> 1197
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1197
Arg Ala Ser Gln Ser Val Ser Thr Thr Phe Leu Ala
1 5 10

<210> 1198

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1198
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 1199
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1199
Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu Ala
1 5 10

<210> 1200
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1200
Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 1201
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1201
Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 1202
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1202
Arg Ala Ser Gln Arg Val Ala Ser Asn Tyr Leu Ala
1 5 10

<210> 1203
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1203
Arg Ala Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala
1 5 10

<210> 1204
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1204
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 1205
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1205
Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 1206
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1206
Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu Ala
1 5 10

<210> 1207
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1207
Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser
1 5 10

<210> 1208
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1208
Arg Ala Ser Glu Ser Val Ser Val Ile Gly Ala His Leu Ile His
1 5 10 15

<210> 1209
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1209
Arg Ala Ser Glu Ser Val Thr Ile Leu Gly Ser His Leu Ile Tyr
1 5 10 15

<210> 1210
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1210
Arg Ala Ser Glu Ser Val Thr Ile Leu Gly Ser His Leu Ile Tyr
1 5 10 15

<210> 1211
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1211
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 1212
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1212
Gly Ala Ser Arg Arg Ala Thr
1 5

<210> 1213
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1213
Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 1214

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1214
Glu Val Ser Asn Arg Phe Ser
1 5

<210> 1215
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1215
Leu Gly Ser Lys Arg Ala Ser
1 5

<210> 1216
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1216
Gly Ala Ser Thr Leu Ala Ser
1 5

<210> 1217
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1217
Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 1218
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1218
Gly Ala Ser Thr Arg Ala Ser
1 5

<210> 1219
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1219
Gly Ala Ser Ile Arg Ala Thr
1 5

<210> 1220
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1220
Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 1221
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1221
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 1222
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1222
Glu Val Ser Asn Arg Asp Ser
1 5

<210> 1223
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1223
Asp Ala Ser Thr Leu Gln Thr
1   5

<210> 1224
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1224
Gly Ala Ser Thr Arg Ala Thr
1   5

<210> 1225
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1225
Gly Ala Ser Ser Arg Ala Ser
1   5

<210> 1226
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1226
Ser Ala Thr Ser Pro Val Pro
1   5

<210> 1227
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1227
Ala Ala Asn Lys Ser Gln Ser
1 5

<210> 1228
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1228
Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 1229
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1229
Asp Asp Ser Val Arg Pro Ser
1 5

<210> 1230

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1230
Arg Asp Lys Glu Arg Pro Ser
1 5

<210> 1231
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1231
Ala Ala Ser Asn Leu Gln Ser
1 5

<210> 1232
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1232
Gly Lys Asn Asn Arg Pro Ser
1 5

<210> 1233
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1233
Gly Thr Asn Asn Arg Pro Ser
1 5

<210> 1234
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1234
Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 1235
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1235
Asp Ala Ser Ser Arg Ala Thr
1 5

<210> 1236
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1236
Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 1237
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1237
Gly Ser Ser Asn Arg Ala Thr
1 5

<210> 1238
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1238
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 1239
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1239
Gly Ala Ser Gln Arg Ala Thr
1   5

<210> 1240
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1240
Gly Ala Ser Ser Arg Ala Thr
1   5

<210> 1241
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1241
Gly Ala Ser Ser Arg Ala Thr
1   5

<210> 1242
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1242
Gly Ala Ser Ser Arg Ala Thr
1   5

<210> 1243
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1243
Gly Ala Ser Asn Trp Ala Thr
1 5

<210> 1244
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1244
Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 1245
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1245
Gly Thr Ser Ser Arg Ala Thr
1 5

<210> 1246

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1246
Gly Ala Ser Gly Arg Ala Thr
1 5

<210> 1247
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1247
Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 1248
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1248
Leu Ala Ser Asn Leu Glu Thr
1 5

<210> 1249
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1249
Leu Ala Ser Asn Val Gln Thr
1 5

<210> 1250
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1250
Leu Ala Ser Asn Val Gln Thr
1 5

<210> 1251
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1251
Gln Gln Ser Tyr Ser Thr Pro Tyr Thr
1 5

<210> 1252
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1252
Gln Gln Tyr His Ser Ser Pro Ser Trp Thr
1 5 10

<210> 1253
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1253
Met Gln Ala Leu Gln Thr Pro Tyr Thr
1 5

<210> 1254
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1254
Met Gln Asn Ile Gln Phe Pro Ser
1 5

<210> 1255
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1255
Met Gln Ala Leu Gln Thr Pro Tyr Thr
1   5

<210> 1256
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1256
Gln Gln Ser Tyr Lys Arg Ala Ser
1   5

<210> 1257
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1257
Met Gln Gly Arg Gln Phe Pro Tyr Ser
1   5

<210> 1258
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1258
Gln Gln Tyr Gly Ser Ser Leu Thr
1   5

<210> 1259
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1259
Gln Gln Tyr Gly Ser Ser Ser Trp Thr
1 5

<210> 1260
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1260
Gln Gln Tyr Gly Ser Ser Pro Pro Trp Thr
1 5 10

<210> 1261
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1261
Gln Gln Ser Tyr Thr Leu Ala
1 5

<210> 1262

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1262
Met Gln Gly Thr His Trp Pro Gly Thr
1 5

<210> 1263
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1263
Gln Gln Tyr Glu Ser Leu Pro Leu Thr
1 5

<210> 1264
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1264
Gln Gln Tyr Asn Asp Trp Leu Pro Val Thr
1 5 10

<210> 1265
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1265
Gln Gln Tyr Ala Gly Ser Pro Pro Phe Thr
1 5 10

<210> 1266
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1266
Leu Gln His Asp Asn Phe Pro Leu Thr
1 5

<210> 1267
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1267
Gln His Tyr Tyr Arg Phe Pro Tyr Ser
1 5

<210> 1268
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1268
Met Gln Ala Leu Gln Thr Pro Tyr Thr
1 5

<210> 1269
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1269
Gln Val Trp Asp Ser Asp Ser Glu His Val Val
1 5 10

<210> 1270
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1270
Gln Ala Trp Asp Asp Thr Thr Val Val
1 5

<210> 1271
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1271
Gln Lys Tyr Asn Ser Ala Pro Phe Thr
1 5

<210> 1272
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1272
Ser Ser Arg Asp Ser Ser Gly Asp His Leu Arg Val
1 5 10

<210> 1273
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1273
Asn Ser Arg Asp Ser Ser Gly His His Leu Leu
1 5 10

<210> 1274
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1274
Gln His Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe Thr
1 5 10

<210> 1275
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1275
Gln Gln Phe Gly Thr Ser Ser Gly Leu Thr
1 5 10

<210> 1276
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1276
Gln Gln Tyr His Ser Ser Pro Ser Trp Thr
1 5 10

<210> 1277
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1277
Gln Gln Tyr His Ser Ser Pro Ser Trp Thr
1 5 10

<210> 1278

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1278
Gln Gln Ser Tyr Ser Thr Pro Tyr Ser
1 5

<210> 1279
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1279
Gln His Tyr Glu Ser Ser Pro Ser Trp Thr
1 5 10

<210> 1280
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1280
Gln Gln Tyr Gly Ser Pro Pro Arg Phe Thr
1 5 10

<210> 1281
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1281
Gln His Tyr Gly Ser Ser Pro Ser Trp Thr
1 5 10

<210> 1282
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1282
Gln His Tyr Asp Ser Ser Pro Ser Trp Thr
1 5 10

<210> 1283
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1283
Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr
1 5 10

<210> 1284
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1284
Met Gln Ala Leu Gln Thr Pro Leu Thr
1 5

<210> 1285
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1285
Gln His Tyr Gly Asn Ser Pro Pro Lys Phe Thr
1 5 10

<210> 1286
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1286
Gln His Tyr Gly Gly Ser Pro Arg Leu Thr
1 5 10

<210> 1287
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1287
Gln Gln His Tyr Ser Thr Pro Trp Thr
1   5

<210> 1288
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1288
Leu Gln Ser Arg Ile Phe Pro Arg Thr
1   5

<210> 1289
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1289
Leu Gln Ser Arg Thr Ile Pro Arg Thr
1   5

<210> 1290
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1290
Leu Gln Ser Arg Thr Ile Pro Arg Thr
1   5

<210> 1291
<211> 521
<212> DNA
<213> Unknown

<220>
<221> source
<223> /note="Description of Unknown:
PGK Promoter sequence"

<400> 1291
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac gagggaccgc gacaggcaga 240

cgctcccatg atcactctgc acgccgaagg caaatagtgc aggccgtgcg gcgcttggcg 300

ttccttggaa gggctgaatc cccgcctcgt ccttcgcagc ggccccccgg gtgttcccat 360

cgccgcttct aggcccactg cgacgcttgc ctgcacttct tacacgctct gggtcccagc 420

cgcggcgacg caaagggcct tggtgcgggt ctcgtcggcg cagggacgcg tttgggtccc 480

gacggaacct tttccgcgtt ggggttgggg caccataagc t 521

<210> 1292
<211> 118
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1292
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtg 118

<210> 1293
<211> 221
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1293
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac g 221

<210> 1294
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1294
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac gagggaccgc gacaggcaga 240

cgctcccatg atcactctgc acgccgaagg caaatagtgc aggccgtgcg gcgcttggcg 300

ttccttggaa gggctgaatc cccg 324

<210> 1295
<211> 422
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1295
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac gagggaccgc gacaggcaga 240

cgctcccatg atcactctgc acgccgaagg caaatagtgc aggccgtgcg gcgcttggcg 300

ttccttggaa gggctgaatc cccgcctcgt ccttcgcagc ggccccccgg gtgttcccat 360

cgccgcttct aggcccactg cgacgcttgc ctgcacttct tacacgctct gggtcccagc 420

cg 422

<210> 1296
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(3)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(21)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 1296

Gly Ser Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp Val Glu
1 5 10 15

Glu Asn Pro Gly Pro
20

<210> 1297
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<220>
<221> VARIANT
<222> (1)..(3)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(22)
<223> /note="Variant residues given in the sequence have no preference with respect to those in the annotations for variant positions"

<400> 1297
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1 5 10 15

Glu Glu Asn Pro Gly Pro
20

<210> 1298
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<220>
<221> VARIANT
<222> (1)..(3)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(23)
<223> /note="Variant residues given in the sequence have no preference with respect to those in the annotations for variant positions"

<400> 1298
Gly Ser Gly Gln Cys Thr Asn Tyr Ala Leu Leu Lys Leu Ala Gly Asp
1 5 10 15

Val Glu Ser Asn Pro Gly Pro
20

<210> 1299
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<220>
<221> VARIANT
<222> (1)..(3)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(25)
<223> /note="Variant residues given in the sequence have no preference with respect to those in the annotations for variant positions"

<400> 1299

Gly Ser Gly Val Lys Gln Thr Leu Asn Phe Asp Leu Leu Lys Leu Ala
1 5 10 15

Gly Asp Val Glu Ser Asn Pro Gly Pro
20 25

<210> 1300
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1300
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu
20 25 30

Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr
50 55 60

Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
85 90 95

Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr

```
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140

Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser
145                 150                 155                 160

Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
        195                 200                 205

Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys
    210                 215                 220

Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
```

```
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 1301

<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1301
atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg 60

ccggacatcc agatgacaca gactacatcc tccctgtctg cctctctggg agacagagtc 120

accatcagtt gcagggcaag tcaggacatt agtaaatatt taaattggta tcagcagaaa 180

ccagatggaa ctgttaaact cctgatctac catacatcaa gattacactc aggagtccca 240

tcaaggttca gtggcagtgg gtctggaaca gattattctc tcaccattag caacctggag 300

caagaagata ttgccactta cttttgccaa cagggtaata cgcttccgta cacgttcgga 360

gggggggacca agctggagat cacaggtggc ggtggctcgg gcggtggtgg gtcgggtggc 420

ggcggatctg aggtgaaact gcaggagtca ggacctggcc tggtggcgcc ctcacagagc 480

ctgtccgtca catgcactgt ctcaggggtc tcattacccg actatggtgt aagctggatt 540

cgccagcctc cacgaaaggg tctggagtgg ctgggagtaa tatggggtag tgaaaccaca 600

tactataatt cagctctcaa atccagactg accatcatca aggacaactc caagagccaa 660

gttttcttaa aaatgaacag tctgcaaact gatgacacag ccatttacta ctgtgccaaa 720

cattattact acggtggtag ctatgctatg gactactggg gccaaggaac ctcagtcacc 780

gtctcctcaa ccacgacgcc agcgccgcga ccaccaacac cggcgcccac catcgcgtcg 840

cagcccctgt ccctgcgccc agaggcgtgc cggccagcgg cgggggcgc agtgcacacg 900

agggggctgg acttcgcctg tgatatctac atctgggcgc ccttggccgg gacttgtggg 960

gtccttctcc tgtcactggt tatcaccctt tactgcaaac ggggcagaaa gaaactcctg 1020

tatatattca aacaaccatt tatgagacca gtacaaacta ctcaagagga agatggctgt 1080

agctgccgat ttccagaaga agaagaagga ggatgtgaac tgagagtgaa gttcagcagg 1140

agcgcagacg cccccgcgta caagcagggc cagaaccagc tctataacga gctcaatcta 1200

ggacgaagag aggagtacga tgttttggac aagagacgtg gccgggaccc tgagatgggg 1260

ggaaagccga gaaggaagaa ccctcaggaa ggcctgtaca atgaactgca gaaagataag 1320

atggcggagg cctacagtga gattgggatg aaaggcgagc gccggagggg caaggggcac 1380

gatggccttt accagggtct cagtacagcc accaaggaca cctacgacgc ccttcacatg 1440

caggccctgc cccctcgc 1458

<210> 1302
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1302
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
180 185 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
195 200 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225 230 235 240

Ser Ser

<210> 1303
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 1303

```
Gln Val Gln Leu Leu Glu Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1               5                   10                  15


Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20                  25                  30


Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50                  55                  60


Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80


Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Ser Cys
                85                  90                  95


Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Gly Gly Gly Ser Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Ser Glu Leu Val Leu Thr Gln Ser Pro Lys
    130                 135                 140


Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Val Thr Cys Lys Ala
145                 150                 155                 160


Ser Gln Asn Val Gly Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Gln Ser Pro Lys Pro Leu Ile Tyr Ser Ala Thr Tyr Arg Asn Ser Gly
```

180 185 190

Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Thr Asn Val Gln Ser Lys Asp Leu Ala Asp Tyr Phe Cys Gln
210 215 220

Tyr Asn Arg Tyr Pro Tyr Thr Ser Phe Phe Phe Thr Lys Leu Glu Ile
225 230 235 240

Lys Arg Arg Ser

<210> 1304
<211> 464
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1304
Gln Val Gln Leu Leu Glu Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

```
Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Ser Cys
                85                  90                  95

Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Gly Gly Gly Ser Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Ser Glu Leu Val Leu Thr Gln Ser Pro Lys
    130                 135                 140

Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Val Thr Cys Lys Ala
145                 150                 155                 160

Ser Gln Asn Val Gly Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ser Pro Lys Pro Leu Ile Tyr Ser Ala Thr Tyr Arg Asn Ser Gly
            180                 185                 190

Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Thr Asn Val Gln Ser Lys Asp Leu Ala Asp Tyr Phe Cys Gln
    210                 215                 220

Tyr Asn Arg Tyr Pro Tyr Thr Ser Phe Phe Phe Thr Lys Leu Glu Ile
225                 230                 235                 240

Lys Arg Arg Ser Lys Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp
                245                 250                 255

Asn Glu Lys Ser Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu
            260                 265                 270
```

```
Cys Pro Ser Pro Leu Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu
        275                 280                 285

Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val
    290                 295                 300

Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His
305                 310                 315                 320

Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys
                325                 330                 335

His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
            340                 345                 350

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
        355                 360                 365

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
    370                 375                 380

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
385                 390                 395                 400

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
                405                 410                 415

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
            420                 425                 430

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
        435                 440                 445

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
    450                 455                 460
```

<210> 1305
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1305
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
100 105 110

Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
115 120 125

Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
130 135 140

```
Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145                 150                 155                 160


Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
                165                 170                 175


Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
            180                 185                 190


Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
        195                 200                 205


Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
    210                 215                 220


Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225                 230                 235                 240


Val Thr Val Ser Ser Glu
                245


<210> 1306
<211> 439
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1306
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1               5                   10                  15


Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30
```

```
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
            100                 105                 110

Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
        115                 120                 125

Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
    130                 135                 140

Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145                 150                 155                 160

Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
                165                 170                 175

Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
            180                 185                 190

Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
        195                 200                 205

Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
    210                 215                 220
```

```
Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225                 230                 235                 240


Val Thr Val Ser Ser Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
                245                 250                 255


Pro Met Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
            260                 265                 270


Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Lys Arg Gly
        275                 280                 285


Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
    290                 295                 300


Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Glu Glu Glu
305                 310                 315                 320


Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
                325                 330                 335


Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
            340                 345                 350


Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
        355                 360                 365


Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
    370                 375                 380


Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
385                 390                 395                 400


Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
                405                 410                 415
```

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
420 425 430

Gln Ala Leu Pro Pro Arg Leu
435

<210> 1307
<211> 819
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1307
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
100 105 110

Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys

```
        115                 120                 125

Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
    130                 135                 140

Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145                 150                 155                 160

Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
                165                 170                 175

Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
            180                 185                 190

Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
        195                 200                 205

Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
    210                 215                 220

Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225                 230                 235                 240

Val Thr Val Ser Ser Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
                245                 250                 255

Pro Met Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr
            260                 265                 270

Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Lys Arg Gly
        275                 280                 285

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
    290                 295                 300

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Glu Glu Glu
```

```
305                 310                 315                 320

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
                325                 330                 335

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
            340                 345                 350

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
        355                 360                 365

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
    370                 375                 380

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
385                 390                 395                 400

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
                405                 410                 415

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
            420                 425                 430

Gln Ala Leu Pro Pro Arg Leu Glu Gly Gly Gly Glu Gly Arg Gly Ser
        435                 440                 445

Leu Leu Thr Cys Gly Asp Val Glu Glu Asn Pro Gly Pro Arg Met Leu
    450                 455                 460

Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro Ala Phe
465                 470                 475                 480

Leu Leu Ile Pro Arg Lys Val Cys Asn Gly Ile Gly Ile Gly Glu Phe
                485                 490                 495

Lys Asp Ser Leu Ser Ile Asn Ala Thr Asn Ile Lys His Phe Lys Asn
```

```
            500                 505                 510

Cys Thr Ser Ile Ser Gly Asp Leu His Ile Leu Pro Val Ala Phe Arg
        515                 520                 525

Gly Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu Leu Asp
    530                 535                 540

Ile Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile Gln Ala
545                 550                 555                 560

Trp Pro Glu Asn Arg Thr Asp Leu His Ala Phe Glu Asn Leu Glu Ile
                565                 570                 575

