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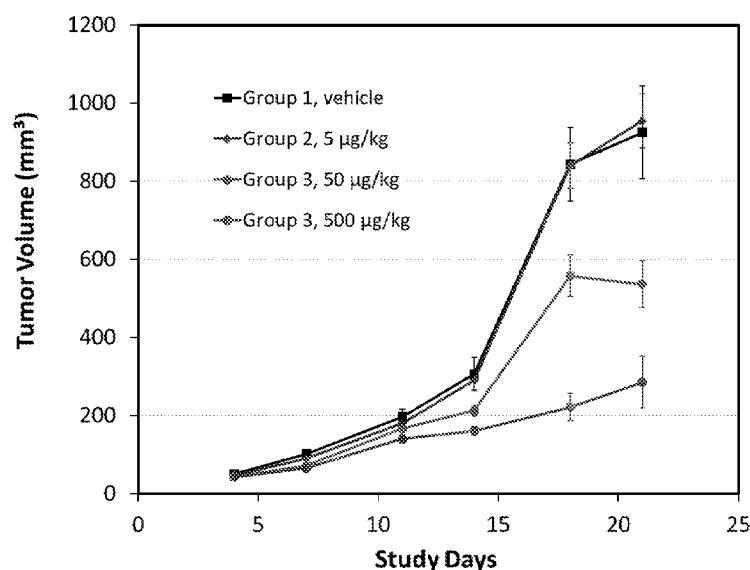
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(54) Title: B CELL MATURATION ANTIGEN BINDING PROTEINS

FIG. 29

Mean Tumor Volume $\pm$ SEM

(57) Abstract: Disclosed herein are B cell maturation antigen binding proteins with improved binding affinities and improved ability to mediate killing of cancer cells expressing B cell maturation antigen (BCMA). Pharmaceutical compositions comprising the binding proteins disclosed herein and methods of treatment of a cancer or a metastasis thereof using such formulations are further provided.

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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B CELL MATURATION ANTIGEN BINDING PROTEINS

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/572,375 filed October 13, 2017 which is incorporated by reference herein in its entirety.

SEQUENCE LISTING

[0001.1] 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 October 11, 2018, is named 47517-722_601_SL.txt and is 232,688 bytes in size.

BACKGROUND OF THE INVENTION

[0002] Cancer is the second leading cause of human death next to coronary disease. Worldwide, millions of people die from cancer every year. In the United States alone, cancer causes the death of well over a half-million people each year, with some 1.4 million new cases diagnosed per year. While deaths from heart disease have been declining significantly, those resulting from cancer generally are on the rise. In the early part of the next century, cancer is predicted to become the leading cause of death.

[0003] Moreover, even for those cancer patients that initially survive their primary cancers, common experience has shown that their lives are dramatically altered. Many cancer patients experience strong anxieties driven by the awareness of the potential for recurrence or treatment failure. Many cancer patients experience significant physical debilitations following treatment.

[0004] Generally speaking, the fundamental problem in the management of the deadliest cancers is the lack of effective and non-toxic systemic therapies. Cancer is a complex disease characterized by genetic mutations that lead to uncontrolled cell growth. Cancerous cells are present in all organisms and, under normal circumstances, their excessive growth is tightly regulated by various physiological factors.

SUMMARY OF THE INVENTION

[0005] The present disclosure provides single domain B cell maturation antigen (BCMA) binding proteins which can be used for diagnosing and treating indications correlated to the expression of BCMA.

[0006] Provided herein is a single domain B cell maturation agent (BCMA) binding protein, comprising complementarity determining regions CDR1, CDR2, and CDR3, wherein (a) the amino acid sequence of CDR1 is as set forth in X₁X₂X₃X₄X₅X₆X₇PX₈G (SEQ ID NO: 1),

wherein X_1 is T or S; X_2 is N, D, or S; X_3 is I, D, Q, H, V, or E; X_4 is F, S, E, A, T, M, V, I, D, Q, P, R, or G; X_5 is S, M, R, or N; X_6 is I, K, S, T, R, E, D, N, V, H, L, A, Q, or G; X_7 is S, T, Y, R, or N; and X_8 is M, G, or Y; (b) the amino acid sequence of CDR2 is as set forth in AIX₉GX₁₀X₁₁TX₁₂YADSVK (SEQ ID NO: 2), wherein X_9 is H, N, or S; X_{10} is F, G, K, R, P, D, Q, H, E, N, T, S, A, I, L, or V; X_{11} is S, Q, E, T, K, or D; and X_{12} is L, V, I, F, Y, or W; and (c) the amino acid sequence of CDR3 is as set forth in VPWGX₁₃YHPX₁₄X₁₅VX₁₆ (SEQ ID NO: 3), wherein X_{13} is D, I, T, K, R, A, E, S, or Y; X_{14} is R, G, L, K, T, Q, S, or N; X_{15} is N, K, E, V, R, M, or D; and X_{16} is Y, A, V, K, H, L, M, T, R, Q, C, S, or N.