Ile Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala Val Val
            580                 585                 590

Ser Leu Asn Ile Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu Ile Ser
        595                 600                 605

Asp Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala Asn
    610                 615                 620

Thr Ile Asn Trp Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys Thr Lys
625                 630                 635                 640

Ile Ile Ser Asn Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly Gln Val
                645                 650                 655

Cys His Ala Leu Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu Pro Arg
            660                 665                 670

Asp Cys Val Ser Cys Arg Asn Val Ser Arg Gly Arg Glu Cys Val Asp
        675                 680                 685

Lys Cys Asn Leu Leu Glu Gly Glu Pro Arg Glu Phe Val Glu Asn Ser
```

690 695 700

Glu Cys Ile Gln Cys His Pro Glu Cys Leu Pro Gln Ala Met Asn Ile
705 710 715 720

Thr Cys Thr Gly Arg Gly Pro Asp Asn Cys Ile Gln Cys Ala His Tyr
725 730 735

Ile Asp Gly Pro His Cys Val Lys Thr Cys Pro Ala Gly Val Met Gly
740 745 750

Glu Asn Asn Thr Leu Val Trp Lys Tyr Ala Asp Ala Gly His Val Cys
755 760 765

His Leu Cys His Pro Asn Cys Thr Tyr Gly Cys Thr Gly Pro Gly Leu
770 775 780

Glu Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser Ile Ala Thr Gly
785 790 795 800

Met Val Gly Ala Leu Leu Leu Leu Leu Val Val Ala Leu Gly Ile Gly
805 810 815

Leu Phe Met

<210> 1308
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1308
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

```
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
            100                 105                 110

Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
        115                 120                 125

Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
    130                 135                 140

Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145                 150                 155                 160

Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
                165                 170                 175

Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
            180                 185                 190

Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
        195                 200                 205
```

```
Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
    210                 215                 220


Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225                 230                 235                 240


Val Thr Val Ser Ser
                245


<210> 1309
<211> 467
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1309
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1               5                   10                  15


Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45


Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80


Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95
```

```
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
            100                 105                 110

Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
        115                 120                 125

Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
    130                 135                 140

Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145                 150                 155                 160

Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
                165                 170                 175

Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
            180                 185                 190

Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
        195                 200                 205

Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
    210                 215                 220

Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225                 230                 235                 240

Val Thr Val Ser Ser Ala Ala Ala Ile Glu Val Met Tyr Pro Pro Pro
                245                 250                 255

Tyr Leu Asp Asn Glu Lys Ser Asn Gly Thr Ile Ile His Val Lys Gly
            260                 265                 270

Lys His Leu Cys Pro Ser Pro Leu Phe Pro Gly Pro Ser Lys Pro Phe
        275                 280                 285
```

```
Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
    290                 295                 300


Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser Arg
305                 310                 315                 320


Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly Pro
                325                 330                 335


Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala Ala
            340                 345                 350


Tyr Arg Ser Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
        355                 360                 365


Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
    370                 375                 380


Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
385                 390                 395                 400


Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
                405                 410                 415


Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
            420                 425                 430


Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
        435                 440                 445


Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
    450                 455                 460


Pro Pro Arg
465
```

<210> 1310
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1310
Gln Val Gln Leu Leu Glu Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Ser Cys
85 90 95

Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr
115

<210> 1311
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1311
Glu Leu Val Leu Thr Gln Ser Pro Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Pro Leu Ile
35 40 45

Tyr Ser Ala Thr Tyr Arg Asn Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Asn Val Gln Ser
65 70 75 80

Lys Asp Leu Ala Asp Tyr Phe Tyr Phe Cys Gln Tyr Asn Arg Tyr Pro
85 90 95

Tyr Thr Ser Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Arg Ser
100 105 110

<210> 1312
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1312
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

```
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205
```

```
Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220


Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225                 230                 235                 240


Ser Ser



<210> 1313
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1313
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30


Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45


Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60


Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80


Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95
```

```
Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285
```

```
Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480
```

Gln Ala Leu Pro Pro Arg
485

<210> 1314
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1314
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
180 185 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
195 200 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 1315
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1315
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagcc accaccatca tcaccatcac cat 813

<210> 1316
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1316
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala

```
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
```

```
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
```

435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 1317
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1317
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 1318
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1318
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

```
Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220
```

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225 230 235 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Leu Val Thr Val Ser Ser His His His His His His His His
260 265 270

<210> 1319
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1319
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln

100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
180 185 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
210 215 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225 230 235 240

Ile Lys

<210> 1320
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1320
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20   25   30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35   40   45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50   55   60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65   70   75   80

Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85   90   95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100   105   110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115   120   125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130   135   140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145   150   155   160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165   170   175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
            180   185   190

```
Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
        195                 200                 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
                245                 250                 255

Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380
```

```
Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400


Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415


Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430


Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445


Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460


Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480


Gln Ala Leu Pro Pro Arg
                485


<210> 1321
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1321
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30
```

```
Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
    210                 215                 220
```

```
Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225                 230                 235                 240


Ile Lys



<210> 1322
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1322
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30


Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45


Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80


Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95


Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110
```

```
Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
        195                 200                 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
                245                 250                 255

Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300
```

```
Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 1323
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1323
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly

145 150 155 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
165 170 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 1324
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1324
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

```
Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240
```

```
Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430
```

```
Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445


Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460


His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480


Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 1325
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1325
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
```

```
Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145                 150                 155                 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
                165                 170                 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
        195                 200                 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
    210                 215                 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Leu Val Thr Val Ser Ser
                245
```

<210> 1326
<211> 491
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1326

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30


Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45


Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60


Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80


Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95


Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110


Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160
```

```
Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350
```

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
355 360 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
370 375 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385 390 395 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
405 410 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
420 425 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
435 440 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1327
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1327
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

```
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
    130                 135                 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145                 150                 155                 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
            180                 185                 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
```

195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 1328
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1328
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
35 40 45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

```
Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285
```

```
Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480
```

```
Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 1329
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1329
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30


Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
    50                  55                  60


Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125
```

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
    130                 135                 140


Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145                 150                 155                 160


Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
            180                 185                 190


Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220


Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225                 230                 235                 240


Gly Thr Lys Leu Glu Ile Lys
                245


<210> 1330
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1330
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205
```

```
Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400
```

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
405 410 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
420 425 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
435 440 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1331
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1331
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly

```
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145                 150                 155                 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
                165                 170                 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
        195                 200                 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
    210                 215                 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Leu Val Thr Val Ser Ser
```

245

<210> 1332
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1332
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

```
Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335
```

```
Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 1333
<211> 247
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1333

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                  10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30


Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys
    50                  55                  60


Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
    130                 135                 140


Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145                 150                 155                 160


Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
                165                 170                 175
```

```
Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
            180                 185                 190


Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220


Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225                 230                 235                 240


Gly Thr Lys Leu Glu Ile Lys
                245


<210> 1334
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1334
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30


Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45


Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60
```

```
Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255
```

```
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445
```

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1335
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1335
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser

100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
180 185 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
195 200 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 1336
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1336
```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190
```

```
Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380
```

```
Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400


Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415


Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430


Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445


Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460


His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480


Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 1337
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1337
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30
```

```
Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
    210                 215                 220
```

```
Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225                 230                 235                 240


Ile Lys



<210> 1338
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1338
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30


Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45


Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60


Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80


Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95


Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110
```

```
Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300
```

```
Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 1339
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1339
Asp Tyr Gly Val Ser
1 5

<210> 1340
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1340
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
1 5 10 15

<210> 1341
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1341
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 1342
<211> 11
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1342
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 1343
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1343
His Thr Ser Arg Leu His Ser
1 5

<210> 1344
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1344
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 1345
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1345
Asp Tyr Gly Val Ser
1 5

<210> 1346
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1346
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
1 5 10 15

<210> 1347
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1347
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 1348
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1348
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 1349
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1349
His Thr Ser Arg Leu His Ser
1 5

<210> 1350
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1350
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 1351
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1351
Asp Tyr Gly Val Ser

1 5

<210> 1352
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1352
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
1 5 10 15

<210> 1353
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1353
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 1354
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1354
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 1355
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1355
His Thr Ser Arg Leu His Ser
1 5

<210> 1356
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1356
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 1357
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1357
Asp Tyr Gly Val Ser
1 5

<210> 1358
<211> 16
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1358
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
1 5 10 15

<210> 1359
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1359
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 1360
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1360
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 1361
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1361
His Thr Ser Arg Leu His Ser
1 5

<210> 1362
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1362
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 1363
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1363
Asn Tyr Asn Leu His
1 5

<210> 1364
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1364
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1   5   10   15

Gly

<210> 1365
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1365
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10

<210> 1366
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1366
Gly Tyr Thr Phe Thr Asn Tyr
1   5

<210> 1367
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1367
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 1368
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1368
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1369
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1369
Gly Tyr Thr Phe Thr Asn Tyr Asn
1 5

<210> 1370
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1370

Ile Tyr Pro Gly Asn Tyr Asp Thr
1 5

<210> 1371
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1371
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 1372
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1372
Gly Tyr Thr Phe Thr Asn Tyr Asn Leu His
1 5 10

<210> 1373
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1373
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1374
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1374
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1375
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1375
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1376
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1376
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac ctggagcatc cgtgaaagtg 60

tcttgcaaag cctccggcta caccttcacc aactacaacc tccattgggt cagacaggcc 120

cccggacaag gactcgaatg gatgggagcg atctacccgg gaaactacga caccagctac 180

aaccagaagt tcaagggccg cgtgactatg accgccgata agagcacctc caccgcctac 240

atggaactgt cctcgctgag gtccgaggac actgcggtgt actactgcgc ccgcgtggac 300

ttcggacact cacggtattg gtacttcgac gtctggggac agggcactac cgtgaccgtg 360

tcgagc 366

<210> 1377
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1377
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1378
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1378
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1379
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1379
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1380
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1380
Thr Ser Ser Val Ser Ser
1   5

<210> 1381
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1381
Ala Thr Ser
1

<210> 1382
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1382
Trp Thr Phe Asn Pro Pro
1   5

<210> 1383
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1383
Ser Ser Val Ser Ser
1   5

<210> 1384
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1384
Ala Thr Ser
1

<210> 1385
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1385
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1386
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1386
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1387

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1387
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1388
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1388
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1389
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1389
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

```
Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile His
        35                  40                  45


Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60


Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65                  70                  75                  80


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
                85                  90                  95


Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105


<210> 1390
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1390
gatatccagc tgactcagtc cccgtcattc ctgtccgcct ccgtgggaga cagagtgacc       60

atcacctgtc gggccacttc ctccgtgtca agcatgaact ggtatcagca gaagcccggg      120

aaggccccaa agccgctgat tcacgcgacg tccaacctgg cttccggcgt gccgagccgg      180

ttctccggct cggggagcgg gactgagtac accctgacta tttcctcgct tcaacccgag      240

gactttgcta cctactactg ccaacagtgg accttcaatc ctccgacatt cggacagggt      300

accaagttgg aaatcaag                                                    318


<210> 1391
<211> 20
<212> PRT
<213> Artificial Sequence
```

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1391
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 1392
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1392
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

```
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile His Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Leu Glu Ile Lys
                245
```

<210> 1393
<211> 744
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1393
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac ctggagcatc cgtgaaagtg 60

tcttgcaaag cctccggcta caccttcacc aactacaacc tccattgggt cagacaggcc 120

cccggacaag gactcgaatg gatgggagcg atctacccgg gaaactacga caccagctac 180

aaccagaagt tcaagggccg cgtgactatg accgccgata agagcacctc caccgcctac 240

atggaactgt cctcgctgag gtccgaggac actgcggtgt actactgcgc ccgcgtggac 300

ttcggacact cacggtattg gtacttcgac gtctggggac agggcactac cgtgaccgtg 360

tcgagcggcg gaggaggttc gggaggggggc ggatcagggg gcggcggcag cggtggaggg 420

ggctcggata tccagctgac tcagtccccg tcattcctgt ccgcctccgt gggagacaga 480

gtgaccatca cctgtcgggc cacttcctcc gtgtcaagca tgaactggta tcagcagaag 540

cccgggaagg ccccaaagcc gctgattcac gcgacgtcca acctggcttc cggcgtgccg 600

agccggttct ccggctcggg gagcgggact gagtacaccc tgactatttc ctcgcttcaa 660

cccgaggact ttgctaccta ctactgccaa cagtggacct tcaatcctcc gacattcgga 720

cagggtacca agttggaaat caag 744

<210> 1394
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1394
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val

```
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val
            180                 185                 190

Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
```

```
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
```

405 410 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1395
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1395
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtccggtgca gaagtcaaga aacctggagc atccgtgaaa 120

gtgtcttgca aagcctccgg ctacaccttc accaactaca acctccattg ggtcagacag 180

gcccccggac aaggactcga atggatggga gcgatctacc cgggaaacta cgacaccagc 240

tacaaccaga agttcaaggg ccgcgtgact atgaccgccg ataagagcac ctccaccgcc 300

tacatggaac tgtcctcgct gaggtccgag gacactgcgg tgtactactg cgcccgcgtg 360

gacttcggac actcacggta ttggtacttc gacgtctggg gacagggcac taccgtgacc 420

gtgtcgagcg gcggaggagg ttcgggaggg ggcggatcag ggggcggcgg cagcggtgga 480

gggggctcgg atatccagct gactcagtcc ccgtcattcc tgtccgcctc cgtgggagac 540

agagtgacca tcacctgtcg ggccacttcc tccgtgtcaa gcatgaactg gtatcagcag 600

aagcccggga aggccccaaa gccgctgatt cacgcgacgt ccaacctggc ttccggcgtg 660

ccgagccggt tctccggctc ggggagcggg actgagtaca ccctgactat ttcctcgctt 720

caacccgagg actttgctac ctactactgc caacagtgga ccttcaatcc tccgacattc 780

ggacagggta ccaagttgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1396
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1396

Ser Tyr Asn Met His
1 5

<210> 1397
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1397
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1398
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1398
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1399
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1399
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 1400
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1400
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1401
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1401
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1402
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1402
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1403
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1403
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1404
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1404
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10 15

<210> 1405
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1405
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1 5 10

<210> 1406

<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1406
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1407
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1407
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1408
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1408
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1409
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1409
caagtgcagc tcgtccagtc cggtgcagaa gtcaagaaac ccggtgcttc agtgaaagtg 60

tcctgcaagg cctccggtta caccttcacc tcctacaaca tgcactgggt ccgccaagcc 120

ccgggccagg gactcgaatg gatgggagcc atctaccctg gcaacgggga cacctcatac 180

aaccctaagt tcaagggcag agtgaccatg actgcggaca agtccactag aacagcgtac 240

atggagctga gcagcctgcg gtccgaggat actgccgtgt actactgcgc ccgctcctac 300

ttctacggaa gctcgtcgtg gtacttcgat gtctggggac agggcaccac tgtgactgtg 360

tcctcc 366

<210> 1410
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1410
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1411
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1411
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1412
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1412
Gln Gln Trp Ile Phe Asn Pro Pro Thr

1 5

<210> 1413
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1413
Ser Ser Ser Val Ser Ser
1 5

<210> 1414
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1414
Ala Thr Ser
1

<210> 1415
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1415
Trp Ile Phe Asn Pro Pro
1 5

<210> 1416
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1416
Ser Ser Val Ser Ser
1 5

<210> 1417
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1417
Ala Thr Ser
1

<210> 1418
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1418
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1419
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1419
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1420
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1420
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1421
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1421
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1422
<211> 106
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1422
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1423
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1423
gaaattgtgc tgactcagag ccccgccacc ctgagcttgt cccccgggga aagggcaacg 60

ctgtcatgcc gcgcctcgtc atccgtgtcc tccatgcatt ggtaccagca gaagccggga 120

caggcccctc ggccgctgat cttcgccacc tccaatctcg cttccggcat tccggcccgg 180

ttctcgggaa gcgggtcggg gaccgactat accctgacca tctctagcct tgaacctgag 240

gacgccgcgg tgtactattg tcaacagtgg atctttaacc ccccaacctt cggtggaggc 300

accaaagtgg agattaag 318

<210> 1424
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1424
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1425
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1425
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

```
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160

Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
    210                 215                 220

Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
```

225 230 235 240

Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1426
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1426
caagtgcagc tcgtccagtc cggtgcagaa gtcaagaaac ccggtgcttc agtgaaagtg 60

tcctgcaagg cctccggtta caccttcacc tcctacaaca tgcactgggt ccgccaagcc 120

ccgggccagg gactcgaatg gatgggagcc atctaccctg gcaacgggga cacctcatac 180

aaccctaagt tcaagggcag agtgaccatg actgcggaca agtccactag aacagcgtac 240

atggagctga gcagcctgcg gtccgaggat actgccgtgt actactgcgc ccgctcctac 300

ttctacggaa gctcgtcgtg gtacttcgat gtctggggac agggcaccac tgtgactgtg 360

tcctccggtg gcggaggctc gggcggaggc ggaagcggcg gcgggggatc gggaggagga 420

gggtccgaaa ttgtgctgac tcagagcccc gccaccctga gcttgtcccc cggggaaagg 480

gcaacgctgt catgccgcgc ctcgtcatcc gtgtcctcca tgcattggta ccagcagaag 540

ccgggacagg cccctcggcc gctgatcttc gccacctcca atctcgcttc cggcattccg 600

gcccggttct cgggaagcgg gtcggggacc gactataccc tgaccatctc tagccttgaa 660

cctgaggacg ccgcggtgta ctattgtcaa cagtggatct ttaacccccc aaccttcggt 720

ggaggcacca aagtggagat taag 744

<210> 1427
<211> 492
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1427

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65                  70                  75                  80


Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
                85                  90                  95


Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
        115                 120                 125


Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160
```

```
Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350
```

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
355 360 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
370 375 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385 390 395 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
405 410 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1428
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1428
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtcca gtccggtgca gaagtcaaga aacccggtgc ttcagtgaaa 120

gtgtcctgca aggcctccgg ttacaccttc acctcctaca acatgcactg ggtccgccaa 180

gccccgggcc agggactcga atggatggga gccatctacc ctggcaacgg ggacacctca 240

tacaacccta agttcaaggg cagagtgacc atgactgcgg acaagtccac tagaacagcg 300

tacatggagc tgagcagcct gcggtccgag gatactgccg tgtactactg cgcccgctcc 360

tacttctacg gaagctcgtc gtggtacttc gatgtctggg gacagggcac cactgtgact 420

gtgtcctccg gtggcggagg ctcgggcgga ggcggaagcg gcggcggggg atcgggagga 480

ggagggtccg aaattgtgct gactcagagc cccgccaccc tgagcttgtc ccccggggaa 540

agggcaacgc tgtcatgccg cgcctcgtca tccgtgtcct ccatgcattg gtaccagcag 600

aagccgggac aggcccctcg gccgctgatc ttcgccacct ccaatctcgc ttccggcatt 660

ccggcccggt tctcgggaag cgggtcgggg accgactata ccctgaccat ctctagcctt 720

gaacctgagg acgccgcggt gtactattgt caacagtgga tctttaaccc cccaaccttc 780

ggtggaggca ccaaagtgga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1429
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1429
Asn Tyr Trp Met His
1 5

<210> 1430
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1430
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1431
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1431
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr

1 5 10

<210> 1432
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1432
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1433
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1433
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1434
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1434
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1435
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1435
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1436
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1436
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1437
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1437
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1438
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1438
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His
1 5 10

<210> 1439
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1439
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1440
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1440
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1441
<211> 122

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1441
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1442
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1442
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaaac caggcgcatc cgtgaaagtc 60

tcctgcaaag cctccggcta cacattcact aactattgga tgcattgggt gcgccaggcc 120

ccgggacagg ggctggagtg gatggggttc attaccccta ccaccggcta ccctgagtac 180

aaccagaagt tcaaggatag ggtcaccatg accgctgaca agtccacctc caccgcgtac 240

atggaactgt catcgctccg gtccgaggat accgcggtgt actactgcgc ccggagaaaa 300

gtcggaaagg gagtgtatta cgccttggac tactggggac aggggactac cgtgaccgtg 360

tcgagc 366

<210> 1443
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1443
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1444
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1444
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1445
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1445
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1446
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1446
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1447
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1447
Asn Thr Lys
1

<210> 1448
<211> 6

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1448
Phe Trp Ser Ser Pro Trp
1 5

<210> 1449
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1449
Gly Asn Ile His Asn Tyr
1 5

<210> 1450
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1450
Asn Thr Lys
1

<210> 1451
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1451
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1452
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1452
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1453
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1453
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1454
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1454
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1455
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1455
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1456
<211> 321

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1456
gacatccaga tgacccagtc cccgtcaagc cttagcgcct ccgtgggcga ccgcgtgacc 60

attacttgtc gggcgtcggg aaacatccac aactacctcg cctggtacca gcagaagccg 120

ggaaaggtcc ccaagctgct gatctacaat accaagactc tggccgacgg agtgccttcc 180

cgcttttccg gttcgggaag cgggactgac tacaccctga ctatctcctc gctgcaaccc 240

gaagatgtgg ctacgtacta ctgccagcac ttctggtcct ctccctggac cttcggcggt 300

ggcactaagg tcgagattaa g 321

<210> 1457
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1457
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1458
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1458
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100   105   110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115   120   125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130   135   140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145   150   155   160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165   170   175

Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile Tyr Asn
180 185 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
210 215 220

Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1459
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1459
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaaac caggcgcatc cgtgaaagtc 60

tcctgcaaag cctccggcta cacattcact aactattgga tgcattgggt gcgccaggcc 120

ccgggacagg ggctggagtg gatggggttc attaccccta ccaccggcta ccctgagtac 180

aaccagaagt tcaaggatag ggtcaccatg accgctgaca agtccacctc caccgcgtac 240

atggaactgt catcgctccg gtccgaggat accgcggtgt actactgcgc ccggagaaaa 300

gtcggaaagg gagtgtatta cgccttggac tactggggac aggggactac cgtgaccgtg 360

tcgagcggtg gaggcggctc cggcggagga ggaagcgggg gaggcggttc agggggcgga 420

ggaagcgaca tccagatgac ccagtccccg tcaagcctta gcgcctccgt gggcgaccgc 480

gtgaccatta cttgtcgggc gtcgggaaac atccacaact acctcgcctg gtaccagcag 540

aagccgggaa aggtccccaa gctgctgatc tacaatacca agactctggc cgacggagtg 600

ccttcccgct tttccggttc gggaagcggg actgactaca ccctgactat ctcctcgctg 660

caacccgaag atgtggctac gtactactgc cagcacttct ggtcctctcc ctggaccttc 720

ggcggtggca ctaaggtcga gattaag 747

<210> 1460
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1460
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

```
Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
        115                 120                 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190

His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys
        195                 200                 205

Leu Leu Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255

Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300
```

```
Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 1461
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1461
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtcaaga aaccaggcgc atccgtgaaa 120

gtctcctgca aagcctccgg ctacacattc actaactatt ggatgcattg ggtgcgccag 180

gccccgggac aggggctgga gtggatgggg ttcattaccc ctaccaccgg ctaccctgag 240

tacaaccaga agttcaagga tagggtcacc atgaccgctg acaagtccac ctccaccgcg 300

tacatggaac tgtcatcgct ccggtccgag gataccgcgg tgtactactg cgcccggaga 360

aaagtcggaa agggagtgta ttacgccttg gactactggg gacaggggac taccgtgacc 420

gtgtcgagcg gtggaggcgg ctccggcgga ggaggaagcg ggggaggcgg ttcagggggc 480

ggaggaagcg acatccagat gacccagtcc ccgtcaagcc ttagcgcctc cgtgggcgac 540

cgcgtgacca ttacttgtcg ggcgtcggga aacatccaca actacctcgc ctggtaccag 600

cagaagccgg gaaaggtccc caagctgctg atctacaata ccaagactct ggccgacgga 660

gtgccttccc gcttttccgg ttcgggaagc gggactgact acaccctgac tatctcctcg 720

ctgcaacccg aagatgtggc tacgtactac tgccagcact tctggtcctc tccctggacc 780

ttcggcggtg gcactaaggt cgagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct accagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 1462
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1462
Asn Tyr Trp Met His
1 5

<210> 1463
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1463
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1464
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1464
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1465
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1465
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1466
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1466
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1467
<211> 13

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1467
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1468
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1468
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1469
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1469
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1470
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1470
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1471
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1471
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His
1 5 10

<210> 1472
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1472
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1473
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1473
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1474
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1474
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1475
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1475
caagtccaac tcgtccaatc aggagcagaa gtcaagaagc ccggaagctc tgtcaaagtg 60

tcctgcaagg cctccggtta caccttcacc aactattgga tgcactgggt cagacaggcc 120

ccgggacagg gcttggaatg gatgggtttc atcactccaa ccaccggtta cccggagtac 180

aaccagaagt ttaaggaccg cgtgaccatt actgccgaca agtccacgag caccgcttac 240

atggaactta gcagcctgcg gtccgaggac actgccgtgt attactgcgc gcggaggaag 300

gtcggaaagg gagtgtacta cgcactggac tactggggcc agggaaccac cgtgactgtg 360

tcctcc   366

<210> 1476
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1476
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1   5   10

<210> 1477

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1477
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1478
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1478
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1479
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1479
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1480
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1480
Asn Thr Lys
1

<210> 1481
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1481
Phe Trp Ser Ser Pro Trp
1 5

<210> 1482
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1482
Gly Asn Ile His Asn Tyr
1 5

<210> 1483
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1483
Asn Thr Lys
1

<210> 1484
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1484
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1485
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1485
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1486
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1486
Asn Thr Lys Thr Leu Ala Asp
1   5

<210> 1487
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1487
Gln His Phe Trp Ser Ser Pro Trp Thr
1   5

<210> 1488
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1488
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35   40   45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1489
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1489
gatattcaga tgacccagtc cccttcatcc ctgagcgcct cagtgggcga tagagtgacc 60

atcacttgtc gcgcctcggg caatatccac aactacctcg cctggtacca gcagaagccg 120

ggaaaagtgc ctaagctgct gatctacaac actaagaccc tggcggatgg agtgcccagc 180

cggttctccg gctccggcag cggcacagac tacaccctca ccatctcctc gctgcaacca 240

gaggacgtgg ctacctacta ctgccagcat ttctggtcgt ccccctggac tttcggaggg 300

gggaccaaag tggagattaa g 321

<210> 1490
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1490
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
            20

<210> 1491
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1491
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100   105   110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115   120   125

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140


Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160


Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165                 170                 175


Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile Tyr Asn
            180                 185                 190


Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205


Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220


Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225                 230                 235                 240


Gly Gly Gly Thr Lys Val Glu Ile Lys
                245


<210> 1492
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1492
caagtccaac tcgtccaatc aggagcagaa gtcaagaagc ccggaagctc tgtcaaagtg       60

tcctgcaagg cctccggtta caccttcacc aactattgga tgcactgggt cagacaggcc      120
```

ccgggacagg gcttggaatg gatgggtttc atcactccaa ccaccggtta cccggagtac 180

aaccagaagt ttaaggaccg cgtgaccatt actgccgaca agtccacgag caccgcttac 240

atggaactta gcagcctgcg gtccgaggac actgccgtgt attactgcgc gcggaggaag 300

gtcggaaagg gagtgtacta cgcactggac tactggggcc agggaaccac cgtgactgtg 360

tcctccggtg gcggagggtc gggaggggggg ggctcgggag gaggagggtc cgggggcggt 420

ggctcagata ttcagatgac ccagtcccct tcatccctga gcgcctcagt gggcgataga 480

gtgaccatca cttgtcgcgc ctcgggcaat atccacaact acctcgcctg gtaccagcag 540

aagccgggaa aagtgcctaa gctgctgatc tacaacacta agaccctggc ggatggagtg 600

cccagccggt tctccggctc cggcagcggc acagactaca ccctcaccat ctcctcgctg 660

caaccagagg acgtggctac ctactactgc cagcatttct ggtcgtcccc ctggactttc 720

ggaggggggga ccaaagtgga gattaag 747

<210> 1493
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1493
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

```
Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
        115                 120                 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190

His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys
        195                 200                 205

Leu Leu Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255
```

```
Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445
```

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450   455   460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465   470   475   480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485   490

<210> 1494
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1494
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca atcaggagca gaagtcaaga agcccggaag ctctgtcaaa 120

gtgtcctgca aggcctccgg ttacaccttc accaactatt ggatgcactg ggtcagacag 180

gccccgggac agggcttgga atggatgggt ttcatcactc caaccaccgg ttacccggag 240

tacaaccaga agtttaagga ccgcgtgacc attactgccg acaagtccac gagcaccgct 300

tacatggaac ttagcagcct gcggtccgag gacactgccg tgtattactg cgcgcggagg 360

aaggtcggaa agggagtgta ctacgcactg gactactggg gccagggaac caccgtgact 420

gtgtcctccg gtggcggagg gtcgggaggg gggggctcgg gaggaggagg gtccgggggc 480

ggtggctcag atattcagat gacccagtcc ccttcatccc tgagcgcctc agtgggcgat 540

agagtgacca tcacttgtcg cgcctcgggc aatatccaca actacctcgc ctggtaccag 600

cagaagccgg gaaaagtgcc taagctgctg atctacaaca ctaagaccct ggcggatgga 660

gtgcccagcc ggttctccgg ctccggcagc ggcacagact acaccctcac catctcctcg 720

ctgcaaccag aggacgtggc tacctactac tgccagcatt tctggtcgtc cccctggact 780

ttcggagggg ggaccaaagt ggagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct accagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 1495
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1495
Asn Tyr Trp Met His
1 5

<210> 1496
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1496
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1497
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1497
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1498
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1498
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1499
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1499
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1500
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1500
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1501
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1501
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1502
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1502
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1503
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1503
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1504
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1504
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His
1 5 10

<210> 1505
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1505
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1   5   10   15

Asp

<210> 1506
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1506
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1   5   10

<210> 1507
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1507
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe

50 55 60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1508
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1508
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac ccggagcttc cgtgaaagtg 60

tcctgcaaag cctccggtta cacctttacg aactactgga tgcattgggt gcgccaggcc 120

ccgggacagg ggctggaatg gatgggcttc attaccccca ccaccggata ccccgagtac 180

aatcagaagt tcaaggaccg ggtcaccatg accgccgaca agtcaacctc tactgcttac 240

atggagctgt ccagcctgcg gtcggaagat accgccgtgt attactgcgc gagaaggaaa 300

gtcggaaagg gagtgtacta tgccctggac tactggggac aggggaccac tgtgactgtg 360

tcaagc 366

<210> 1509
<211> 11
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1509
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1510
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1510
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1511
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1511
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1512
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1512
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1513
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1513
Asn Thr Lys
1

<210> 1514
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1514
Phe Trp Ser Ser Pro Trp
1 5

<210> 1515
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1515
Gly Asn Ile His Asn Tyr
1   5

<210> 1516
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1516
Asn Thr Lys
1

<210> 1517
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1517
Gln His Phe Trp Ser Ser Pro Trp Thr
1   5

<210> 1518
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1518
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala

1 5 10

<210> 1519
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1519
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1520
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1520
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1521
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1521
Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1522
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1522
gcgatccgca tgacccagag cccgttctcc ctgtccgcgt ccgtggggga ccgcgtgact 60

atcacgtgtc gggcctccgg gaacatccac aactacctcg catggtacca gcagaagccg 120

gccaaggccc ctaagttgtt catctacaac accaagactc ttgccgacgg agtgccgtcc 180

cggtttagcg gaagcggttc cggcaccgac tacaccctga ctatctcgag cctgcaacca 240

gaagatttcg ccacttacta ctgccagcac ttctggtcgt ccccttggac attcggcggc 300

ggcaccaagg tcgagattaa g 321

<210> 1523
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1523
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 1524
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1524
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ile
    130                 135                 140

Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile Tyr Asn
            180                 185                 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 1525
<211> 747

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1525
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac ccggagcttc cgtgaaagtg 60

tcctgcaaag cctccggtta cacctttacg aactactgga tgcattgggt gcgccaggcc 120

ccgggacagg ggctggaatg gatgggcttc attaccccca ccaccggata ccccgagtac 180

aatcagaagt tcaaggaccg ggtcaccatg accgccgaca agtcaacctc tactgcttac 240

atggagctgt ccagcctgcg gtcggaagat accgccgtgt attactgcgc gagaaggaaa 300

gtcggaaagg gagtgtacta tgccctggac tactggggac aggggaccac tgtgactgtg 360

tcaagcggag gcggaggctc gggggggcgga ggttcgggcg gaggaggatc agggggcggc 420

ggttccgcga tccgcatgac ccagagcccg ttctccctgt ccgcgtccgt gggggaccgc 480

gtgactatca cgtgtcgggc ctccgggaac atccacaact acctcgcatg gtaccagcag 540

aagccggcca aggcccctaa gttgttcatc tacaacacca agactcttgc cgacggagtg 600

ccgtcccggt ttagcggaag cggttccggc accgactaca ccctgactat ctcgagcctg 660

caaccagaag atttcgccac ttactactgc cagcacttct ggtcgtcccc ttggacattc 720

ggcggcggca ccaaggtcga gattaag 747

<210> 1526
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1526
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
        115                 120                 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190

His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys
```

```
        195                 200                 205

Leu Phe Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255

Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
```

385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1527
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1527
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtccggtgca gaagtcaaga aacccggagc ttccgtgaaa 120

gtgtcctgca aagcctccgg ttacaccttt acgaactact ggatgcattg ggtgcgccag 180

gccccgggac aggggctgga atggatgggc ttcattaccc ccaccaccgg ataccccgag 240

tacaatcaga agttcaagga ccgggtcacc atgaccgccg acaagtcaac ctctactgct 300

tacatggagc tgtccagcct gcggtcggaa gataccgccg tgtattactg cgcgagaagg 360

aaagtcggaa agggagtgta ctatgccctg gactactggg gacaggggac cactgtgact 420

gtgtcaagcg gaggcggagg ctcgggggc ggaggttcgg gcggaggagg atcaggggc 480

ggcggttccg cgatccgcat gacccagagc ccgttctccc tgtccgcgtc cgtgggggac 540

cgcgtgacta tcacgtgtcg ggcctccggg aacatccaca actacctcgc atggtaccag 600

cagaagccgg ccaaggcccc taagttgttc atctacaaca ccaagactct tgccgacgga 660

gtgccgtccc ggtttagcgg aagcggttcc ggcaccgact acaccctgac tatctcgagc 720

ctgcaaccag aagatttcgc cacttactac tgccagcact tctggtcgtc cccttggaca 780

ttcggcggcg gcaccaaggt cgagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct accagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 1528
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1528
Asn Tyr Trp Met His
1 5

<210> 1529
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1529
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1530
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1530
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1531
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1531
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1532
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1532
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1533
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1533
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1534
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1534
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1535
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1535
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1536
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1536
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1537
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1537
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His

1 5 10

<210> 1538
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1538
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1539
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1539
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1540
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1540

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1541
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1541
caagtccaac tcgtccaaag cggtgcagaa gtcaagaagc ccggttcctc cgtgaaagtg 60

tcctgcaaag cctcgggcta caccttcact aattactgga tgcattgggt ccgccaggcg 120

cccggacagg gattggaatg gatggggttc atcacgccga ccaccggata cccggagtac 180

aaccagaagt tcaaggacag agtgaccatt accgccgata agtccacctc caccgcttac 240

atggagctct cctcactgcg gtccgaagat acagccgtgt actattgtgc tcgccggaaa 300

gtcggaaagg gagtgtacta cgccctggac tattggggcc agggcaccac cgtgaccgtg 360

tcctcg 366

<210> 1542
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1542
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1543
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1543
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1544
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1544
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1545
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1545
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1546
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1546
Asn Thr Lys
1

<210> 1547
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1547

Phe Trp Ser Ser Pro Trp
1 5

<210> 1548
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1548
Gly Asn Ile His Asn Tyr
1 5

<210> 1549
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1549
Asn Thr Lys
1

<210> 1550
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1550
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1551
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1551
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1552
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1552
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1553
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1553
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1554
<211> 107

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1554
Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1555
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1555

gccattagga tgactcagtc ccctttctcc ctctccgcga gcgtgggcga ccgcgtgacg 60

atcacttgcc gggcctcggg gaacattcac aactacctgg cctggtacca gcagaagccg 120

gccaaggccc ctaagctgtt catctacaac accaagaccc ttgcggacgg agtgccatcg 180

agattttccg gctcgggctc tgggaccgat tacactctga ctatctcaag cctgcaacct 240

gaggacttcg ccacttacta ctgccagcac ttctggagca gcccctggac tttcggtggc 300

gggaccaagg tcgaaatcaa g 321

<210> 1556
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1556
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1557
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1557
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr

```
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ile
    130                 135                 140

Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile Tyr Asn
            180                 185                 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
```

210 215 220

Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1558
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1558
caagtccaac tcgtccaaag cggtgcagaa gtcaagaagc ccggttcctc cgtgaaagtg 60

tcctgcaaag cctcgggcta caccttcact aattactgga tgcattgggt ccgccaggcg 120

cccggacagg gattggaatg gatggggttc atcacgccga ccaccggata cccggagtac 180

aaccagaagt tcaaggacag agtgaccatt accgccgata agtccacctc caccgcttac 240

atggagctct cctcactgcg gtccgaagat acagccgtgt actattgtgc tcgccggaaa 300

gtcggaaagg gagtgtacta cgccctggac tattggggcc agggcaccac cgtgaccgtg 360

tcctcgggag gagggggttc gggcggaggc ggctccggtg gaggcggaag cggaggggc 420

ggatcagcca ttaggatgac tcagtcccct ttctccctct ccgcgagcgt gggcgaccgc 480

gtgacgatca cttgccgggc ctcggggaac attcacaact acctggcctg gtaccagcag 540

aagccggcca aggcccctaa gctgttcatc tacaacacca agacccttgc ggacggagtg 600

ccatcgagat tttccggctc gggctctggg accgattaca ctctgactat ctcaagcctg 660

caacctgagg acttcgccac ttactactgc cagcacttct ggagcagccc ctggactttc 720

ggtggcggga ccaaggtcga aatcaag 747

<210> 1559
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1559
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
115 120 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
130 135 140

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160


Gly Gly Ser Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala
                165                 170                 175


Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190


His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys
        195                 200                 205


Leu Phe Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220


Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240


Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255


Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270


Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285


Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300


Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320


Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335
```

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1560
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 1560
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca aagcggtgca gaagtcaaga agcccggttc ctccgtgaaa 120

gtgtcctgca aagcctcggg ctacaccttc actaattact ggatgcattg ggtccgccag 180

gcgcccggac agggattgga atggatgggg ttcatcacgc cgaccaccgg atacccggag 240

tacaaccaga agttcaagga cagagtgacc attaccgccg ataagtccac ctccaccgct 300

tacatggagc tctcctcact gcggtccgaa gatacagccg tgtactattg tgctcgccgg 360

aaagtcggaa agggagtgta ctacgccctg gactattggg gccagggcac caccgtgacc 420

gtgtcctcgg gaggaggggg ttcgggcgga ggcggctccg gtggaggcgg aagcggaggg 480

ggcggatcag ccattaggat gactcagtcc cctttctccc tctccgcgag cgtgggcgac 540

cgcgtgacga tcacttgccg ggcctcgggg aacattcaca actacctggc ctggtaccag 600

cagaagccgg ccaaggcccc taagctgttc atctacaaca ccaagaccct tgcggacgga 660

gtgccatcga gattttccgg ctcgggctct gggaccgatt acactctgac tatctcaagc 720

ctgcaacctg aggacttcgc cacttactac tgccagcact tctggagcag cccctggact 780

ttcggtggcg ggaccaaggt cgaaatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct accagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 1561
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1561
Asn Tyr Asn Leu His
1 5

<210> 1562
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1562
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1563
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1563
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1564
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1564
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1565
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1565
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 1566
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1566

Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10

<210> 1567
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1567
Gly Tyr Thr Phe Thr Asn Tyr Asn
1   5

<210> 1568
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1568
Ile Tyr Pro Gly Asn Tyr Asp Thr
1   5

<210> 1569
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1569
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10   15

<210> 1570
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1570
Gly Tyr Thr Phe Thr Asn Tyr Asn Leu His
1 5 10

<210> 1571
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1571
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1572
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1572
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1573
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1573
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1574
<211> 366
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1574
caagtccaac tcgtccaatc cggtgcagaa gtcaagaaac ccggtgcatc cgtgaaagtg 60

tcatgcaaag cctccgggta caccttcact aactacaacc tccactgggt ccgccaggcc 120

ccgggacagg gactggagtg gatgggggcc atctacccgg gaaactacga cacttcatac 180

aaccagaagt tcaagggcag agtgaccatg actgccgaca agagcacatc gaccgcctac 240

atggaactca gctccctgcg ctccgaggat actgccgtct actactgtgc ccgggtggac 300

ttcggccact cccggtattg gtatttcgat gtctggggac agggaaccac cgtgactgtg 360

tccagc 366

<210> 1575
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1575
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1576
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1576
Ala Thr Ser Asn Leu Ala Ser
1   5

<210> 1577
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1577
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1   5

<210> 1578
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1578
Thr Ser Ser Val Ser Ser
1   5

<210> 1579
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1579
Ala Thr Ser
1

<210> 1580
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1580
Trp Thr Phe Asn Pro Pro
1 5

<210> 1581
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1581
Ser Ser Val Ser Ser
1 5

<210> 1582
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1582
Ala Thr Ser
1

<210> 1583

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1583
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1584
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1584
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1585
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1585
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1586
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1586
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1587
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1587
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1588
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1588
gaaatcgtgc tgacccagtc ccctgcgact ctgagcctga gccctgggga acgcgccact 60

ttgtcatgcc gggccacctc ctccgtgtcc tccatgaact ggtaccagca gaagcccgga 120

caggctccgc ggccgctgat ccatgccacc tccaacctgg ccagcggcat tcccgcgagg 180

ttttccggct cgggctctgg taccgactac accctgacca tctcgagcct tgagccagaa 240

gatgctgcgg tgtactactg ccaacagtgg accttcaatc cgcctacgtt cggacagggg 300

accaagctgg agattaag 318

<210> 1589
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1589
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1590
<211> 248
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1590

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30


Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140


Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160
```

Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His Ala Thr
180 185 190

Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
210 215 220

Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 1591
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1591
caagtccaac tcgtccaatc cggtgcagaa gtcaagaaac ccggtgcatc cgtgaaagtg 60

tcatgcaaag cctccgggta caccttcact aactacaacc tccactgggt ccgccaggcc 120

ccgggacagg gactggagtg gatgggggcc atctacccgg gaaactacga cacttcatac 180

aaccagaagt tcaagggcag agtgaccatg actgccgaca agagcacatc gaccgcctac 240

atggaactca gctccctgcg ctccgaggat actgccgtct actactgtgc ccgggtggac 300

ttcggccact cccggtattg gtatttcgat gtctggggac agggaaccac cgtgactgtg 360

tccagcgggg gcggaggatc gggtggcgga ggttcggggg gaggaggatc aggcggcggc 420

ggatcggaaa tcgtgctgac ccagtcccct gcgactctga gcctgagccc tggggaacgc 480

gccactttgt catgccgggc cacctcctcc gtgtcctcca tgaactggta ccagcagaag 540

cccggacagg ctccgcggcc gctgatccat gccacctcca acctggccag cggcattccc 600

gcgaggtttt ccggctcggg ctctggtacc gactacaccc tgaccatctc gagccttgag 660

ccagaagatg ctgcggtgta ctactgccaa cagtggacct tcaatccgcc tacgttcgga 720

caggggacca agctggagat taag 744

<210> 1592
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1592
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65 70 75 80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
85 90 95

```
Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125


Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160


Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175


Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val
            180                 185                 190


Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205


Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220


Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240


Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255


Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270


Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285
```

```
Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480
```

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1593
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1593
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca atccggtgca gaagtcaaga aacccggtgc atccgtgaaa 120

gtgtcatgca aagcctccgg gtacaccttc actaactaca acctccactg ggtccgccag 180

gccccgggac agggactgga gtggatgggg gccatctacc cgggaaacta cgacacttca 240

tacaaccaga agttcaaggg cagagtgacc atgactgccg acaagagcac atcgaccgcc 300

tacatggaac tcagctccct gcgctccgag gatactgccg tctactactg tgcccgggtg 360

gacttcggcc actcccggta ttggtatttc gatgtctggg gacagggaac caccgtgact 420

gtgtccagcg ggggcggagg atcgggtggc ggaggttcgg ggggaggagg atcaggcggc 480

ggcggatcgg aaatcgtgct gacccagtcc cctgcgactc tgagcctgag ccctggggaa 540

cgcgccactt tgtcatgccg ggccacctcc tccgtgtcct ccatgaactg gtaccagcag 600

aagcccggac aggctccgcg gccgctgatc catgccacct ccaacctggc cagcggcatt 660

cccgcgaggt tttccggctc gggctctggt accgactaca ccctgaccat ctcgagcctt 720

gagccagaag atgctgcggt gtactactgc caacagtgga ccttcaatcc gcctacgttc 780

ggacagggga ccaagctgga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1594
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1594
Asn Tyr Asn Leu His
1 5

<210> 1595
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1595
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1596
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1596
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1597
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1597
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1598
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1598
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 1599
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1599
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1600
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1600
Gly Tyr Thr Phe Thr Asn Tyr Asn
1 5

<210> 1601
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1601
Ile Tyr Pro Gly Asn Tyr Asp Thr
1 5

<210> 1602

<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1602
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 1603
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1603
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1604
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1604
caagtccaac tcgtccagtc gggagcagaa gtcaagaagc ccggatcatc cgtgaaagtg 60

tcctgcaaag cctcaggcta cacctttacc aactacaact tgcactgggt cagacaggcc 120

ccgggacagg gcctggagtg gatgggcgcc atctaccccg gaaactatga cacctcgtac 180

aaccagaagt tcaagggtcg cgtgactatc acggctgaca agtccactag caccgcgtac 240

atggaacttt cctcactgcg gtccgaggat actgcggtgt actactgcgc ccgggtggac 300

ttcggacact cgagatattg gtacttcgat gtctggggac aggggaccac cgtgactgtg 360

tcctcc 366

<210> 1605
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1605
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1606
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1606
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1607
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1607
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1608
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1608
Thr Ser Ser Val Ser Ser
1 5

<210> 1609

<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1609
Ala Thr Ser
1

<210> 1610
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1610
Trp Thr Phe Asn Pro Pro
1 5

<210> 1611
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1611
Ser Ser Val Ser Ser
1 5

<210> 1612
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1612
Ala Thr Ser
1

<210> 1613
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1613
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1614
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1614
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1615
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1615
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1616
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1616
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1617
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1617
Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1618
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1618
gaaattgtgc tgacccagtc tcccgcaacc ctgtccctga gccctggaga gcgcgccacc 60

ctgtcctgcc gggccacatc ctccgtgtcg tccatgaact ggtaccagca gaagcccggc 120

caagccccga ggcctctgat tcatgctacc tcaaatctgg ccagcggaat cccggcgcgc 180

ttctccggct cgggcagcgg tactgactac actctcacca tctcgtccct cgaaccggag 240

gacgccgccg tctactactg tcagcagtgg accttcaacc cacctacttt cggacaaggg 300

accaagctgg agatcaag 318

<210> 1619
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1619
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
1 5 10 15

Gly Gly Ser

<210> 1620
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1620
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ile
130 135 140

Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly Asp Arg
145 150 155 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
165 170 175

Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile Tyr Asn
180 185 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
210 215 220

Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1621
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1621
caagtccaac tcgtccagtc gggagcagaa gtcaagaagc ccggatcatc cgtgaaagtg 60

tcctgcaaag cctcaggcta cacctttacc aactacaact tgcactgggt cagacaggcc 120

ccgggacagg gcctggagtg gatgggcgcc atctaccccg gaaactatga cacctcgtac 180

aaccagaagt tcaagggtcg cgtgactatc acggctgaca agtccactag caccgcgtac 240

atggaacttt cctcactgcg gtccgaggat actgcggtgt actactgcgc ccgggtggac 300

ttcggacact cgagatattg gtacttcgat gtctggggac aggggaccac cgtgactgtg 360

tcctccgggg gcggtggcag cgggggaggc ggaagcggcg gagggggttc cgggggtgga 420

ggaagcgaaa ttgtgctgac ccagtctccc gcaaccctgt ccctgagccc tggagagcgc 480

gccaccctgt cctgccgggc cacatcctcc gtgtcgtcca tgaactggta ccagcagaag 540

cccggccaag ccccgaggcc tctgattcat gctacctcaa atctggccag cggaatcccg 600

gcgcgcttct ccggctcggg cagcggtact gactacactc tcaccatctc gtccctcgaa 660

ccggaggacg ccgccgtcta ctactgtcag cagtggacct tcaacccacc tactttcgga 720

caagggacca agctggagat caag 744

<210> 1622
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1622
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

```
Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val
            180                 185                 190

Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240
```

```
Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430
```

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1623
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1623
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtcgggagca gaagtcaaga agcccggatc atccgtgaaa 120

gtgtcctgca aagcctcagg ctacaccttt accaactaca acttgcactg ggtcagacag 180

gccccgggac agggcctgga gtggatgggc gccatctacc ccggaaacta tgacacctcg 240

tacaaccaga agttcaaggg tcgcgtgact atcacggctg acaagtccac tagcaccgcg 300

tacatggaac tttcctcact gcggtccgag gatactgcgg tgtactactg cgcccgggtg 360

gacttcggac actcgagata ttggtacttc gatgtctggg gacaggggac caccgtgact 420

gtgtcctccg ggggcggtgg cagcggggga ggcggaagcg gcggaggggg ttccgggggt 480

ggaggaagcg aaattgtgct gacccagtct cccgcaaccc tgtccctgag ccctggagag 540

cgcgccaccc tgtcctgccg ggccacatcc tccgtgtcgt ccatgaactg gtaccagcag 600

aagcccggcc aagccccgag gcctctgatt catgctacct caaatctggc cagcggaatc 660

ccggcgcgct tctccggctc gggcagcggt actgactaca ctctcaccat ctcgtccctc 720

gaaccggagg acgccgccgt ctactactgt cagcagtgga ccttcaaccc acctactttc 780

ggacaaggga ccaagctgga gatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1624
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1624
Asn Tyr Asn Leu His
1 5

<210> 1625
<211> 17

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1625
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1626
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1626
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1627
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1627
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1628

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1628
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 1629
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1629
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1630
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1630
Gly Tyr Thr Phe Thr Asn Tyr Asn
1 5

<210> 1631
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1631
Ile Tyr Pro Gly Asn Tyr Asp Thr
1 5

<210> 1632
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1632
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 1633
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1633
Gly Tyr Thr Phe Thr Asn Tyr Asn Leu His
1 5 10

<210> 1634
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1634
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1635
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1635
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 1636
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1636
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1637
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1637
caagtccaac tcgtccagtc gggagcagaa gtcaagaagc ccggatcatc cgtgaaagtg 60

tcctgcaaag cctcaggcta cacctttacc aactacaact tgcactgggt cagacaggcc 120

ccgggacagg gcctggagtg gatgggcgcc atctaccccg gaaactatga cacctcgtac 180

aaccagaagt tcaagggtcg cgtgactatc acggctgaca agtccactag caccgcgtac 240

atggaacttt cctcactgcg gtccgaggat actgcggtgt actactgcgc ccgggtggac 300

ttcggacact cgagatattg gtacttcgat gtctggggac aggggaccac cgtgactgtg 360

tcctcc   366

<210> 1638
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1638
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 1639
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1639
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1640
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1640
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1641
<211> 6
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1641
Thr Ser Ser Val Ser Ser
1   5

<210> 1642
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1642
Ala Thr Ser
1

<210> 1643
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1643
Trp Thr Phe Asn Pro Pro
1   5

<210> 1644
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1644
Ser Ser Val Ser Ser
1 5

<210> 1645
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1645
Ala Thr Ser
1

<210> 1646
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1646
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 1647
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1647
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1   5   10

<210> 1648
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1648
Ala Thr Ser Asn Leu Ala Ser
1   5

<210> 1649
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1649
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1   5

<210> 1650
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1650
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly

1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1651
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1651
gaaattgtgc tgacccagtc tcccgcaacc ctgtccctga gccctggaga gcgcgccacc 60

ctgtcctgcc gggccacatc ctccgtgtcg tccatgaact ggtaccagca gaagcccggc 120

caagccccga ggcctctgat tcatgctacc tcaaatctgg ccagcggaat cccggcgcgc 180

ttctccggct cgggcagcgg tactgactac actctcacca tctcgtccct cgaaccggag 240

gacgccgccg tctactactg tcagcagtgg accttcaacc cacctacttt cggacaaggg 300

accaagctgg agatcaag 318

<210> 1652
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1652
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1653
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1653
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

```
Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140


Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160


Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His Ala Thr
            180                 185                 190


Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
    210                 215                 220


Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240


Gln Gly Thr Lys Leu Glu Ile Lys
                245
```

<210> 1654
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1654
caagtccaac tcgtccaatc cggcgcagaa gtcaagaaac caggatcgtc cgtgaaagtg 60

tcctgcaagg cgtccgggta caccttcact aattacaacc tccactgggt cagacaggcc 120

ccaggacagg gcctggaatg gatgggcgcc atctaccctg gaaactacga tacctcgtac 180

aaccagaagt tcaagggccg cgtgactatt accgccgaca agagcacctc caccgcctat 240

atggaactgt cgtccctgcg gtccgaggac actgccgtgt actactgtgc aagggtggac 300

ttcggtcact cccggtattg gtacttcgac gtctggggac aggggaccac tgtgaccgtg 360

tcgtcgggag gcggtggaag cggcggtggc ggaagcggag gcggcggatc agggggcgga 420

ggaagcgaca ttcagcttac ccagtcaccg tccttcctga gcgcctccgt gggagatcgc 480

gtgaccatca catgccgcgc cacttcctcg gtgtcctcca tgaactggta ccagcagaag 540

cccggaaagg ctcctaagcc tctgatccat gcgacctcca acttggcttc cggggtgccg 600

tcacggttca gcggcagcgg ttcaggaact gagtacaccc tgactattag ctctctccaa 660

cccgaggact tcgccaccta ctactgccag cagtggacct tcaacccgcc cacgtttggg 720

cagggtacca agctggagat caag 744

<210> 1655
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1655

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val
            180                 185                 190
```

```
Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380
```

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385 390 395 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
405 410 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1656
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1656
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca atccggcgca gaagtcaaga aaccaggatc gtccgtgaaa 120

gtgtcctgca aggcgtccgg gtacaccttc actaattaca acctccactg ggtcagacag 180

gccccaggac agggcctgga atggatgggc gccatctacc ctggaaacta cgatacctcg 240

tacaaccaga agttcaaggg ccgcgtgact attaccgccg acaagagcac ctccaccgcc 300

tatatggaac tgtcgtccct gcggtccgag gacactgccg tgtactactg tgcaagggtg 360

gacttcggtc actcccggta ttggtacttc gacgtctggg gacaggggac cactgtgacc 420

gtgtcgtcgg gaggcggtgg aagcggcggt ggcggaagcg gaggcggcgg atcaggggggc 480

ggaggaagcg acattcagct tacccagtca ccgtccttcc tgagcgcctc cgtgggagat 540

cgcgtgacca tcacatgccg cgccacttcc tcggtgtcct ccatgaactg gtaccagcag 600

aagcccggaa aggctcctaa gcctctgatc catgcgacct ccaacttggc ttccggggtg 660

ccgtcacggt tcagcggcag cggttcagga actgagtaca ccctgactat tagctctctc 720

caacccgagg acttcgccac ctactactgc cagcagtgga ccttcaaccc gcccacgttt 780

gggcagggta ccaagctgga gatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1657
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1657
Ser Tyr Asn Met His
1 5

<210> 1658
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1658
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1659
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1659
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1660
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1660
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 1661
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1661
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1662
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1662
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1663
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1663
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1664
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1664
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1665
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1665
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10 15