[0006a] Provided herein is a single domain B cell maturation agent (BCMA) binding protein, wherein the single domain BCMA binding protein comprises a complementarity determining region 1 (CDR1), a CDR2, and a CDR3, and wherein:

- (a) the CDR1 has the amino acid sequence of SEQ ID NO: 11, the CDR2 has the amino acid sequence of SEQ ID NO: 125, and the CDR3 has the amino acid sequence of SEQ ID NO: 239;
- (b) the CDR1 has the amino acid sequence of SEQ ID NO: 95, the CDR2 has the amino acid sequence of SEQ ID NO: 209, and the CDR3 has the amino acid sequence of SEQ ID NO: 323;
- (c) the CDR1 has the amino acid sequence of SEQ ID NO: 84, the CDR2 has the amino acid sequence of SEQ ID NO: 198, and the CDR3 has the amino acid sequence of SEQ ID NO: 312;
- (d) the CDR1 has the amino acid sequence of SEQ ID NO: 41, the CDR2 has the amino acid sequence of SEQ ID NO: 155, and the CDR3 has the amino acid sequence of SEQ ID NO: 269;
- (e) the CDR1 has the amino acid sequence of SEQ ID NO: 10, the CDR2 has the amino acid sequence of SEQ ID NO: 124, and the CDR3 has the amino acid sequence of SEQ ID NO: 238;
- (f) the CDR1 has the amino acid sequence of SEQ ID NO: 99, the CDR2 has the amino acid sequence of SEQ ID NO: 213, and the CDR3 has the amino acid sequence of SEQ ID NO: 327;
- (g) the CDR1 has the amino acid sequence of SEQ ID NO: 76, the CDR2 has the amino acid sequence of SEQ ID NO: 190, and the CDR3 has the amino acid sequence of SEQ ID NO: 304;
- (h) the CDR1 has the amino acid sequence of SEQ ID NO: 39, the CDR2 has the amino acid sequence of SEQ ID NO: 153, and the CDR3 has the amino acid sequence of SEQ ID NO: 267;

- (i) the CDR1 has the amino acid sequence of SEQ ID NO: 70, the CDR2 has the amino acid sequence of SEQ ID NO: 184, and the CDR3 has the amino acid sequence of SEQ ID NO: 298;
- (j) the CDR1 has the amino acid sequence of SEQ ID NO: 82, the CDR2 has the amino acid sequence of SEQ ID NO: 196, and the CDR3 has the amino acid sequence of SEQ ID NO: 310;
- (k) the CDR1 has the amino acid sequence of SEQ ID NO: 38, the CDR2 has the amino acid sequence of SEQ ID NO: 152, and the CDR3 has the amino acid sequence of SEQ ID NO: 266;
- (l) the CDR1 has the amino acid sequence of SEQ ID NO: 66, the CDR2 has the amino acid sequence of SEQ ID NO: 180, and the CDR3 has the amino acid sequence of SEQ ID NO: 294;
- (m) the CDR1 has the amino acid sequence of SEQ ID NO: 102, the CDR2 has the amino acid sequence of SEQ ID NO: 216, and the CDR3 has the amino acid sequence of SEQ ID NO: 330;
- (n) the CDR1 has the amino acid sequence of SEQ ID NO: 34, the CDR2 has the amino acid sequence of SEQ ID NO: 137, and the CDR3 has the amino acid sequence of SEQ ID NO: 251;
- (o) the CDR1 has the amino acid sequence of SEQ ID NO: 42, the CDR2 has the amino acid sequence of SEQ ID NO: 145, and the CDR3 has the amino acid sequence of SEQ ID NO: 259;
- (p) the CDR1 has the amino acid sequence of SEQ ID NO: 81, the CDR2 has the amino acid sequence of SEQ ID NO: 195, and the CDR3 has the amino acid sequence of SEQ ID NO: 309;
- (q) the CDR1 has the amino acid sequence of SEQ ID NO: 101, the CDR2 has the amino acid sequence of SEQ ID NO: 215, and the CDR3 has the amino acid sequence of SEQ ID NO: 329;
- (r) the CDR1 has the amino acid sequence of SEQ ID NO: 17, the CDR2 has the amino acid sequence of SEQ ID NO: 131, and the CDR3 has the amino acid sequence of SEQ ID NO: 245;
- (s) the CDR1 has the amino acid sequence of SEQ ID NO: 57, the CDR2 has the amino acid sequence of SEQ ID NO: 171, and the CDR3 has the amino acid sequence of SEQ ID NO: 285;
- (t) the CDR1 has the amino acid sequence of SEQ ID NO: 64, the CDR2 has the amino acid sequence of SEQ ID NO: 178, and the CDR3 has the amino acid sequence of SEQ ID NO: 292;

(u) the CDR1 has the amino acid sequence of SEQ ID NO: 47, the CDR2 has the amino acid sequence of SEQ ID NO: 161, and the CDR3 has the amino acid sequence of SEQ ID NO: 275;

(v) the CDR1 has the amino acid sequence of SEQ ID NO: 65, the CDR2 has the amino acid sequence of SEQ ID NO: 179, and the CDR3 has the amino acid sequence of SEQ ID NO: 293;

(w) the CDR1 has the amino acid sequence of SEQ ID NO: 97, the CDR2 has the amino acid sequence of SEQ ID NO: 211, and the CDR3 has the amino acid sequence of SEQ ID NO: 325;

(x) the CDR1 has the amino acid sequence of SEQ ID NO: 26, the CDR2 has the amino acid sequence of SEQ ID NO: 140, and the CDR3 has the amino acid sequence of SEQ ID NO: 254;

(y) the CDR1 has the amino acid sequence of SEQ ID NO: 94, the CDR2 has the amino acid sequence of SEQ ID NO: 208, and the CDR3 has the amino acid sequence of SEQ ID NO: 322;

(z) the CDR1 has the amino acid sequence of SEQ ID NO: 77, the CDR2 has the amino acid sequence of SEQ ID NO: 191, and the CDR3 has the amino acid sequence of SEQ ID NO: 305;

(aa) the CDR1 has the amino acid sequence of SEQ ID NO: 49, the CDR2 has the amino acid sequence of SEQ ID NO: 163, and the CDR3 has the amino acid sequence of SEQ ID NO: 277;

(bb) the CDR1 has the amino acid sequence of SEQ ID NO: 68, the CDR2 has the amino acid sequence of SEQ ID NO: 182, and the CDR3 has the amino acid sequence of SEQ ID NO: 296;