<210> 1666
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1666
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1 5 10

<210> 1667
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1667
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1668
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1668
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1669
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 1669

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 1670
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1670

```
caagtccaac tcgtccagtc aggagcagaa gtcaagaaac ctggagcttc cgtgaaagtg       60
```

tcgtgcaagg cctccggcta caccttcacc tcttacaaca tgcactgggt cagacaggcc 120

cctggtcaag gactggaatg gatgggagcg atctacccgg gcaacggaga cacttcgtac 180

aaccccaagt tcaagggacg ggtcactatg accgccgata agagcacgcg caccgcgtac 240

atggaactga gcagcctgcg ctccgaggac actgccgtgt attactgcgc gaggagctac 300

ttctacggat catcgtcgtg gtacttcgac gtctggggcc agggcaccac cgtgaccgtg 360

tcatcc 366

<210> 1671
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1671
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1672
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1672
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1673
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1673
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 1674
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1674
Ser Ser Ser Val Ser Ser
1   5

<210> 1675
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1675
Ala Thr Ser
1

<210> 1676
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1676
Trp Ile Phe Asn Pro Pro
1 5

<210> 1677
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1677
Ser Ser Val Ser Ser
1 5

<210> 1678
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1678
Ala Thr Ser
1

<210> 1679
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1679

Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1680
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1680
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1681
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1681
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1682
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1682
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1683
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1683
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1684
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 1684
gatattcagc tgacccagag cccgtcattc ctgtccgcct ccgtgggaga cagagtgacc 60

atcacttgtc gggccagctc ctcggtgtcc tccatgcatt ggtatcagca gaagcctggg 120

aaggctccca agcccctcat cttcgccaca tcaaatcttg cctccggggt gccaagccgg 180

ttctccggga gcggctccgg tactgagtac actctgacca tttcctcctt gcaacccgag 240

gactttgcca cctactactg ccagcagtgg atctttaacc cgccgacctt cggaggagga 300

accaaagtgg agatcaag 318

<210> 1685
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1685
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1686
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1686
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205
```

Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
210 215 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225 230 235 240

Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1687
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1687
caagtccaac tcgtccagtc aggagcagaa gtcaagaaac ctggagcttc cgtgaaagtg 60

tcgtgcaagg cctccggcta caccttcacc tcttacaaca tgcactgggt cagacaggcc 120

cctggtcaag gactggaatg gatgggagcg atctacccgg gcaacggaga cacttcgtac 180

aaccccaagt tcaagggacg ggtcactatg accgccgata agagcacgcg caccgcgtac 240

atggaactga gcagcctgcg ctccgaggac actgccgtgt attactgcgc gaggagctac 300

ttctacggat catcgtcgtg gtacttcgac gtctggggcc agggcaccac cgtgaccgtg 360

tcatccggtg gcggaggatc ggggggcgga ggaagcggcg gggggggctc cggcggtgga 420

ggctcggata ttcagctgac ccagagcccg tcattcctgt ccgcctccgt gggagacaga 480

gtgaccatca cttgtcgggc cagctcctcg gtgtcctcca tgcattggta tcagcagaag 540

cctgggaagg ctcccaagcc cctcatcttc gccacatcaa atcttgcctc cggggtgcca 600

agccggttct ccgggagcgg ctccggtact gagtacactc tgaccatttc ctccttgcaa 660

cccgaggact ttgccaccta ctactgccag cagtggatct ttaacccgcc gaccttcgga 720

ggaggaacca aagtggagat caag 744

<210> 1688
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1688
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65 70 75 80

Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
85 90 95

Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
115 120 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly

```
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
```

325 330 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
340 345 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
355 360 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
370 375 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385 390 395 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
405 410 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1689
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1689
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtcaggagca gaagtcaaga aacctggagc ttccgtgaaa 120

gtgtcgtgca aggcctccgg ctacaccttc acctcttaca acatgcactg ggtcagacag 180

gcccctggtc aaggactgga atggatggga gcgatctacc cgggcaacgg agacacttcg 240

tacaacccca agttcaaggg acgggtcact atgaccgccg ataagagcac gcgcaccgcg 300

tacatggaac tgagcagcct gcgctccgag gacactgccg tgtattactg cgcgaggagc 360

tacttctacg gatcatcgtc gtggtacttc gacgtctggg gccagggcac caccgtgacc 420

gtgtcatccg gtggcggagg atcgggggggc ggaggaagcg gcgggggggg ctccggcggt 480

ggaggctcgg atattcagct gacccagagc ccgtcattcc tgtccgcctc cgtgggagac 540

agagtgacca tcacttgtcg ggccagctcc tcggtgtcct ccatgcattg gtatcagcag 600

aagcctggga aggctcccaa gcccctcatc ttcgccacat caaatcttgc ctccggggtg 660

ccaagccggt tctccgggag cggctccggt actgagtaca ctctgaccat ttcctccttg 720

caacccgagg actttgccac ctactactgc cagcagtgga tctttaaccc gccgaccttc 780

ggaggaggaa ccaaagtgga gatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1690
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1690
Ser Tyr Asn Met His
1 5

<210> 1691
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1691
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1692
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1692
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1693
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1693
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 1694
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1694
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1695
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1695
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1696
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1696
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1697
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1697
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1698
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1698

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1   5   10   15

<210> 1699
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1699
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1   5   10

<210> 1700
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1700
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1   5   10   15

Gly

<210> 1701
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1701
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1702
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1702
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1703
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1703
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc ctggttcatc ggtgaaagtg 60

tcctgcaaag cgtcgggcta caccttcacc tcgtacaaca tgcactgggt ccgccaggcc 120

cccggacaag gactggaatg gatgggtgct atctaccccg gaaacggaga taccagctac 180

aaccccaagt tcaagggacg cgtgaccatt actgccgaca agtccacaag aaccgcctac 240

atggaactgt ccagcctgag atccgaggac actgcggtgt actactgtgc gaggtcctac 300

ttctacgggt cctcctcttg gtacttcgac gtctggggac agggcactac tgtgaccgtg 360

tccagc 366

<210> 1704
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1704
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1705
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1705
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1706
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1706
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1707
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1707
Ser Ser Ser Val Ser Ser
1 5

<210> 1708
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1708
Ala Thr Ser
1

<210> 1709
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1709
Trp Ile Phe Asn Pro Pro
1 5

<210> 1710
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1710
Ser Ser Val Ser Ser
1 5

<210> 1711
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1711
Ala Thr Ser
1

<210> 1712
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1712
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1713
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1713
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1714
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1714
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1715

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1715
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1716
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1716
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1717
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1717
gagatcgtgc tgacgcagtc gccggccacc ctgagccttt caccgggaga acgcgccact 60

ctgtcatgcc gggccagcag ctccgtgtcc tccatgcatt ggtaccagca gaagccgggg 120

caggccccgc ggcctctcat cttcgccacc tccaatctgg cctccggcat ccctgctcgg 180

tttagcggaa gcggcagcgg aactgactat accttgacca tctcctcgct ggaaccagag 240

gatgcagccg tgtactattg ccagcagtgg atcttcaacc cgccaacctt cggcggcggc 300

accaaggtcg agattaag 318

<210> 1718
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1718
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1719
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1719
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
130 135 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg

145 150 155 160

Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe Ala Thr
180 185 190

Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
210 215 220

Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225 230 235 240

Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1720
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1720
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc ctggttcatc ggtgaaagtg 60

tcctgcaaag cgtcgggcta caccttcacc tcgtacaaca tgcactgggt ccgccaggcc 120

cccggacaag gactggaatg gatgggtgct atctaccccg gaaacggaga taccagctac 180

aaccccaagt tcaagggacg cgtgaccatt actgccgaca agtccacaag aaccgcctac 240

atggaactgt ccagcctgag atccgaggac actgcggtgt actactgtgc gaggtcctac 300

ttctacgggt cctcctcttg gtacttcgac gtctggggac agggcactac tgtgaccgtg 360

tccagcgggg gaggcggtag cgggggggt ggatcgggcg gcggcggatc aggaggagga 420

gggtccgaga tcgtgctgac gcagtcgccg gccaccctga gcctttcacc gggagaacgc 480

gccactctgt catgccgggc cagcagctcc gtgtcctcca tgcattggta ccagcagaag 540

ccggggcagg ccccgcggcc tctcatcttc gccacctcca atctggcctc cggcatccct 600

gctcggttta gcggaagcgg cagcggaact gactatacct tgaccatctc ctcgctggaa 660

ccagaggatg cagccgtgta ctattgccag cagtggatct tcaacccgcc aaccttcggc 720

ggcggcacca aggtcgagat taag 744

<210> 1721
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1721
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65 70 75 80

```
Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270
```

```
Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460
```

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1722
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1722
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtcaaga agcctggttc atcggtgaaa 120

gtgtcctgca aagcgtcggg ctacaccttc acctcgtaca acatgcactg ggtccgccag 180

gcccccggac aaggactgga atggatgggt gctatctacc ccggaaacgg agataccagc 240

tacaacccca agttcaaggg acgcgtgacc attactgccg acaagtccac aagaaccgcc 300

tacatggaac tgtccagcct gagatccgag gacactgcgg tgtactactg tgcgaggtcc 360

tacttctacg ggtcctcctc ttggtacttc gacgtctggg gacagggcac tactgtgacc 420

gtgtccagcg ggggaggcgg tagcgggggg ggtggatcgg gcggcggcgg atcaggagga 480

ggagggtccg agatcgtgct gacgcagtcg ccggccaccc tgagcctttc accgggagaa 540

cgcgccactc tgtcatgccg ggccagcagc tccgtgtcct ccatgcattg gtaccagcag 600

aagccggggc aggccccgcg gcctctcatc ttcgccacct ccaatctggc ctccggcatc 660

cctgctcggt ttagcggaag cggcagcgga actgactata ccttgaccat ctcctcgctg 720

gaaccagagg atgcagccgt gtactattgc cagcagtgga tcttcaaccc gccaaccttc 780

ggcggcggca ccaaggtcga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1723
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1723
Ser Tyr Asn Met His
1 5

<210> 1724
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1724

Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1   5   10   15

Gly

<210> 1725
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1725
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1   5   10

<210> 1726
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1726
Gly Tyr Thr Phe Thr Ser Tyr
1   5

<210> 1727
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1727
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1728
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1728
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1729
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1729
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1730
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1730
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1731
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1731
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10 15

<210> 1732
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1732
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1 5 10

<210> 1733
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1733
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1734
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1734
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1735
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1735
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 1736
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1736
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc caggttcctc ggtgaaagtg       60

tcctgcaaag cctcgggtta caccttcacc tcgtacaata tgcactgggt ccgccaagct      120

ccgggacaag gcctggaatg gatgggagcg atctaccccg gaaacggcga cacgtcctac      180

aacccgaagt tcaagggaag agtgaccatc accgccgaca agtccacccg caccgcgtac      240

atggagctta gcagcctgcg gagcgaggac actgccgtgt attactgcgc ccggtcctac      300

ttctatggat catcctcgtg gtacttcgat gtctggggcc aggggaccac cgtgaccgtg      360

tccagc                                                                 366


<210> 1737
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"
```

<400> 1737
Arg Ala Ser Ser Ser Val Ser Ser Met His
1   5   10

<210> 1738
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1738
Ala Thr Ser Asn Leu Ala Ser
1   5

<210> 1739
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1739
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 1740
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1740
Ser Ser Ser Val Ser Ser

1 5

<210> 1741
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1741
Ala Thr Ser
1

<210> 1742
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1742
Trp Ile Phe Asn Pro Pro
1 5

<210> 1743
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1743
Ser Ser Val Ser Ser
1 5

<210> 1744
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1744
Ala Thr Ser
1

<210> 1745
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1745
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1746
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1746
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1747
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1747
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1748
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1748
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1749
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1749
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe
35 40 45

```
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60


Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65                  70                  75                  80


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
                85                  90                  95


Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 1750
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1750
gatatccagc tgacccagag cccttccttc ctgtccgctt ccgtgggaga cagagtcact       60

attacttgtc gggcctcctc atccgtgtca tccatgcact ggtaccagca gaagccggga      120

aaggccccaa agcccttgat ctttgccact tccaacctgg catccggcgt gccctcgagg      180

ttctccggga gcggttcagg gaccgagtac actctgacca ttagcagcct ccagcctgag      240

gactttgcca cctactactg ccagcagtgg attttcaacc cgcctacatt cggagggggc      300

actaaggtcg aaatcaag                                                    318


<210> 1751
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
```

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1751
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1752
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1752
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140


Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160


Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe Ala Thr
            180                 185                 190


Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 1753
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 1753
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc caggttcctc ggtgaaagtg 60

tcctgcaaag cctcgggtta caccttcacc tcgtacaata tgcactgggt ccgccaagct 120

ccgggacaag gcctggaatg gatgggagcg atctaccccg gaaacggcga cacgtcctac 180

aacccgaagt tcaagggaag agtgaccatc accgccgaca agtccacccg caccgcgtac 240

atggagctta gcagcctgcg gagcgaggac actgccgtgt attactgcgc ccggtcctac 300

ttctatggat catcctcgtg gtacttcgat gtctggggcc aggggaccac cgtgaccgtg 360

tccagcggtg gcggaggcag cggcggagga gggtctggag gaggcggctc gggggggaggg 420

ggctcggata tccagctgac ccagagccct tccttcctgt ccgcttccgt gggagacaga 480

gtcactatta cttgtcgggc ctcctcatcc gtgtcatcca tgcactggta ccagcagaag 540

ccgggaaagg ccccaaagcc cttgatcttt gccacttcca acctggcatc cggcgtgccc 600

tcgaggttct ccgggagcgg ttcagggacc gagtacactc tgaccattag cagcctccag 660

cctgaggact ttgccaccta ctactgccag cagtggattt tcaacccgcc tacattcgga 720

gggggcacta aggtcgaaat caag 744

<210> 1754
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1754
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

```
Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65                  70                  75                  80

Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220
```

```
Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240


Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255


Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270


Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285


Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300


His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320


Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335


Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350


Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365


Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380


Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400


Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415
```

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1755
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1755
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtcaaga agccaggttc ctcggtgaaa 120

gtgtcctgca aagcctcggg ttacaccttc acctcgtaca atatgcactg ggtccgccaa 180

gctccgggac aaggcctgga atggatggga gcgatctacc ccggaaacgg cgacacgtcc 240

tacaacccga agttcaaggg aagagtgacc atcaccgccg acaagtccac ccgcaccgcg 300

tacatggagc ttagcagcct gcggagcgag gacactgccg tgtattactg cgcccggtcc 360

tacttctatg gatcatcctc gtggtacttc gatgtctggg gccaggggac caccgtgacc 420

gtgtccagcg gtggcggagg cagcggcgga ggagggtctg gaggaggcgg ctcgggggga 480

```
gggggctcgg atatccagct gacccagagc ccttccttcc tgtccgcttc cgtgggagac      540

agagtcacta ttacttgtcg ggcctcctca tccgtgtcat ccatgcactg gtaccagcag      600

aagccgggaa aggccccaaa gcccttgatc tttgccactt ccaacctggc atccggcgtg      660

ccctcgaggt tctccgggag cggttcaggg accgagtaca ctctgaccat tagcagcctc      720

cagcctgagg actttgccac ctactactgc cagcagtgga ttttcaaccc gcctacattc      780

ggaggggca ctaaggtcga aatcaagacc actaccccag caccgaggcc acccaccccg      840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct      900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc      960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc     1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact     1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg     1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc     1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga     1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac     1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc     1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc     1440

tatgacgctc ttcacatgca ggccctgccg cctcgg                               1476


<210> 1756
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1756
Arg Tyr Asn Met His
1               5
```

<210> 1757
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1757
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1758
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1758
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1759
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1759
Gly Tyr Thr Phe Thr Arg Tyr

1 5

<210> 1760
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1760
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1761
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1761
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1762
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1762
Gly Tyr Thr Phe Thr Arg Tyr Asn
1 5

<210> 1763
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1763
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1764
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1764
Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10 15

<210> 1765
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1765
Gly Tyr Thr Phe Thr Arg Tyr Asn Met His
1 5 10

<210> 1766
<211> 17
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1766
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1767
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1767
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1768
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1768
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1769
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1769
caagtccaac tcgtccagtc aggagcagaa gtcaagaaac caggagcatc cgtgaaagtg 60

tcgtgcaaag cctctggcta caccttcacc cggtacaaca tgcactgggt cagacaggcc 120

ccgggacagc ggctcgagtg gatgggtgcc atctaccccg gcaacgggga cacctcctac 180

tcccaaaagt tcaagggtcg cgtgaccatc acggcggata agtcggccag cactgcgtac 240

atggaattgt catccctgcg ctccgaggat accgccgtgt attactgcgc gcggtccttc 300

ttctacggct cctccgattg gtacttcgac gtctggggac agggaactac cgtgaccgtg 360

tcctcc 366

<210> 1770
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1770
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1771
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1771
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1772
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1772
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1773
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1773
Ser Ser Ser Val Asn Asn
1 5

<210> 1774
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1774
Ala Thr Ser
1

<210> 1775
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1775
Trp Ile Phe Asn Pro Pro
1 5

<210> 1776
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1776
Ser Ser Val Asn Asn
1 5

<210> 1777
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1777
Ala Thr Ser
1

<210> 1778
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1778
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1779
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1779
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1780
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1780
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1781
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1781
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1782
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 1782
Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1783
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1783
gaaatcgtgc tgactcagtc gccggacttc caaagcgtga ccccaaagga gaaggtcacc 60

atcacctgta gagcctcatc gtccgtgaac aatatgcact ggtaccagca gaagccggac 120

cagtccccta agcccctgat ctacgccact tccaacctgg cctccggcgt gccgtcgagg 180

ttcagcggct cgggcagcgg gaccgactac accctgacca tcaacagcct tgaagctgag 240

gacgccgcta cctactactg ccagcagtgg attttcaacc ctcccacatt tggacagggc 300

actaagctgg agattaag 318

<210> 1784
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1784
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1785
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1785
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

```
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140

Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Pro Leu Ile Tyr Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Tyr Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240
```

Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 1786
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1786
caagtccaac tcgtccagtc aggagcagaa gtcaagaaac caggagcatc cgtgaaagtg 60

tcgtgcaaag cctctggcta caccttcacc cggtacaaca tgcactgggt cagacaggcc 120

ccgggacagc ggctcgagtg gatgggtgcc atctaccccg gcaacgggga cacctcctac 180

tcccaaaagt tcaagggtcg cgtgaccatc acggcggata agtcggccag cactgcgtac 240

atggaattgt catccctgcg ctccgaggat accgccgtgt attactgcgc gcggtccttc 300

ttctacggct cctccgattg gtacttcgac gtctggggac agggaactac cgtgaccgtg 360

tcctccgggg gtggcgggag cggagggggc ggaagcgggg gtggaggatc aggaggcgga 420

ggctccgaaa tcgtgctgac tcagtcgccg gacttccaaa gcgtgacccc aaaggagaag 480

gtcaccatca cctgtagagc ctcatcgtcc gtgaacaata tgcactggta ccagcagaag 540

ccggaccagt cccctaagcc cctgatctac gccacttcca acctggcctc cggcgtgccg 600

tcgaggttca gcggctcggg cagcgggacc gactacaccc tgaccatcaa cagccttgaa 660

gctgaggacg ccgctaccta ctactgccag cagtggattt tcaaccctcc cacatttgga 720

cagggcacta agctggagat taag 744

<210> 1787
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1787

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Arg Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Arg Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65                  70                  75                  80

Tyr Ser Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
                165                 170                 175
```

```
Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Asn Asn Met His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Pro
        195                 200                 205

Leu Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Asn Ser Leu
225                 230                 235                 240

Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365
```

```
Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 1788
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1788
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtcaggagca gaagtcaaga aaccaggagc atccgtgaaa 120

gtgtcgtgca aagcctctgg ctacaccttc acccggtaca acatgcactg ggtcagacag 180

gccccgggac agcggctcga gtggatgggt gccatctacc ccggcaacgg ggacacctcc 240

tactcccaaa agttcaaggg tcgcgtgacc atcacggcgg ataagtcggc cagcactgcg 300

tacatggaat tgtcatccct gcgctccgag gataccgccg tgtattactg cgcgcggtcc 360

ttcttctacg gctcctccga ttggtacttc gacgtctggg gacagggaac taccgtgacc 420

gtgtcctccg ggggtggcgg gagcggaggg ggcggaagcg ggggtggagg atcaggaggc 480

ggaggctccg aaatcgtgct gactcagtcg ccggacttcc aaagcgtgac cccaaaggag 540

aaggtcacca tcacctgtag agcctcatcg tccgtgaaca atatgcactg gtaccagcag 600

aagccggacc agtcccctaa gcccctgatc tacgccactt ccaacctggc ctccggcgtg 660

ccgtcgaggt tcagcggctc gggcagcggg accgactaca ccctgaccat caacagcctt 720

gaagctgagg acgccgctac ctactactgc cagcagtgga ttttcaaccc tcccacattt 780

ggacagggca ctaagctgga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1789
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1789
Arg Tyr Asn Met His
1 5

<210> 1790
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1790
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1791
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1791
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1792
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1792
Gly Tyr Thr Phe Thr Arg Tyr
1 5

<210> 1793
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1793
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1794
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1794
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1795
<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1795
Gly Tyr Thr Phe Thr Arg Tyr Asn
1 5

<210> 1796
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1796
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1797
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1797
Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10 15

<210> 1798
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1798
Gly Tyr Thr Phe Thr Arg Tyr Asn Met His
1 5 10

<210> 1799
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1799
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1800
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1800
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1801
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1801
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1802
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1802
caagtgcaac tcgtccaatc cggcgcggaa gtcaaaaagc ctggagcctc cgtcaaagtg 60

tcctgcaagg cctccggtta cactttcact cgctacaaca tgcattgggt gcggcaggcc 120

ccgggacagc gcctggaatg gatgggcgca atctaccccg gcaacggaga cacctcctat 180

tcccaaaagt tcaagggaag ggtcacaatc acggccgaca agagcgcctc aactgcctac 240

atggagctga gcagcctcag atccgaagat accgcggtgt actactgcgc ccggagcttc 300

ttctacggtt cgtctgattg gtactttgac gtctggggcc agggaaccac cgtgaccgtg 360

tcgtcc 366

<210> 1803
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1803
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1804
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1804
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1805

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1805
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1806
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1806
Ser Ser Ser Val Asn Asn
1 5

<210> 1807
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1807
Ala Thr Ser
1

<210> 1808
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1808
Trp Ile Phe Asn Pro Pro
1 5

<210> 1809
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1809
Ser Ser Val Asn Asn
1 5

<210> 1810
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1810
Ala Thr Ser
1

<210> 1811
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1811
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1812
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1812
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1813
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1813
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1814
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1814
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 1815
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1815
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met
            20   25   30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Tyr
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65   70   75   80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
                85   90   95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 1816
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1816
gacatccagc ttacccagtc gccatcattc ctgtccgcat cagtgggtga tcgcgtgacc 60

attacctgtc gggcgtcctc ctccgtgaac aacatgcact ggtaccagca gaagccgggg 120

aaggctccca agcctctgat ctacgccact agcaatttgg ccagcggcgt gccttcgaga 180

ttctcggggt cgggctcagg aaccgagtat accctgacca tttcctccct ccaaccggag 240

gactttgcta cttactactg ccagcagtgg attttcaacc ccccgacttt cggacagggc 300

accaagctgg aaatcaag 318

<210> 1817
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1817
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1818
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1818
```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20                  25                  30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Tyr Ala Thr
            180                 185                 190
```

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
210 215 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 1819
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1819
caagtgcaac tcgtccaatc cggcgcggaa gtcaaaaagc ctggagcctc cgtcaaagtg 60

tcctgcaagg cctccggtta cactttcact cgctacaaca tgcattgggt gcggcaggcc 120

ccgggacagc gcctggaatg gatgggcgca atctaccccg gcaacggaga cacctcctat 180

tcccaaaagt tcaagggaag ggtcacaatc acggccgaca agagcgcctc aactgcctac 240

atggagctga gcagcctcag atccgaagat accgcggtgt actactgcgc ccggagcttc 300

ttctacggtt cgtctgattg gtactttgac gtctggggcc agggaaccac cgtgaccgtg 360

tcgtccggtg gcggagggag cggtggagga ggctccgggg gaggaggcag cggcgggga 420

ggcagcgaca tccagcttac ccagtcgcca tcattcctgt ccgcatcagt gggtgatcgc 480

gtgaccatta cctgtcgggc gtcctcctcc gtgaacaaca tgcactggta ccagcagaag 540

ccggggaagg ctcccaagcc tctgatctac gccactagca atttggccag cggcgtgcct 600

tcgagattct cggggtcggg ctcaggaacc gagtataccc tgaccatttc ctccctccaa 660

ccggaggact ttgctactta ctactgccag cagtggattt tcaacccccc gactttcgga 720

cagggcacca agctggaaat caag 744

<210> 1820
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1820
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Arg Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65 70 75 80

Tyr Ser Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
85 90 95

Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp

```
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Asn Asn Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
```

```
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 1821

<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1821
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca atccggcgcg gaagtcaaaa agcctggagc ctccgtcaaa 120

gtgtcctgca aggcctccgg ttacactttc actcgctaca acatgcattg ggtgcggcag 180

gccccgggac agcgcctgga atggatgggc gcaatctacc ccggcaacgg agacacctcc 240

tattcccaaa agttcaaggg aagggtcaca atcacggccg acaagagcgc ctcaactgcc 300

tacatggagc tgagcagcct cagatccgaa gataccgcgg tgtactactg cgcccggagc 360

ttcttctacg gttcgtctga ttggtacttt gacgtctggg gccagggaac caccgtgacc 420

gtgtcgtccg gtggcggagg gagcggtgga ggaggctccg ggggaggagg cagcggcggg 480

ggaggcagcg acatccagct tacccagtcg ccatcattcc tgtccgcatc agtgggtgat 540

cgcgtgacca ttacctgtcg ggcgtcctcc tccgtgaaca acatgcactg gtaccagcag 600

aagccgggga aggctcccaa gcctctgatc tacgccacta gcaatttggc cagcggcgtg 660

ccttcgagat tctcggggtc gggctcagga accgagtata ccctgaccat ttcctccctc 720

caaccggagg actttgctac ttactactgc cagcagtgga ttttcaaccc cccgactttc 780

ggacagggca ccaagctgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1822
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1822
Arg Tyr Asn Met His
1 5

<210> 1823
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1823
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1824

<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1824
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1825
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1825
Gly Tyr Thr Phe Thr Arg Tyr
1 5

<210> 1826
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1826
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1827
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1827
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1828
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1828
Gly Tyr Thr Phe Thr Arg Tyr Asn
1 5

<210> 1829
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1829
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1830
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1830
Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10 15

<210> 1831
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1831
Gly Tyr Thr Phe Thr Arg Tyr Asn Met His
1 5 10

<210> 1832
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1832
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1833
<211> 13
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1833
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1834
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1834
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1835
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1835
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc ctggttcctc cgtgaaagtg 60

tcctgcaaag cgtctggcta caccttcacc cggtacaata tgcactgggt cagacaggcg 120

cccggacagg gcctggagtg gatgggggcc atctaccctg ggaacggcga cactagctac 180

tcccaaaagt tcaagggccg cgtgacgatt accgccgaca agtcaaccag cactgcctat 240

atggagctga gctcgcttcg gagcgaagat accgccgtgt actactgcgc tcggagcttc 300

ttctacgggt cctcggattg gtacttcgac gtctggggcc aggggactac tgtgaccgtg 360

tcctcc 366

<210> 1836
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1836
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1837
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1837
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1838
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1838
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1839
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1839
Ser Ser Ser Val Asn Asn
1 5

<210> 1840
<211> 3
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1840
Ala Thr Ser
1

<210> 1841
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1841
Trp Ile Phe Asn Pro Pro
1 5

<210> 1842
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1842
Ser Ser Val Asn Asn
1 5

<210> 1843
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1843
Ala Thr Ser
1

<210> 1844
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1844
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1845
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1845
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1846
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1846
Ala Thr Ser Asn Leu Ala Ser

1 5

<210> 1847
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1847
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1848
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1848
Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1849
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1849
gaaatcgtgc tgacccagtc cccggacttt cagtcagtga ctcccaagga gaaggtcacc 60

attacttgtc gcgcctcctc ctcggtgaac aacatgcact ggtaccagca gaagccggac 120

cagtccccga agcccctgat ctatgctacc tccaacttgg cgtccggcgt gccgtcaagg 180

ttcagcggat cgggttccgg gacagactac accctgacta ttaactcact cgaggccgag 240

gatgccgcca cctactactg ccagcagtgg atcttcaacc ctccaacctt cggacaagga 300

accaagctgg aaatcaag 318

<210> 1850
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1850
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
            20

<210> 1851
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1851
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
    50   55   60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115   120   125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile

130 135 140

Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys
145 150 155 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met His Trp
165 170 175

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Pro Leu Ile Tyr Ala Thr
180 185 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Tyr Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
210 215 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 1852
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1852
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc ctggttcctc cgtgaaagtg 60

tcctgcaaag cgtctggcta caccttcacc cggtacaata tgcactgggt cagacaggcg 120

cccggacagg gcctggagtg gatgggggcc atctaccctg ggaacggcga cactagctac 180

tcccaaaagt tcaagggccg cgtgacgatt accgccgaca agtcaaccag cactgcctat 240

atggagctga gctcgcttcg gagcgaagat accgccgtgt actactgcgc tcggagcttc 300

ttctacgggt cctcggattg gtacttcgac gtctggggcc aggggactac tgtgaccgtg 360

tcctccgggg gaggaggatc gggcggaggc ggttcgggag gcggcggaag cggaggcgga 420

ggttcagaaa tcgtgctgac ccagtccccg gactttcagt cagtgactcc caaggagaag 480

gtcaccatta cttgtcgcgc ctcctcctcg gtgaacaaca tgcactggta ccagcagaag 540

ccggaccagt ccccgaagcc cctgatctat gctacctcca acttggcgtc cggcgtgccg 600

tcaaggttca gcggatcggg ttccgggaca gactacaccc tgactattaa ctcactcgag 660

gccgaggatg ccgccaccta ctactgccag cagtggatct tcaaccctcc aaccttcgga 720

caaggaacca agctggaaat caag 744

<210> 1853
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1853
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Arg Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

```
Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65                  70                  75                  80

Tyr Ser Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val
                165                 170                 175

Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Asn Asn Met His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Pro
        195                 200                 205

Leu Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Asn Ser Leu
225                 230                 235                 240

Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255
```

```
Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445
```

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1854
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1854
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtcaaga agcctggttc ctccgtgaaa 120

gtgtcctgca aagcgtctgg ctacaccttc acccggtaca atatgcactg ggtcagacag 180

gcgcccggac agggcctgga gtggatgggg gccatctacc ctgggaacgg cgacactagc 240

tactcccaaa agttcaaggg ccgcgtgacg attaccgccg acaagtcaac cagcactgcc 300

tatatggagc tgagctcgct tcggagcgaa gataccgccg tgtactactg cgctcggagc 360

ttcttctacg ggtcctcgga ttggtacttc gacgtctggg gccaggggac tactgtgacc 420

gtgtcctccg ggggaggagg atcgggcgga ggcggttcgg gaggcggcgg aagcggaggc 480

ggaggttcag aaatcgtgct gacccagtcc ccggactttc agtcagtgac tcccaaggag 540

aaggtcacca ttacttgtcg cgcctcctcc tcggtgaaca acatgcactg gtaccagcag 600

aagccggacc agtccccgaa gcccctgatc tatgctacct ccaacttggc gtccggcgtg 660

ccgtcaaggt tcagcggatc gggttccggg acagactaca ccctgactat taactcactc 720

gaggccgagg atgccgccac ctactactgc cagcagtgga tcttcaaccc tccaaccttc 780

ggacaaggaa ccaagctgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggcccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1855
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1855
Arg Tyr Asn Met His
1 5

<210> 1856
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1856
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys
1 5 10 15

Gly

<210> 1857
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1857
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1858
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1858
Gly Tyr Thr Phe Thr Arg Tyr
1 5

<210> 1859
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1859
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1860
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1860
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1861
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1861
Gly Tyr Thr Phe Thr Arg Tyr Asn
1 5

<210> 1862
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1862
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1863
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1863
Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10 15

<210> 1864
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1864
Gly Tyr Thr Phe Thr Arg Tyr Asn Met His
1 5 10

<210> 1865
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1865
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe Lys

1 5 10 15

Gly

<210> 1866
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1866
Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 1867
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1867
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
50 55 60

```
Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 1868
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1868
caagtccaac tcgtccagtc tggcgcagaa gtcaagaagc ccggaagctc cgtgaaagtg       60

tcctgcaaag cgtcgggtta cactttcacc cggtacaaca tgcactgggt cagacaggcc      120

cctggacaag gactggagtg gatgggtgcc atctaccctg gaaacggaga tacctcctac      180

tcccaaaagt tcaaggggag agtgaccatt accgccgaca agtcaacttc caccgcttac      240

atggagctca gctccctgcg gtccgaagat actgcggtgt actattgcgc tcgctcattt      300

ttctacggct catcggattg gtacttcgac gtctggggac agggaactac cgtgaccgtg      360

tcctcg                                                                 366


<210> 1869
<211> 10
<212> PRT
<213> Artificial Sequence
```

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1869
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1870
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1870
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1871
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1871
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1872
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1872
Ser Ser Ser Val Asn Asn
1 5

<210> 1873
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1873
Ala Thr Ser
1

<210> 1874
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1874
Trp Ile Phe Asn Pro Pro
1 5

<210> 1875
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1875

Ser Ser Val Asn Asn
1 5

<210> 1876
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1876
Ala Thr Ser
1

<210> 1877
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1877
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1878
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1878
Arg Ala Ser Ser Ser Val Asn Asn Met His
1 5 10

<210> 1879
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1879
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1880
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1880
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1881
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1881
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Tyr
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65   70   75   80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
                85   90   95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 1882
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1882
gacatccagc tgactcagtc cccgtccttc ctgtccgcct ccgtggggga ccgcgtgacg 60

attacttgtc gggcctcctc atccgtgaac aacatgcatt ggtaccagca gaagccagga 120

aaggcaccga agccgcttat ctatgccacc tcgaatctgg ccagcggagt gccttcgagg 180

tttagcggct ccggctccgg caccgagtac actttgacca ttagcagcct ccagccggag 240

gacttcgcca catactactg ccagcagtgg atcttcaacc cccccacctt cggccaagga 300

accaagctgg aaatcaag   318

<210> 1883
<211> 20

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1883
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 1884
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1884
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
    50   55   60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Tyr Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Leu Glu Ile Lys
                245
```

<210> 1885
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1885
caagtccaac tcgtccagtc tggcgcagaa gtcaagaagc ccggaagctc cgtgaaagtg 60

tcctgcaaag cgtcgggtta cactttcacc cggtacaaca tgcactgggt cagacaggcc 120

cctggacaag gactggagtg gatgggtgcc atctaccctg gaaacggaga tacctcctac 180

tcccaaaagt tcaaggggag agtgaccatt accgccgaca agtcaacttc caccgcttac 240

atggagctca gctccctgcg gtccgaagat actgcggtgt actattgcgc tcgctcattt 300

ttctacggct catcggattg gtacttcgac gtctggggac agggaactac cgtgaccgtg 360

tcctcggggg gaggaggatc gggcggaggc ggttcgggag gcggcggaag cggaggcgga 420

ggttcagaca tccagctgac tcagtccccg tccttcctgt ccgcctccgt gggggaccgc 480

gtgacgatta cttgtcgggc ctcctcatcc gtgaacaaca tgcattggta ccagcagaag 540

ccaggaaagg caccgaagcc gcttatctat gccacctcga atctggccag cggagtgcct 600

tcgaggttta gcggctccgg ctccggcacc gagtacactt tgaccattag cagcctccag 660

ccggaggact tcgccacata ctactgccag cagtggatct tcaacccccc caccttcggc 720

caaggaacca agctggaaat caag 744

<210> 1886
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1886
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Arg Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65                  70                  75                  80

Tyr Ser Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Asn Asn Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205
```