(cc) the CDR1 has the amino acid sequence of SEQ ID NO: 90, the CDR2 has the amino acid sequence of SEQ ID NO: 204, and the CDR3 has the amino acid sequence of SEQ ID NO: 318;

(dd) the CDR1 has the amino acid sequence of SEQ ID NO: 43, the CDR2 has the amino acid sequence of SEQ ID NO: 157, and the CDR3 has the amino acid sequence of SEQ ID NO: 271;

(ee) the CDR1 has the amino acid sequence of SEQ ID NO: 89, the CDR2 has the amino acid sequence of SEQ ID NO: 203, and the CDR3 has the amino acid sequence of SEQ ID NO: 317;

(ff) the CDR1 has the amino acid sequence of SEQ ID NO: 112, the CDR2 has the amino acid sequence of SEQ ID NO: 226, and the CDR3 has the amino acid sequence of SEQ ID NO: 340;

(gg) the CDR1 has the amino acid sequence of SEQ ID NO: 103, the CDR2 has the amino acid sequence of SEQ ID NO: 217, and the CDR3 has the amino acid sequence of SEQ ID NO: 331;

(hh) the CDR1 has the amino acid sequence of SEQ ID NO: 21, the CDR2 has the amino acid sequence of SEQ ID NO: 135, and the CDR3 has the amino acid sequence of SEQ ID NO: 249;

(ii) the CDR1 has the amino acid sequence of SEQ ID NO: 92, the CDR2 has the amino acid sequence of SEQ ID NO: 206, and the CDR3 has the amino acid sequence of SEQ ID NO: 320;

(jj) the CDR1 has the amino acid sequence of SEQ ID NO: 87, the CDR2 has the amino acid sequence of SEQ ID NO: 201, and the CDR3 has the amino acid sequence of SEQ ID NO: 315; or

(kk) the CDR1 has the amino acid sequence of SEQ ID NO: 60, the CDR2 has the amino acid sequence of SEQ ID NO: 174, and the CDR3 has the amino acid sequence of SEQ ID NO: 288.

[0007] In one embodiment, the CDR1 does not comprise an amino acid sequence of SEQ ID NO: 473. In one embodiment, the CDR2 does not comprise an amino acid sequence of SEQ ID NO: 474. In one embodiment, the CDR3 does not comprise an amino acid sequence of SEQ ID NO: 475. In one embodiment, the CDR1 and CDR2 do not comprise amino acid sequences of SEQ ID NO: 473 and 474, respectively. In one embodiment, the CDR1 and CDR3 do not comprise amino acid sequences of SEQ ID NO: 473 and 475, respectively. In one embodiment, the CDR2 and CDR3 do not comprise amino acid sequences of SEQ ID NO: 474 and 475, respectively. In one embodiment, the CDR1, CDR2 and CDR3 do not comprise amino acid sequences of SEQ ID NO: 473, 474 and 475, respectively.

[0008] Provided herein is a single domain BCMA binding protein wherein said protein comprises the following formula: f1-r1-f2-r2-f3-r3-f4, wherein, r1 is SEQ ID NO: 1; r2 is SEQ ID NO: 2; and r3 is SEQ ID NO: 3; and wherein f1, f2, f3 and f4 are framework residues selected so that said protein is from about eighty percent (80%) to about 99% identical to the amino acid sequence set forth in SEQ ID NO: 346 or 472. Provided herein is a single domain BCMA binding protein wherein said protein comprises the following formula: f1-r1-f2-r2-f3-r3-f4, wherein, r1 is SEQ ID NO: 1; r2 is SEQ ID NO: 2; and r3 is SEQ ID NO: 3; and wherein f1, f2, f3 and f4 are framework residues selected so that said protein is from about 80% to about 90% identical to the amino acid sequence set forth in SEQ ID NO: 346 or 472. In one embodiment, the amino acid

sequence of the single domain BCMA binding protein does not comprise SEQ ID NO: 472.

[0009] In some non-limiting examples, r1 comprises an amino acid sequence set forth as any one of SEQ ID NOS: 4-117.

[0010] In some non-limiting examples, r2 comprises an amino acid sequence set forth as any one of SEQ ID NOS: 118-231.

[0011] In some non-limiting examples, r3 comprises an amino acid sequence set forth as any one of SEQ ID NOS: 232-345.

[0012] In other non-limiting examples, the protein comprises an amino sequence set forth as any one of SEQ ID NOS: 346-460.

[0012] In other non-limiting examples, the protein comprises an amino sequence set forth as any one of SEQ ID NOS: 346-460.

[0013] In a single domain BCMA binding protein, f1 can comprise SEQ ID NO: 461 or 462.

[0014] In a single domain BCMA binding protein, f2 can comprise SEQ ID NO: 463.

[0015] In a single domain BCMA binding protein, f3 can comprise SEQ ID NO: 464 or 465.

[0016] In a single domain BCMA binding protein, wherein f4 can comprise SEQ ID NO: 466 or 467.

[0017] In one non-limiting example, r1 comprises SEQ ID NO: 76, 114, 115, 116 or 117. In one non-limiting example, r1 comprises SEQ ID NO: 76.

[0018] In one non-limiting example, r1 comprises SEQ ID NO: 76, r2 is SEQ ID NO: 190, and r3 is SEQ ID NO: 304.

[0019] In one non-limiting example, r1 comprises SEQ ID NO: 114, r2 comprises SEQ ID NO: 228 and r3 comprises SEQ ID NO: 342.

[0020] In one non-limiting example, r1 comprises SEQ ID NO: 115, r2 comprises SEQ ID NO: 229 and r3 comprises SEQ ID NO: 343.