```
Leu Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400
```

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
405 410 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1887
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1887
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtctggcgca gaagtcaaga agcccggaag ctccgtgaaa 120

gtgtcctgca aagcgtcggg ttacactttc acccggtaca acatgcactg ggtcagacag 180

gcccctggac aaggactgga gtggatgggt gccatctacc ctggaaacgg agatacctcc 240

tactcccaaa agttcaaggg gagagtgacc attaccgccg acaagtcaac ttccaccgct 300

tacatggagc tcagctccct gcggtccgaa gatactgcgg tgtactattg cgctcgctca 360

ttttttctacg gctcatcgga ttggtacttc gacgtctggg gacagggaac taccgtgacc 420

gtgtcctcgg ggggaggggg gagcggcgga gggggctcgg gcggtggagg aagcggaggc 480

ggcggttcgg acatccagct gactcagtcc ccgtccttcc tgtccgcctc cgtgggggac 540

cgcgtgacga ttacttgtcg ggcctcctca tccgtgaaca acatgcattg gtaccagcag 600

aagccaggaa aggcaccgaa gccgcttatc tatgccacct cgaatctggc cagcggagtg 660

ccttcgaggt ttagcggctc cggctccggc accgagtaca ctttgaccat tagcagcctc 720

cagccggagg acttcgccac atactactgc cagcagtgga tcttcaaccc ccccaccttc 780

ggccaaggaa ccaagctgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 1888
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1888
Gln Val His Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100   105   110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
        115   120

<210> 1889
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1889
caagtgcatc tgcagcagtc gggggccgaa ctggcaaagc caggcgccag cgtgaagatg   60

agctgcaagg cctccgggta caccttcacc aactactgga tgcactgggt caagcagcgc   120

ccgggccagg gactcgagtg gatcgggttc atcacgccga ctaccggcta cccggagtat 180

aaccagaagt tcaaggacaa ggccactctg actgccgaca agtcctcgtc taccgcgtac 240

atgcaactgt cctcactgac ttcggaggat tccgctgtgt actactgcgc gcggaggaaa 300

gtcggaaagg gagtgtacta tgccctggac tactggggcc agggtaccag cgtcactgtg 360

tcctcc 366

<210> 1890
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1890
Asp Ile Leu Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Asn Ser Pro Gln Leu Leu Val
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Thr
65 70 75 80

Glu Asp Phe Gly Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

100 105

<210> 1891
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1891
gacattctga tgacccagtc ccctgcatca ctctccgcgt ccgtgggaga aaccgtgacc 60

atcacgtgta gagcctccgg caacatccac aactacctgg cctggtacca gcagaagcag 120

ggaaactcgc cccaactgct tgtgtacaac accaagacct tggctgacgg agtgccttcc 180

cggttctcgg gttcgggatc aggcacacag tactccctga aaatcaatag cctccagacc 240

gaagattttg gaacctacta ctgccaacac ttctggagct ccccctggac tttcggaggc 300

ggtaccaagc tcgagattaa g 321

<210> 1892
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1892
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Leu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Ala Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1893
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1893
caagtgcagc tgcagcagcc tggtgccgag ctcgtgaagc cgggagcgtc cgtgaagatg 60

agctgcaaag cctcgggcta caccttcacc aattacaact tgcattgggt caagcagacc 120

ccgggccagg gcctcgaatg gatcggagcg atctaccccg ggaactacga tactagctac 180

aaccagaagt tcaagggaaa ggccaccctg accgccgata agtcctcatc caccgcctac 240

atgctgctgt cctcgctgac ttccgaggac tccgctgtgt acttctgcgc ccgcgtggac 300

ttcggacaca gcagatattg gtattttgac gtctggggcg ccgggactac cgtgactgtg 360

tcgtcc 366

<210> 1894
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1894
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Ser Phe Pro Arg Pro Trp Ile His
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
85 90 95

Phe Gly Ala Gly Ala Lys Leu Glu Leu Lys
100 105

<210> 1895
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1895
caaattgtcc tgagccagag cccggctatc ctgtccgcct caccgggcga aaaggtcacc 60

atgacttgtc gggccacttc ctccgtgtca tccatgaact ggtaccagca gaagcctggc 120

agcttccctc ggccatggat tcacgccacg tcaaacctgg catcgggagt gcccgcaagg 180

ttctccgggt ccggcagcgg aacatcctac tccctcacca tctcgcgcgt ggaagcggag 240

gacgctgcca cctactactg ccaacagtgg accttcaacc cccccacctt tggagcggga 300

gccaagctgg aacttaag 318

<210> 1896
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1896
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Arg Thr Ala Tyr
65 70 75 80

Ile His Leu Ser Ser Leu Thr Ser Glu Asp Ser Val Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1897
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1897
caagtgcagc tgcagcagcc gggagcagag ctcgtgaagc ctggagcctc agtgaagatg 60

agctgcaagg cctccggtta caccttcacc tcctacaaca tgcactgggt caagcagacc 120

cccggacaag gcctggaatg gatcggcgcc atctacccgg gaaacgggga cacctcctat 180

aaccccaagt tcaagggaaa agcaaccctg accgcggaca agtccagcag aactgcctac 240

atccatcttt cctcgctgac gtccgaggat tccgtggtgt actactgtgc ccgctcctac 300

ttctacgggt catcctcgtg gtacttcgat gtctggggcg ctggaaccac cgtgactgtg 360

tcctcc 366

<210> 1898
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1898
Gln Ile Ile Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly

1 5 10 15

Glu Lys Val Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Thr Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Ser Leu Glu Ile Lys
100 105

<210> 1899
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1899
cagatcattc tgagccagag cccggccatt ctgtctgcct cgcctggaga aaaagtcacc 60

ctcacttgcc gggccagctc ctccgtgtcc tcaatgcact ggtaccagca gaagcctggc 120

tcaagcccga agccctggat cttcgccacc tccaatctgg cgtcaggagt gcccgcgagg 180

ttcactggat cggggtccgg cacatcgtat tcgctcacca tttcccgggt ggaggccgag 240

gacgccgcta cttactactg ccaacagtgg atcttcaacc caccgacctt tggcggaggg 300

acttccttgg aaatcaag 318

<210> 1900
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1900
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Ser His
20 25 30

Gly Ile Asn Trp Val Lys Gln Ala Pro Arg Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Gly Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Arg Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Tyr Gly Asn Tyr Glu Glu Pro Tyr Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 1901
<211> 363

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1901
caaattcagc tggtgcagtc gggacctgag ctcaagaagc ccggagaaac cgtgaagatc 60

tcctgcaaga cttccgggta cacttttact tcccacggca tcaactgggt caagcaggca 120

ccaaggaagg ggcttaagtg gatgggctgg attaacacct acaccggcga acccacctat 180

ggcgatgact tcaaaggacg gttcgcgttc tccctcgaaa cctcagcaag aaccgcgtat 240

ttgcaaatca acaacctgaa gaacgaggac accgccacct acttctgcgc ccgctacgga 300

aattacgagg aaccttacgc tatggactac tggggccagg gcacttccgt gactgtgtcg 360

tcc 363

<210> 1902
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1902
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Ser Phe Pro Arg Pro Trp Ile His
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser

50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
85 90 95

Phe Gly Ala Gly Ala Lys Leu Glu Leu Lys
100 105

<210> 1903
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1903
cagatcgtgc tgagccagag ccccgccatc ctgagcgctt ccccgggaga aaaggtcacc 60

atgacttgcc gggccactag cagcgtgtcc tccatgaact ggtaccagca gaagccgggc 120

tccttccctc gcccctggat tcatgccacc tcaaacctgg ccagcggagt gccagccaga 180

ttctcgggat ctggatcggg gacgtcctac tccctcacca tctcgcgggt ggaggccgaa 240

gatgccgcca catactactg tcaacagtgg accttcaacc cgccgacctt tggagcgggg 300

gccaagctgg agctgaaa 318

<210> 1904
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1904
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Asn Ile His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Phe
65   70   75   80

Ile His Phe Ser Ser Leu Thr Ser Glu Asp Ser Val Val Tyr Tyr Cys
                85   90   95

Ala Arg Ser Tyr Phe Tyr Gly Ser Asp Ser Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Ala Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1905
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1905
caagtgcagc ttcagcagcc tggggccgaa ctcgtgaagc caggagcctc cgtgaagatg   60

tcatgcaaag cctccggcta cacttttacc tcctacaaca ttcattgggt caagcagaca   120

cctggccagg gcctggaatg gattggtgca atctacccgg gcaacggaga cacctcgtac 180

aaccagaagt ttaaggggaa ggccaccctg accgcggaca agtcaagcac taccgcgttc 240

attcacttct cgtccttgac ctccgaggat agcgtggtgt actactgcgc ccgctcctat 300

ttctacggct ccgattcgtg gtacttcgac gtctggggag ccggaactac cgtgaccgtg 360

tcctcc 366

<210> 1906
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1906
Gln Ile Ile Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Leu Thr Cys Arg Ala Ser Ser Gly Val Pro Ser Leu
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Ser Leu Glu Ile Lys

100 105

<210> 1907
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1907
caaatcatcc tgagccagag cccggccatc ctgtcggctt cacccgggga aaaggtcacg 60

ctgacttgcc gggcctcctc cggcgtgcca agcctccact ggtaccagca aaagcctggc 120

tcgtccccca aaccctggat tttcgccacc tccaacctgg ctagcggagt gccggccaga 180

ttctcgggtt ccgggtccgg caccagctat tctctcacca tctcccgggt cgaggcggag 240

gacgcagcga cttactactg tcaacagtgg atcttcaatc cgcccacctt cggcggagga 300

acttccctgg aaatcaag 318

<210> 1908
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1908
Gln Val Gln Leu Leu Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Ser Gln Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ser Phe Phe Tyr Gly Ser Ser Asp Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Ala Gly Thr Thr Val Ser Val Ser Ser
        115   120

<210> 1909
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1909
caagtgcagc tgctgcagcc cggagccgaa ctcgtgaagc cgggcgcatc cgtgaaaatg 60

agctgcaagg cgtccggtta caccttcact cgctacaaca tgcactgggt caagcagacc 120

cctggacaag gcctggagtg gattggtgct atctacccgg gaaacggaga cactagctac 180

tcgcagaaat tcaagggaaa ggccacgctg accgccgata agtcctcctc cactgcctac 240

atgcaactca gctcactgac ctcagaggac tcggccgtgt actactgcgc gaggtccttc 300

ttctacgggt cctcggattg gtacttcgac gtctggggcg ccggtaccac cgtgtccgtg 360

tcatcc   366

<210> 1910
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1910
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Thr Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Asn Asn Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 1911
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1911
cagatcgtgc tgagccagtc cccggcgatt ctgtccacct cgcctgggga aaaggtcacc 60

ctgacatgta gagcctcctc ctccgtgaac aatatgcatt ggtatcagca gaagccagga 120

tcaagcccca agccctggat ctatgccact tcgaaccttg cctctggagt gccctcacgg 180

ttctccggct cgggatcggg gaccagctac agcttgacta tctcccgggt ggaggctgag 240

gacgccgcaa cctactactg ccagcaatgg atcttcaacc ctccgacttt tggggccgga 300

accaagctgg aactcaag 318

<210> 1912
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1912
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Thr Leu Tyr Leu
65 70 75 80

Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val
115

<210> 1913
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1913
caagtgcagt tggtggaatc aggaggaggt gtcgtgcaac caggaagatc attgaggctc 60

tcatgcgccg ccagcggatt cacctttcgg gattactaca tggcctgggt ccgccaggcc 120

ccggggaagg gactggaatg ggtggcatcc atctcgtacg aagggaaccc ctactatggg 180

gactccgtga agggacggtt caccatctcc cgggacaacg ccaagtccac cctgtacctt 240

caaatgtcct cgctgagggc ggaggatact gctgtctact actgtgcccg ccacgaccat 300

aacaacgtgg actggttcgc ctactggggc cagggaaccc tcgtcaccgt gtcctcg 357

<210> 1914
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1914
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Val Ser Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Glu Asn Lys Lys Asn Tyr Leu Ala Trp Tyr Leu Gln Lys Pro Gly Gln
35 40 45

Ser Pro Gln Leu Leu Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
65 70 75 80

Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Asn Phe Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 1915
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1915
gacattgtga tgacgcagac tcccctgtcg ctctccgtga cccctggcca gcccgtgtcg 60

atgtcgtgca agagctccca gtccctgctg tattccgaga acaagaagaa ttaccttgcg 120

tggtacctcc agaagccggg gcagagcccg cagctgctga ttttctgggc gtccactaga 180

gagtctggag tgcctgaccg gtttagcgga agcggctccg gtactgattt caccctgaaa 240

atctcgcgcg tggaagctga ggacgtgggc gtgtactact gccagcagta ctacaacttc 300

cctactttcg gacaaggaac caagctggaa atcaag 336

<210> 1916
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1916
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 1917
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1917
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
            20   25   30

Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ala Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
    50   55   60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Thr Leu Tyr Leu

65 70 75 80

Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr
130 135 140

Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly Gln Pro Val Ser Met
145 150 155 160

Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Glu Asn Lys Lys Asn
165 170 175

Tyr Leu Ala Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu
180 185 190

Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser
195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu
210 215 220

Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Tyr Asn Phe Pro
225 230 235 240

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
245 250

<210> 1918

<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1918
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Arg Val Thr Ile Thr Arg Asp Asn Ser Ala Ser Thr Leu Tyr Met
65 70 75 80

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 1919
<211> 357
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1919
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac caggagcttc cgtgaaagtg 60

tcgtgcaaag cttcaggctt caccttccgc gactattaca tggcctgggt ccgccaagcg 120

cccggacagc ggctggagtg gatggggtcc atttcctacg aggggaaccc ctactatgga 180

gattccgtga agggcagagt gacgatcact cgggataact ccgcctccac tctctacatg 240

gaactgtcct cgcttcggag cgaagatacc gcggtgtact actgcgcccg ccacgaccat 300

aacaacgtgg actggttcgc ctactgggga caggggaccc tcgtgaccgt gtcctct 357

<210> 1920
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1920
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Glu Asn Lys Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys
35 40 45

Val Pro Lys Leu Leu Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Asn Phe Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 1921
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1921
gacattcaga tgacccagtc cccgagctcg ctgtccgcct ccgtgggaga cagagtgaca 60

atcacttgca agagcagcca gtcactgttg tactccgaga acaagaagaa ctacctcgcc 120

tggtaccagc agaagccggg aaaggtccct aagctgctga tcttctgggc cagcactagg 180

gagtcgggag tgccgtcacg gttcagcgga tcgggatcgg gtaccgactt caccctgact 240

atctcctccc tgcaacctga ggacgtggcc acctactact gtcagcagta ctacaatttt 300

cccaccttcg gccagggtac caagctggaa atcaag 336

<210> 1922
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1922
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1923
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1923
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Arg Val Thr Ile Thr Arg Asp Asn Ser Ala Ser Thr Leu Tyr Met
65 70 75 80

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr

130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Glu Asn Lys Lys Asn
165 170 175

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu
180 185 190

Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Ser Arg Phe Ser
195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
210 215 220

Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Asn Phe Pro
225 230 235 240

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
245 250

<210> 1924
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1924
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Gln Val Thr Ile Ser Arg Asp Asn Ser Ile Ser Thr Leu Tyr Leu
65 70 75 80

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 1925
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1925
gaagtccaac tggtgcagtc aggagcagaa gtcaaaaaac caggagaaag cctcaagatc 60

agctgcaagg gctcgggttt caccttccgg gactactata tggcctgggt cagacagatg 120

ccgggaaagg gactggaatg gatggggtca atcagctacg agggcaaccc ctactacgga 180

gactccgtga agggacaggt cacaatctcc cgggacaact cgatttccac tctgtatctg 240

caatggagct ccctcaaggc ctccgacact gcgatgtact actgtgcgcg gcatgaccac 300

aacaatgtgg attggttcgc ctactgggga cagggaaccc tcgtgaccgt gtccagc 357

<210> 1926
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1926
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Glu Asn Lys Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys
35 40 45

Val Pro Lys Leu Leu Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Asn Phe Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 1927
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1927
gatatccaaa tgacccagtc gccctcctca ctctccgcct ccgtgggaga tcgcgtgacc 60

attacttgca agagctcgca gtccctgctg tactccgaga acaagaagaa ctacttggcc 120

tggtaccagc agaagcccgg caaagtgccg aagctgctta tcttttgggc ctcgaccagg 180

gaaagcggag tgccgtcacg cttctccggc tccgggtctg gcaccgactt cactctgact 240

atttcctccc tgcaacctga ggacgtggct acctactact gccagcagta ctacaacttc 300

cctaccttcg gccaagggac gaagctggag atcaag 336

<210> 1928
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1928
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1929
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1929
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu

```
1               5                   10                  15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Phe Thr Phe Arg Asp Tyr
            20                  25                  30

Tyr Met Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
    50                  55                  60

Gly Gln Val Thr Ile Ser Arg Asp Asn Ser Ile Ser Thr Leu Tyr Leu
65                  70                  75                  80

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
                85                  90                  95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Glu Asn Lys Lys Asn
                165                 170                 175

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu
            180                 185                 190

Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Ser Arg Phe Ser
```

195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
210 215 220

Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Asn Phe Pro
225 230 235 240

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
245 250

<210> 1930
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1930
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Gln Val Thr Ile Ser Arg Asp Asn Ser Ile Ser Thr Leu Tyr Leu
65 70 75 80

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 1931
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1931
gaagtgcagt tggtccaatc aggcgcagaa gtgaagaaac ccggagaatc attgaagatt 60

tcgtgcaaag gaagcgggtt cacattccgc gattactaca tggcgtgggt cagacagatg 120

ccgggaaagg gactcgagtg gatggggtcc atcagctacg aaggaaaccc ttactacggg 180

gactccgtga agggccaggt caccatctcc cgcgacaact caatctccac tctgtatctg 240

caatggtcga gcctcaaggc ctctgatact gcgatgtact actgcgctcg gcatgaccac 300

aacaacgtgg actggttcgc ttactgggga cagggtaccc ttgtgaccgt gtcctcc 357

<210> 1932
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1932
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

```
Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
            20                  25                  30


Glu Asn Lys Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45


Ala Pro Arg Leu Leu Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Ile
    50                  55                  60


Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80


Ile Ser Ser Leu Gln Pro Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
                85                  90                  95


Tyr Tyr Asn Phe Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210> 1933
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 1933
gagatcgtga tgactcagtc ccctgccacc ctctcgctgt cccccgggga gagggccacg       60

ctgtcctgca agagctccca gtcactgctg tattccgaaa acaagaagaa ctacctcgcc      120

tggtaccaac agaagccggg acaggccccg cggcttctga tcttctgggc ctccactcgg      180

gagtccggca ttccggcccg cttctccggc tcggggagcg gaactgactt caccctgacc      240

atcagcagcc tgcagccaga ggacctcgca gtgtactact gtcaacagta ctacaatttc      300

cccacctttg gccagggtac caagctggag attaag                                336
```

<210> 1934
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1934
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1935
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1935
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Gln Val Thr Ile Ser Arg Asp Asn Ser Ile Ser Thr Leu Tyr Leu

```
65                  70                  75                  80

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
                85                  90                  95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
    130                 135                 140

Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
145                 150                 155                 160

Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Glu Asn Lys Lys Asn
                165                 170                 175

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
            180                 185                 190

Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Ala Arg Phe Ser
        195                 200                 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
    210                 215                 220

Pro Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Asn Phe Pro
225                 230                 235                 240

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
                245                 250
```

<210> 1936

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1936
Asp Tyr Ala Met His
1 5

<210> 1937
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1937
Thr Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 1938
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1938
Asp Ile Gln Tyr Gly Asn Tyr Tyr Tyr Gly Met Asp Val
1 5 10

<210> 1939
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1939
Gly Phe Thr Phe Asn Asp Tyr
1 5

<210> 1940
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1940
Ser Trp Asn Ser Gly Ser
1 5

<210> 1941
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1941
Asp Ile Gln Tyr Gly Asn Tyr Tyr Tyr Gly Met Asp Val
1 5 10

<210> 1942
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1942
Gly Phe Thr Phe Asn Asp Tyr Ala
1 5

<210> 1943
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1943
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 1944
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1944
Ala Lys Asp Ile Gln Tyr Gly Asn Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 1945
<211> 122
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1945

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asp Tyr
            20                  25                  30


Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Thr Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95


Ala Lys Asp Ile Gln Tyr Gly Asn Tyr Tyr Tyr Gly Met Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 1946
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1946

gaggtgcagc tggtcgagtc ggggggagga ttggtgcagc cgggcagaag cctgcggctc 60

tcatgtgccg cctccggctt cacctttaac gactacgcaa tgcactgggt cagacaggct 120

cctgggaagg gcctggaatg ggtgtccacc atttcctgga actccgggag catcggctac 180

gctgactccg tgaagggccg cttcacgatt agccgcgata acgcgaaaaa gagcctgtac 240

ctccaaatga actccctgcg ggccgaagat accgcccttt actactgcgc gaaggacatt 300

cagtatggaa actactacta cggaatggac gtctggggac aggggaccac agtgaccgtg 360

tcaagc 366

<210> 1947
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1947
Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 1948
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1948
Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 1949
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1949
Gln Gln Arg Ser Asn Trp Pro Ile Thr
1 5

<210> 1950
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1950
Ser Gln Ser Val Ser Ser Tyr
1 5

<210> 1951
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1951
Asp Ala Ser
1

<210> 1952
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1952
Arg Ser Asn Trp Pro Ile
1 5

<210> 1953
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1953
Gln Ser Val Ser Ser Tyr
1 5

<210> 1954
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1954
Asp Ala Ser
1

<210> 1955
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1955
Gln Gln Arg Ser Asn Trp Pro Ile Thr
1   5

<210> 1956
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1956
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Ile
                85   90   95

Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100   105

<210> 1957
<211> 321
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1957
gaaatcgtgc tgacccagag cccagccact ttgtcactgt cccccggcga aagagccact 60

ctgtcctgcc gggcatcgca gtccgtgtcg tcctacctgg cctggtacca gcaaaagccc 120

ggacaagccc ctcgccttct catctacgac gcctccaatc gcgcgaccgg aatcccggcc 180

aggttctccg ggagcggttc aggcactgac ttcaccctga ccatctcgtc cctggagccg 240

gaggatttcg ccgtgtatta ctgccagcag cggtccaact ggcccatcac cttcggccaa 300

gggactcggc tcgaaatcaa g 321

<210> 1958
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1958
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 1959
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 1959

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Ile Gln Tyr Gly Asn Tyr Tyr Tyr Gly Met Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp
```

180 185 190

Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp
210 215 220

Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Ile Thr Phe
225 230 235 240

Gly Gln Gly Thr Arg Leu Glu Ile Lys
245

<210> 1960
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1960
gaggtgcagc tggtcgagtc ggggggagga ttggtgcagc cgggcagaag cctgcggctc 60

tcatgtgccg cctccggctt cacctttaac gactacgcaa tgcactgggt cagacaggct 120

cctgggaagg gcctggaatg ggtgtccacc atttcctgga actccgggag catcggctac 180

gctgactccg tgaagggccg cttcacgatt agccgcgata acgcgaaaaa gagcctgtac 240

ctccaaatga actccctgcg ggccgaagat accgcccttt actactgcgc gaaggacatt 300

cagtatggaa actactacta cggaatggac gtctggggac aggggaccac agtgaccgtg 360

tcaagcggcg gtggaggatc tggcggagga ggttccggtg gcggtggatc gggaggggga 420

ggatcggaaa tcgtgctgac ccagagccca gccactttgt cactgtcccc cggcgaaaga 480

gccactctgt cctgccgggc atcgcagtcc gtgtcgtcct acctggcctg gtaccagcaa 540

aagcccggac aagcccctcg ccttctcatc tacgacgcct ccaatcgcgc gaccggaatc 600

ccggccaggt tctccgggag cggttcaggc actgacttca ccctgaccat ctcgtccctg 660

gagccggagg atttcgccgt gtattactgc cagcagcggt ccaactggcc catcaccttc 720

ggccaaggga ctcggctcga aatcaag 747

<210> 1961
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1961
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30

Tyr Met Ala Trp Val Arg Gln Ala Pro Lys Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asn Asn Ala Lys Ser Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
85 90 95

Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
        115

<210> 1962
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1962
Asp Ile Val Met Thr Gln Thr Pro Ser Ser Gln Ala Val Ser Ala Gly
1   5   10   15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
            20   25   30

Glu Asn Lys Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45

Ser Pro Lys Leu Leu Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
                85   90   95

Tyr Tyr Asn Phe Pro Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
            100   105   110

<210> 1963
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1963
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 1964
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1964
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
            20   25   30

Tyr Met Ala Trp Val Arg Gln Ala Pro Lys Lys Gly Leu Glu Trp Val
        35   40   45

Ala Ser Ile Ser Tyr Glu Gly Asn Pro Tyr Tyr Gly Asp Ser Val Lys
    50   55   60

Gly Arg Phe Thr Ile Ser Arg Asn Asn Ala Lys Ser Thr Leu Tyr Leu
65   70   75   80

Gln Met Asn Ser Leu Arg Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
                85   90   95

```
Arg His Asp His Asn Asn Val Asp Trp Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr
    130                 135                 140


Gln Thr Pro Ser Ser Gln Ala Val Ser Ala Gly Glu Lys Val Thr Met
145                 150                 155                 160


Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Glu Asn Lys Lys Asn
                165                 170                 175


Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu
            180                 185                 190


Ile Phe Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ile
        195                 200                 205


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln
    210                 215                 220


Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Asn Phe Pro
225                 230                 235                 240


Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
                245                 250


<210> 1965
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
```

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1965
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Asp Tyr Tyr Cys
85 90 95

Ala Arg Ser Asn Tyr Tyr Gly Ser Ser Tyr Trp Phe Phe Asp Val Trp
100 105 110

Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1966
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 1966
gaggtgcaac tgcagcagtc aggagcagaa ctggtcaagc cgggcgcatc cgtcaagatg 60

agctgcaagg cctcaggata caccttcact tcatacaaca tgcactgggt caagcagacg 120

cctgggcagg ggctggagtg gatcggtgcc atctaccccg gaaacggcga cacctcctac 180

aaccagaagt tcaagggaaa ggccaccctc accgctgata agtccagcag caccgcctac 240

atgcaactgt cgtccctgac ttcggaggac agcgctgact actattgcgc ccgctctaat 300

tactacggtt cctcctactg gttcttcgac gtgtggggcg cgggtaccac tgtgactgtc 360

tccagc 366

<210> 1967
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1967
Asp Ile Val Leu Thr Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Asn Tyr Met
20 25 30

Asp Trp Tyr Gln Lys Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1968
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1968
gacatcgtgc tcactcagtc gcccgccatt ctgagcgcta gccccggcga aaaggtcacc 60

atgacctgta gagcgtcatc ctcggtgaac tacatggact ggtaccagaa gaagccggga 120

tcgagcccta agccatggat ctacgccaca tccaatctgg cgtccggcgt gccggcccgg 180

ttcagcggga gcggctcagg cacctcctat tccctcacca tctcgagagt ggaggctgag 240

gatgcagcca cgtactactg tcagcagtgg tcgttcaacc ccccaacctt tggtggtgga 300

accaagctgg aaatcaag 318

<210> 1969
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1969
Gly Ser Thr Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly
1 5 10 15

Ser Ser

<210> 1970
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1970
Asp Ile Val Leu Thr Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Asn Tyr Met
20 25 30

Asp Trp Tyr Gln Lys Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Ser Thr Ser Gly Gly
100 105 110

Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu Val Gln Leu
115 120 125

Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met
130 135 140

Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp

145 150 155 160

Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr
165 170 175

Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala
180 185 190

Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser
195 200 205

Ser Leu Thr Ser Glu Asp Ser Ala Asp Tyr Tyr Cys Ala Arg Ser Asn
210 215 220

Tyr Tyr Gly Ser Ser Tyr Trp Phe Phe Asp Val Trp Gly Ala Gly Thr
225 230 235 240

Thr Val Thr Val Ser Ser
245

<210> 1971
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 1971
gacatcgtgc tcactcagtc gcccgccatt ctgagcgcta gccccggcga aaaggtcacc 60

atgacctgta gagcgtcatc ctcggtgaac tacatggact ggtaccagaa gaagccggga 120

tcgagcccta agccatggat ctacgccaca tccaatctgg cgtccggcgt gccggcccgg 180

ttcagcggga gcggctcagg cacctcctat tccctcacca tctcgagagt ggaggctgag 240

gatgcagcca cgtactactg tcagcagtgg tcgttcaacc ccccaacctt tggtggtgga 300

accaagctgg aaatcaaggg aagcacctcc ggcggaggtt ccggaggagg gtccggaggc 360

ggaggcagct ccgaggtgca actgcagcag tcaggagcag aactggtcaa gccgggcgca 420

tccgtcaaga tgagctgcaa ggcctcagga tacaccttca cttcatacaa catgcactgg 480

gtcaagcaga cgcctgggca ggggctggag tggatcggtg ccatctaccc cggaaacggc 540

gacacctcct acaaccagaa gttcaaggga aaggccaccc tcaccgctga taagtccagc 600

agcaccgcct acatgcaact gtcgtccctg acttcggagg acagcgctga ctactattgc 660

gcccgctcta attactacgg ttcctcctac tggttcttcg acgtgtgggg cgcgggtacc 720

actgtgactg tctccagc 738

<210> 1972
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1972
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

```
Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser
    130                 135                 140

Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val
145                 150                 155                 160

Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
                165                 170                 175

Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
            180                 185                 190

Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
        195                 200                 205

Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
    210                 215                 220

Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225                 230                 235                 240

Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
                245                 250
```

<210> 1973
<211> 238
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1973
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gln
115 120 125

Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser
130 135 140

Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn
145 150 155 160

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met

165 170 175

Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser
180 185 190

Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
195 200 205

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
210 215 220

Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
225 230 235

<210> 1974
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1974
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

```
Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95


Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110


Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120                 125


<210> 1975
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1975
Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln
1               5                   10                  15


Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20                  25                  30


Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45


Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60


Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80


Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95
```

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
100 105 110

<210> 1976
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1976
Gly Asp Ser Met Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1977
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1977
Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 1978
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1978
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1979
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1979
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1980
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1980
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1981
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1981
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1   5   10   15

<210> 1982
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1982
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1   5   10

<210> 1983
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1983
Asp Val Ser Asn Arg Pro Ser
1   5

<210> 1984
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1984

Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1985
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1985
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15

Lys Gly

<210> 1986
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1986
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

```
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Leu Trp Glu Val Arg Ala Leu Pro Ser Val Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 1987
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1987
Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1               5                   10                  15


Thr Ala Arg Ile Thr Cys Gly Ala Asn Asp Ile Gly Ser Lys Ser Val
            20                  25                  30


His Trp Tyr Gln Gln Lys Ala Gly Gln Ala Pro Val Leu Val Val Ser
        35                  40                  45


Glu Asp Ile Ile Arg Pro Ser Gly Ile Pro Glu Arg Ile Ser Gly Ser
    50                  55                  60


Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65                  70                  75                  80
```

```
Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Arg Asp Ser Asp Gln
                85                  90                  95


Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
            100                 105


<210> 1988
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1988
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Ser Asn
            20                  25                  30


Val Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Gly Val Ile Pro Ile Val Asp Ile Ala Asn Tyr Ala Gln Arg Phe
    50                  55                  60


Lys Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Thr Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Thr Leu Gly Leu Val Leu Asp Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110
```

```
Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300
```

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 1989
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1989
Glu Thr Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly

```
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Gly Ser Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Tyr Gly Ala Ser Ser Arg Ala Pro Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Asp Ser Pro
                85                  90                  95

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala
            100                 105                 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
```

195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 1990
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1990
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Tyr Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Gly Tyr Gly Arg Val Asp Glu Trp Gly Arg Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 1991
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1991
Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Leu Ser Asn Ile Gly Arg Asn
20 25 30

Pro Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Leu Asp Asn Leu Arg Leu Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp Ser His
85 90 95

Pro Gly Trp Thr Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1992
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1992
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

```
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys
    210                 215                 220

Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365
```

```
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> 1993
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1993
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
        35                  40                  45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
```

```
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
```

<210> 1994
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1994
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
            20   25   30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
            100   105   110

Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 1995
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1995
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

```
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
        35                  40                  45


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 1996
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1996
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
            100                 105                 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys
    210                 215                 220

Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val
225                 230                 235                 240
```

```
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430
```

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435   440   445

<210> 1997
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1997
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Leu
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala

130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 1998
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1998
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
            100                 105                 110


Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210> 1999
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1999
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60


Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80
```

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 2000
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2000
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 2001
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 2001
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
        35   40   45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 2002
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 2002
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Asp Glu Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 2003
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 2003
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
        35   40   45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 2004
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 2004
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Val Arg Ser Gly Ser Tyr Asn Tyr Tyr Tyr Tyr Gly Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120

<210> 2005
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2005
Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser

50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

Asn Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 2006
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2006
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ala Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Gly Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Arg Asp Tyr Tyr Asp Ile Leu Thr Asp Tyr Tyr Ile His Tyr Trp
100 105 110

Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 2007
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2007
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Cys Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg
100 105

<210> 2008
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2008
Asn Tyr Trp Met Asn
1 5

<210> 2009
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2009
Ala Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Gly Ser Val Lys
1 5 10 15

Gly

<210> 2010
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2010
Asp Tyr Tyr Asp Ile Leu Thr Asp Tyr Tyr Ile His Tyr Trp Tyr Phe
1 5 10 15

Asp Leu

<210> 2011
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2011
Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 2012
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2012
Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 2013
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2013
Gly Ala Ser Ser Arg Ala Thr

1 5

<210> 2014
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2014
Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Gly Ser Leu Tyr Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

```
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335
```

```
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350


Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365


Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380


Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400


Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415


Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430


Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> 2015
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 2015
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Pro Ser Gln Gly Ile Asn Trp Glu
            20                  25                  30
```

```
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Ser Leu Glu Gln Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
```

<210> 2016
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 2016
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Asp Tyr
20 25 30

His Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Val Ile Asn Pro Met Tyr Gly Thr Thr Asp Tyr Asn Gln Arg Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Asp Tyr Phe Thr Gly Thr Gly Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 2017
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 2017
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Arg Ser Leu Val His Ser
20 25 30

Arg Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ile Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Ser
85 90 95

Thr His Leu Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 2018
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 2018
Arg Tyr Gly Ile Ser
1 5

<210> 2019
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 2019
Trp Ile Ser Thr Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> 2020
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 2020
Arg Gln Leu Tyr Phe Asp Tyr
1 5

<210> 2021
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 2021
Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala

1 5 10

<210> 2022
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2022
Asp Ala Ser Thr Arg Ala Thr
1 5

<210> 2023
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2023
Gln Gln Tyr Asp Asn Trp Pro Leu Thr
1 5

<210> 2024
<211> 400
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<220>
<221> misc_feature
<222> (1)..(400)
<223> /note="This sequence may encompass 100-400 nucleotides"

<220>
<221> source
<223> /note="See specification as filed for detailed description of
substitutions and preferred embodiments"

<400> 2024
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 400

<210> 2025
<211> 2000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> misc_feature
<222> (1)..(2000)
<223> /note="This sequence may encompass 50-2000 nucleotides"

<400> 2025
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 960

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1020

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1200

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1680

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980

aaaaaaaaaa aaaaaaaaaa 2000

<210> 2026
<211> 100
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 2026
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60

tttttttttt tttttttttt tttttttttt tttttttttt 100

<210> 2027
<211> 5000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> misc_feature
<222> (1)..(5000)
<223> /note="This sequence may encompass 50-5000 nucleotides"

<400> 2027
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 120

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 180

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 240

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 300

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 360

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 420

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 480

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 540

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 600

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 660

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 720

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 780

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 840

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 900

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 960

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1020

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1080

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1140

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1200

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1260

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1320

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1380

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1440

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1500

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1560

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1620

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1680

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1740

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1800

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1860

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1920

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 1980

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2040

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2100

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2160

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2220

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2280

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2340

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2400

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2460

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2520

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2580

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2640

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2700

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2760

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2820

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2880

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 2940

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3000

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3060

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3120

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3180

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3240

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3300

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3360

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3420

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3480

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3540

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3600

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3660

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3720

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3780

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3840

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3900

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 3960

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4020

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4080

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4140

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4200

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4260

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4320

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4380

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4440

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4500

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4560

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4620

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4680

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4740

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4800

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4860

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4920

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 4980

tttttttttt tttttttttt 5000

<210> 2028
<211> 5000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> misc_feature
<222> (1)..(5000)
<223> /note="This sequence may encompass 100-5000 nucleotides"

<400> 2028
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 960

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1020

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1200

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1680

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2160

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2220

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2280

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2340

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2400

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2460

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2520

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2580

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2640

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2700

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2760

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2820

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2880

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2940

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3000

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3060

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3900

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3960

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4020

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4200

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4260

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4320

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4500

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4560

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4620

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4680

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 4980

aaaaaaaaaa aaaaaaaaaa 5000

<210> 2029
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<220>
<221> VARIANT
<222> (1)..(21)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(486)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 2029
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu
20 25 30

```
Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr
    50                  55                  60

Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
                85                  90                  95

Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140

Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser
145                 150                 155                 160

Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
        195                 200                 205

Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys
    210                 215                 220
```

```
Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys
225                 230                 235                 240


His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255


Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270


Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285


Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300


Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320


Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335


Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350


Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365


Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380


Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400


Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415
```

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 2030
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2030
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln

```
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
```

```
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
    290                 295                 300

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
305                 310                 315                 320

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
                325                 330                 335

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
            340                 345                 350

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
        355                 360                 365

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
    370                 375                 380

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
385                 390                 395                 400

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
                405                 410                 415

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
            420                 425                 430

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
        435                 440                 445

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
```

450 455 460

Arg
465

<210> 2031
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2031
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro
20

<210> 2032
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 2032
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccc 63

<210> 2033
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2033
Leu Ala Glu Ala Ala Ala Lys
1 5

<210> 2034
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
<221> SITE
<222> (1)..(30)
<223> /note="This sequence may encompass 1-6 'Gly Gly Gly Gly Ser' repeating units"

<220>
<221> source
<223> /note="See specification as filed for detailed description of substitutions and preferred embodiments"

<400> 2034
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25 30

<210> 2035
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 2035
Arg Gly Asp Ser
1

<210> 2036
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2036
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
115 120 125

```
Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly
    130                 135                 140

Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp
145                 150                 155                 160

Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val
            180                 185                 190

Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr
        195                 200                 205

Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser
    210                 215                 220

Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu
225                 230                 235                 240

Thr Val Leu
```