[0021] In one non-limiting example, r1 comprises SEQ ID NO: 117, r2 comprises SEQ ID NO: 231 and r3 comprises SEQ ID NO: 345.

[0022] In one non-limiting example, r1 comprises SEQ ID NO: 116, r2 comprises SEQ ID NO: 230 and r3 comprises SEQ ID NO: 344.

[0023] A domain BCMA binding protein can have an elimination half-time of at least 12 hours, at least 20 hours, at least 25 hours, at least 30 hours, at least 35 hours, at least 40 hours, at least 45 hours, at least 50 hours, at least 100 hours or more. In some embodiments, the single domain BCMA binding protein further comprises a Fc domain. In some embodiments, the single domain BCMA binding protein further comprises an anti-cancer agent.

[0024] Provided herein is a single domain BCMA binding protein parental llama anti-BCMA 253BH10 SEQ ID NO: 472 or a humanized version of this llama sequence, BH2T, SEQ ID NO 346, wherein one or more amino acid residues selected from amino acid positions 26, 27, 28, 29, 30, 31, 32 and 34 of CDR1; positions 52, 54, 55 and 57 of CDR2; and positions 101, 105, 106 and 108 of CDR3 are substituted, wherein amino acid position 26, if substituted, is substituted with S; amino acid position 27, if substituted, is substituted with D or S; amino acid position 28, if substituted, is substituted with D, Q, H, V, or E; amino acid position 29, if substituted, is substituted with S, E, A, T, M, V, I, D, Q, P, R, or G; amino acid position 30, if substituted, is substituted with M, R, or N; amino acid position 31, if substituted, is substituted with K, S, T, R, E, D, N, V, H, L, A, Q, or G; amino acid position 32, if substituted, is substituted with T, Y,

R, or N; amino acid position 34, if substituted, is substituted with G or Y; amino acid position 52, if substituted, is substituted with N or S; amino acid position 54, if substituted, is substituted with G, K, R, P, D, Q, H, E, N, T, S, A, I, L, or V; amino acid position 55, if substituted, is substituted with Q, E, T, K, or D; amino acid position 57, if substituted, is substituted with V, I, F, Y, or W; amino acid position 101, if substituted, is substituted with I, T, K, R, A, E, S, or Y; amino acid position 105, if substituted, is substituted with G, L, K, T, Q, S, or N; amino acid position 106, if substituted, is substituted with K, E, V, R, M, or D; and amino acid position 108, if substituted, is substituted with A, V, K, H, L, M, T, R, Q, C, S, or N.

[0025] Such a single domain BCMA binding protein can be human, humanized, affinity matured, or a combination thereof.

[0026] Provided herein is a method for the treatment or amelioration of a B cell lineage cancer in a subject in need thereof, comprising administering to the subject a single domain BCMA binding protein described herein.

[0027] Provided herein is a multispecific binding protein comprising the single domain BCMA binding protein described herein.

[0027a] Provided herein is a multispecific binding protein comprising the single domain BCMA binding protein described herein, a human serum albumin binding domain, and a CD3 binding domain.

[0028] Provided herein is a method for the treatment or amelioration of a B cell lineage cancer in a subject in need thereof, comprising administering to the subject a multispecific binding protein described herein.

[0028a] Provided herein is a method for treating or ameliorating a B cell lineage cancer expressing BCMA in a subject in need thereof, comprising administering to the subject a single domain BCMA binding protein described herein or a multispecific binding protein described herein.

[0028b] Provided herein is the use of a single domain BCMA binding protein described herein or a multispecific binding protein described herein, in the manufacture of a medicament for treating or ameliorating a B cell lineage cancer expressing BCMA in a subject in need thereof.

[0029] The B cell lineage cancer can be a primary cancer or a metastatic cancer.

[0030] A B cell lineage cancer to be treated with the methods described herein can be a multiple myeloma, a leukemia, a lymphoma.

INCORPORATION BY REFERENCE

[0031] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

[0031a] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each of the appended claims.

[0031b] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

BRIEF DESCRIPTION OF THE DRAWINGS

[0032] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0033] **Fig. 1** illustrates the effect of exemplary BCMA targeting molecules (01H08, 01F07, 02F02, and BH253), containing an anti-BCMA binding protein according to the present disclosure in killing of EJM cells that express BCMA compared to a negative control.

[0034] **Fig. 2** is an image of an SDS-PAGE of representative purified BCMA trispecific molecules. Lane 1: 01F07-M34Y TriTAC non-reduced; Lane 2: 01F07-M34G-TriTAC non-reduced; Lane 3: 02B05 TriTAC non-reduced; Lane 4: 02G02-M34Y TriTAC non-reduced; Lane 5: 02G02 M34G TriTAC non-reduced; Lane 6: Broad Range SDS-PAGE Standard (Bio-Rad #1610317); Lane 7: 01F07-M34Y TriTAC non-reduced; Lane 8: 01F07-M34G-TriTAC non-reduced; Lane 9: 02B05 TriTAC non-reduced; Lane 10: 02G02-M34Y TriTAC non-reduced; Lane 11: 02G02 M34G TriTAC non-reduced; and Lane 12: Broad Range SDS-PAGE Standard (Bio-Rad #1610317).

[0035] **Figs. 3A-3I** illustrate the effect of exemplary BCMA trispecific targeting molecules containing an anti-BCMA binding protein according to the present disclosure in killing of Jeko1 (**Figs. 3A-3C**), MOLP-8 (**Figs. 3D-3F**) or OPM-2 (**Figs. 3G-3I**) cells that express BCMA compared to a negative control.

[0036] **Figs. 4A-4D** illustrate binding of an exemplary BCMA trispecific targeting protein containing a BCMA binding protein of this disclosure (02B05) to purified T Cells from four different human donors, donor 02 (**Fig. 4A**), donor 35 (**Fig. 4B**), donor 81 (**Fig. 4C**), donor 86 (**Fig. 4D**).

[0037] **Figs. 5A-5F** illustrate binding of an exemplary BCMA trispecific targeting protein (02B05) to cells expressing BCMA, NCI-H929 (**Fig. 5A**), EJM (**Fig. 5B**), OPM2 (**Fig. 5D**), RPMI8226 (**Fig. 5E**); or cell lines lacking expression of BCMA, NCI-H510A (**Fig. 5C**), and DMS-153 (**Fig. 5F**).

[0038] **Fig. 6** illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05) and BCMA expressing EJM cells, in presence or absence of human serum albumin (HSA).

[0039] **Fig. 7** illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05) and BCMA expressing EJM cells, using varying effector cells to target cells ratio.

[0040] **Fig. 8** illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05) and BCMA expressing OPM2 cells, using varying effector cells to target cells ratio.

[0041] Fig. 9 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05) and BCMA expressing NCI-H929 cells, using varying time-points and a 1:1 effector cells to target cells ratio.

[0042] Fig. 10 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA expressing EJM cells, and T cells from four different donors, in presence of human serum albumin (HSA).

[0043] Fig. 11 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA expressing NCI-H929 cells, and T cells from four different donors, in presence of human serum albumin (HSA).

[0044] Fig. 12 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA expressing OPM2 cells, and T cells from four different donors, in presence of human serum albumin (HSA).

[0045] Fig. 13 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA expressing RPMI8226 cells, and T cells from four different donors, in presence of human serum albumin (HSA).

[0046] Fig. 14 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA non-expressing OVCAR8 cells, and T cells from four different donors, in presence of human serum albumin (HSA).

[0047] Fig. 15 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA non-expressing NCI-H510A cells, and T cells from four different donors, in presence of human serum albumin (HSA).

[0048] Fig. 16 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein (02B05), BCMA expressing NCI-H929 cells, and peripheral blood mononuclear cells (PBMC) from two different cynomolgus, in presence of human serum albumin (HSA).

[0049] Fig. 17 illustrates the results of a TDCC assay using an exemplary BCMA trispecific targeting protein containing a BCMA binding protein of this disclosure (02B05), BCMA expressing RPMI8226 cells, and peripheral blood mononuclear cells (PBMC) from two different cynomolgus donors, in presence of human serum albumin (HSA).

[0050] Fig. 18 illustrates the expression level of T cell activation biomarker CD69, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA expressing cells EJM.

[0051] **Fig. 19** illustrates the expression level of T cell activation biomarker CD25, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA expressing cells EJM.

[0052] **Fig. 20** illustrates the expression level of T cell activation biomarker CD69, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA expressing cells OPM2.

[0053] **Fig. 21** illustrates the expression level of T cell activation biomarker CD25, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA expressing cells OPM2.

[0054] **Fig. 22** illustrates the expression level of T cell activation biomarker CD69, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA expressing cells RPMI8226.

[0055] **Fig. 23** illustrates the expression level of T cell activation biomarker CD25, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA expressing cells RPMI8226.

[0056] **Fig. 24** illustrates the expression level of T cell activation biomarker CD69, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA non-expressing cells OVCAR8.

[0057] **Fig. 25** illustrates the expression level of T cell activation biomarker CD25, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA non-expressing cells OVCAR8.

[0058] **Fig. 26** illustrates the expression level of T cell activation biomarker CD69, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA non-expressing cells NCI-H510A.

[0059] **Fig. 27** illustrates the expression level of T cell activation biomarker CD25, following a TDCC assay using an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) and BCMA non-expressing cells NCI-H510A.

[0060] **Fig. 28** illustrates the expression level a cytokine, TNF- α , in co-cultures of T cells and BCMA expressing target cells (EJM cells) treated with increasing concentrations of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) or with a negative control GFP trispecific protein.

[0061] **Fig. 29** illustrates tumor growth reduction in RPMI8226 xenograft model, treated with an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05), at varying concentrations, or with a control vehicle.

[0062] **Fig. 30** illustrates tumor growth reduction in Jeko1 xenograft model, treated with an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05), at varying concentrations, or with a control vehicle.

[0063] **Fig. 31** illustrates concentration of BCMA targeting trispecific protein in serum samples from cynomolgus monkeys dosed with varying concentrations of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05).

[0064] **Fig. 32** the results of a TDCC assay using BCMA trispecific targeting protein obtained from serum samples of cynomolgus monkeys dosed with varying concentrations of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05), BCMA expressing EJM cells, and purified human T cells, in presence of serum from cynomolgus monkeys that were not exposed to a BCMA targeting trispecific protein.

DETAILED DESCRIPTION OF THE INVENTION

[0065] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

Certain definitions

[0066] The terminology used herein is for the purpose of describing particular cases only and is not intended to be limiting. As used herein, the singular forms “a”, “an” and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms “including”, “includes”, “having”, “has”, “with”, or variants thereof are used in either the detailed description and/or the claims, such terms are intended to be inclusive in a manner similar to the term “comprising.”

[0067] The term “about” or “approximately” means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, *e.g.*, the limitations of the measurement system. For example, “about” can mean within 1 or more than 1 standard deviation, per the practice in the given value. Where particular values are described in the application and claims, unless otherwise stated the term “about” should be assumed to mean an acceptable error range for the particular value.

[0068] The terms “individual,” “patient,” or “subject” are used interchangeably. None of the terms require or are limited to situation characterized by the supervision (e.g. constant or intermittent) of a health care worker (e.g. a doctor, a registered nurse, a nurse practitioner, a physician’s assistant, an orderly, or a hospice worker).

[0069] An “antibody” typically refers to a Y-shaped tetrameric protein comprising two heavy (H) and two light (L) polypeptide chains held together by covalent disulfide bonds and non-covalent interactions. Human light chains comprise a variable domain (VL) and a constant domain (CL) wherein the constant domain may be readily classified as kappa or lambda based on amino acid sequence and gene loci. Each heavy chain comprises one variable domain (VH) and a constant region, which in the case of IgG, IgA, and IgD, comprises three domains termed CH1, CH2, and CH3 (IgM and IgE have a fourth domain, CH4). In IgG, IgA, and IgD classes the CH1 and CH2 domains are separated by a flexible hinge region, which is a proline and cysteine rich segment of variable length (generally from about 10 to about 60 amino acids in IgG). The variable domains in both the light and heavy chains are joined to the constant domains by a “J” region of about 12 or more amino acids and the heavy chain also has a “D” region of about 10 additional amino acids. Each class of antibody further comprises inter-chain and intra-chain disulfide bonds formed by paired cysteine residues. There are two types of native disulfide bridges or bonds in immunoglobulin molecules: inter-chain and intra-chain disulfide bonds. The location and number of inter-chain disulfide bonds vary according to the immunoglobulin class and species. Inter-chain disulfide bonds are located on the surface of the immunoglobulin, are accessible to solvent and are usually relatively easily reduced. In the human IgG1 isotype there are four inter-chain disulfide bonds, one from each heavy chain to the light chain and two between the heavy chains. The inter-chain disulfide bonds are not required for chain association. As is well known the cysteine rich IgG1 hinge region of the heavy chain has generally been held to consist of three parts: an upper hinge, a core hinge, and a lower hinge. Those skilled in the art will appreciate that the IgG1 hinge region contain the cysteines in the heavy chain that comprise the inter-chain disulfide bonds (two heavy/heavy, two heavy/light), which provide structural flexibility that facilitates Fab movements. The inter-chain disulfide bond between the light and heavy chain of IgG1 are formed between C214 of the kappa or lambda light chain and C220 in the upper hinge region of the heavy chain. The inter-chain disulfide bonds between the heavy chains are at positions C226 and C229 (all numbered per the EU index according to Kabat, *et al.*, *infra.*)

[0070] As used herein the term “antibody” includes polyclonal antibodies, multiclonal antibodies, monoclonal antibodies, chimeric antibodies, humanized and primatized antibodies,

CDR grafted antibodies, human antibodies, recombinantly produced antibodies, intrabodies, multispecific antibodies, bispecific antibodies, monovalent antibodies, multivalent antibodies, anti-idiotypic antibodies, synthetic antibodies, including muteins and variants thereof, immunospecific antibody fragments such as Fd, Fab, F(ab')₂, F(ab') fragments, single-chain fragments (*e.g.*, ScFv and ScFvFc), disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (VH, VL, or VHH domains (such as a heavy chain only antibody devoid of a light chain)); and derivatives thereof including Fc fusions and other modifications, and any other immunoreactive molecule so long as it comprises a domain having a binding site for preferential association or binding with a BCMA protein. Moreover, unless dictated otherwise by contextual constraints the term further comprises all classes of antibodies (*i.e.* IgA, IgD, IgE, IgG, and IgM) and all subclasses (*i.e.*, IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2). Heavy-chain constant domains that correspond to the different classes of antibodies are typically denoted by the corresponding lower case Greek letter alpha, delta, epsilon, gamma, and mu, respectively. Light chains of the antibodies from any vertebrate species can be assigned to one of two clearly distinct types, called kappa (kappa) and lambda (lambda), based on the amino acid sequences of their constant domains.

[0071] The term “Framework” or “FR” residues (or regions) refer to variable domain residues other than the CDR or hypervariable region residues as herein defined. A “human consensus framework” is a framework which represents the most commonly occurring amino acid residue in a selection of human immunoglobulin VL or VH framework sequences.

[0072] As used herein, “Variable region” or “variable domain” refers to the fact that certain portions of the variable domains differ extensively in sequence among antibodies and are used in the binding and specificity of each particular antibody for its particular antigen. However, the variability is not evenly distributed throughout the variable domains of antibodies. It is concentrated in three segments called complementarity-determining regions (CDRs) or hypervariable regions both in the light-chain and the heavy-chain variable domains. The more highly conserved portions of variable domains are called the framework (FR). The variable domains of native heavy and light chains each comprise four FR regions, largely adopting a β -sheet configuration, connected by three CDRs, which form loops connecting, and in some cases forming part of, the β sheet structure. The CDRs in each chain are held together in close proximity by the FR regions and, with the CDRs from the other chain, contribute to the formation of the antigen-binding site of antibodies (*see*, Kabat *et al.*, Sequences of Proteins of Immunological Interest, Fifth Edition, National Institute of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody-dependent cellular toxicity.

“Variable domain residue numbering as in Kabat” or “amino acid position numbering as in Kabat,” and variations thereof, refers to the numbering system used for heavy chain variable domains or light chain variable domains of the compilation of antibodies in Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th *Ed.* Public Health Service, National Institutes of Health, Bethesda, Md. (1991). Using this numbering system, the actual linear amino acid sequence may contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or CDR of the variable domain. For example, a heavy chain variable domain may include a single amino acid insert (residue 52a according to Kabat) after residue 52 of H2 and inserted residues (*e.g.*, residues 82a, 82b, and 82c, etc according to Kabat) after heavy chain FR residue 82. The Kabat numbering of residues may be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a “standard” Kabat numbered sequence. It is not intended that CDRs of the present disclosure necessarily correspond to the Kabat numbering convention.

[0073] In some embodiments, the BCMA binding proteins comprise a heavy chain only antibody, such as a VH or a VHH domain. In some cases, the BCMA binding proteins comprise a heavy chain only antibody that is an engineered human VH domain. In some examples, the engineered human VH domain is produced by panning of phage display libraries. In some embodiments, the BCMA binding proteins comprise a VHH. The term “VHH,” as used herein, refers to single chain antibody binding domain devoid of light chain. In some cases, a VHH is derived from an antibody of the type that can be found in Camelidae or cartilaginous fish which are naturally devoid of light chains or to a synthetic and non-immunized VHH which can be constructed accordingly. Each heavy chain comprises a variable region encoded by V-, D- and J exons. A VHH, in some cases, is a natural VHH, such as a Camelid-derived VHH, or a recombinant protein comprising a heavy chain variable domain. In some embodiments, the VHH is derived from a species selected from the group consisting of camels, llamas, vicuñas, guanacos, and cartilaginous fish (such as, but not limited to, sharks). In another embodiment, the VHH is derived from an alpaca (such as, but not limited to, a Huacaya Alpaca or a Suri alpaca).

[0074] As used herein, the term “Percent (%) amino acid sequence identity” with respect to a sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software programs such as EMBOSS MATCHER, EMBOSS WATER, EMBOSS STRETCHER, EMBOSS NEEDLE, EMBOSS LALIGN, BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate

parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared.

[0075] As used herein, “elimination half-time” is used in its ordinary sense, as is described in *Goodman and Gillman's The Pharmaceutical Basis of Therapeutics* 21-25 (Alfred Goodman Gilman, Louis S. Goodman, and Alfred Gilman, eds., 6th ed. 1980). Briefly, the term is meant to encompass a quantitative measure of the time course of drug elimination. The elimination of most drugs is exponential (*i.e.*, follows first-order kinetics), since drug concentrations usually do not approach those required for saturation of the elimination process. The rate of an exponential process may be expressed by its rate constant, k , which expresses the fractional change per unit of time, or by its half-time, $t_{1/2}$ the time required for 50% completion of the process. The units of these two constants are time^{-1} and time, respectively. A first-order rate constant and the half-time of the reaction are simply related ($k \times t_{1/2} = 0.693$) and may be interchanged accordingly. Since first-order elimination kinetics dictates that a constant fraction of drug is lost per unit time, a plot of the log of drug concentration versus time is linear at all times following the initial distribution phase (*i.e.* after drug absorption and distribution are complete). The half-time for drug elimination can be accurately determined from such a graph.

[0076] As used herein, the term “binding affinity” refers to the affinity of the proteins described in the disclosure to their binding targets, and is expressed numerically using “Kd” values. If two or more proteins are indicated to have comparable binding affinities towards their binding targets, then the Kd values for binding of the respective proteins towards their binding targets, are within ± 2 -fold of each other. If two or more proteins are indicated to have comparable binding affinities towards single binding target, then the Kd values for binding of the respective proteins towards said single binding target, are within ± 2 -fold of each other. If a protein is indicated to bind two or more targets with comparable binding affinities, then the Kd values for binding of said protein to the two or more targets are within ± 2 -fold of each other. In general, a higher Kd value corresponds to a weaker binding. In some embodiments, the “Kd” is measured by a radiolabeled antigen binding assay (RIA) or surface plasmon resonance assays using a BIACORE®-2000 or a BIACORE®-3000 (BIAcore, Inc., Piscataway, N.J.). In certain embodiments, an “on-rate” or “rate of association” or “association rate” or “kon” and an “off-rate” or “rate of dissociation” or “dissociation rate” or “koff” are also determined with the surface plasmon resonance technique using a BIACORE®-2000 or a BIACORE®-3000 (BIAcore, Inc., Piscataway, N.J.). In additional embodiments, the “Kd”, “kon”, and “koff” are measured using the OCTET® Systems (Pall Life Sciences). In an exemplary method for measuring binding affinity using the OCTET® Systems, the ligand, *e.g.*, biotinylated human BCMA, is immobilized on the OCTET® streptavidin capillary sensor tip surface which streptavidin tips are then activated according to manufacturer's instructions using about 20-50 $\mu\text{g/ml}$ human BCMA protein. A

solution of PBS/Casein is also introduced as a blocking agent. For association kinetic measurements, BCMA binding protein variants are introduced at a concentration ranging from about 10 ng/mL to about 100 µg/mL, about 50 ng/mL to about 5 µg/mL, or about 2 ng/mL to about 20 µg/mL. In some embodiments, the BCMA binding single domain proteins are used at a concentration ranging from about 2 ng/mL to about 20 µg/mL. Complete dissociation is observed in case of the negative control, assay buffer without the binding proteins. The kinetic parameters of the binding reactions are then determined using an appropriate tool, *e.g.*, ForteBio software.

[0077] Described herein are BCMA binding proteins, pharmaceutical compositions as well as nucleic acids, recombinant expression vectors, and host cells for making such BCMA binding proteins. Also provided are methods of using the disclosed BCMA binding proteins in the prevention, and/or treatment of diseases, conditions and disorders. The BCMA binding proteins are capable of specifically binding to BCMA. In some embodiments, the BCMA binding proteins include additional domains, such as a CD3 binding domain and an albumin binding domain.

B cell maturation antigen (BCMA)

[0078] B cell maturation antigen (BCMA, TNFRSF17, CD269) is a transmembrane protein belonging to the tumor necrosis family receptor (TNFR) super family that is primarily expressed on terminally differentiated B cells. BCMA expression is restricted to the B cell lineage and mainly present on plasma cells and plasmablasts and to some extent on memory B cells, but virtually absent on peripheral and naive B cells. BCMA is also expressed on multiple myeloma (MM) cells, on leukemia cells and lymphoma cells.

[0079] BCMA was identified through molecular analysis of a t(4;16)(q26;p13) translocation found in a human intestinal T cell lymphoma and an in-frame sequence was mapped to the 16p13.1 chromosome band.

[0080] Human BCMA cDNA has an open reading frame of 552 bp that encodes a 184 amino acid polypeptide. The BCMA gene is organized into three exons that are separated by two introns, each flanked by GT donor and AG acceptor consensus splicing sites, and codes for a transcript of 1.2 kb. The structure of BCMA protein includes an integral transmembrane protein based on a central 24 amino acid hydrophobic region in an alpha-helix structure.

[0081] The murine BCMA gene is located on chromosome 16 syntenic to the human 16p13 region, and also includes three exons that are separated by two introns. The gene encodes a 185 amino acid protein. Murine BCMA mRNA is expressed as a 404 bp transcript at the highest levels in plasmacytoma cells (J558) and at modest levels in the A20 B cell lymphoma line. Murine BCMA mRNA transcripts have also been detected at low levels in T cell lymphoma

(EL4, BW5147) and dendritic cell (CB1D6, D2SC1) lines in contrast to human cell lines of T cell and dendritic cell origin. The murine BCMA cDNA sequence has 69.3% nucleotide identity with the human BCMA cDNA sequence and slightly higher identity (73.7%) when comparing the coding regions between these two cDNA sequences. Mouse BCMA protein is 62% identical to human BCMA protein and, like human BCMA, contains a single hydrophobic region, which may be an internal transmembrane segment. The N-terminal 40 amino acid domain of both murine and human BCMA protein have six conserved cysteine residues, consistent with the formation of a cysteine repeat motif found in the extracellular domain of TNFRs. Similar to members of the TNFR superfamily, BCMA protein contains a conserved aromatic residue four to six residues C-terminal from the first cysteine.

[0082] BCMA is not expressed at the cell surface, but rather, is located on the Golgi apparatus. The amount of BCMA expression is proportional to the stage of cellular differentiation (highest in plasma cells).

[0083] BCMA is involved in B cell development and homeostasis due to its interaction with its ligands BAFF (B cell activating factor, also designated as TALL-1 or TNFSF13B) and APRIL (A proliferation inducing ligand).

[0084] BCMA regulates different aspects of humoral immunity, B cell development and homeostasis along with its family members TACI (transmembrane activator and cyclophilin ligand interactor) and BAFF-R (B cell activation factor receptor, also known as tumor necrosis factor receptor superfamily member 13C). Expression of BCMA appears rather late in B cell differentiation and contributes to the long term survival of plasmablasts and plasma cells in the bone marrow. BCMA also supports growth and survival of multiple myeloma (MM) cells.

[0085] BCMA is mostly known for its functional activity in mediating the survival of plasma cells that maintain long-term humoral immunity.

[0086] There is a need for having treatment options for solid tumor diseases related to the overexpression of BCMA, such as cancer multiple myeloma, leukemias and lymphomas. The present disclosure provides, in certain embodiments, single domain proteins which specifically bind to BCMA on the surface of tumor target cells.

BCMA binding proteins

[0087] Contemplated herein are BCMA binding proteins. Provided herein in certain embodiments are binding proteins, such as anti-BCMA single domain antibodies or antibody variants, which bind to an epitope in the BCMA protein. In some embodiments, the BCMA binding protein binds to a human BCMA protein comprising the sequence of SEQ ID NO: 468. In some embodiments, the BCMA binding protein binds to a human BCMA protein comprising

a truncated sequence compared to SEQ ID NO: 468. In one non-limiting example, the BCMA binding protein binds to a human BCMA protein comprising amino acid residues 5-51 of SEQ ID NO: 468.

[0088] In some embodiments, the BCMA binding proteins of the present disclosure can be expressed within a multidomain protein that includes additional immunoglobulin domains. Such multidomain proteins can act via immunotoxin-based inhibition of tumor growth and induction of antibody-dependent cellular cytotoxicity (ADCC). In some embodiments, the multidomain proteins containing the BCMA binding proteins of the present disclosure exhibit complement-dependent cytotoxicity (CDC) activity. In some embodiments, the multidomain proteins containing the BCMA binding proteins of the present disclosure exhibit both ADCC and CDC activity, against cancer cells expressing BCMA. An amino acid sequence of a Fc domain can be added on to the BCMA binding proteins described herein to induce ADCC or CDC. Amino acid sequences of Fc domains are known in the art and are contemplated herein.

[0089] A BCMA binding protein described herein binds to the extracellular domain of BCMA. In one instance, a BCMA binding protein described herein binds to amino acid residues 5-51 of human BCMA.

[0090] In some embodiments, the BCMA binding protein is an anti-BCMA antibody or an antibody variant. As used herein, the term "antibody variant" refers to variants and derivatives of an antibody described herein. In certain embodiments, amino acid sequence variants of the anti-BCMA antibodies described herein are contemplated. For example, in certain embodiments amino acid sequence variants of anti-BCMA antibodies described herein are contemplated to improve the binding affinity and/or other biological properties of the antibodies. Exemplary methods for preparing amino acid variants include, but are not limited to, introducing appropriate modifications into the nucleotide sequence encoding the antibody, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of residues within the amino acid sequences of the antibody.

[0091] Any combination of deletion, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics, *e.g.*, antigen-binding. In certain embodiments, antibody variants having one or more amino acid substitutions are provided. Sites of interest for substitution mutagenesis include the CDRs and framework regions. Examples of such substitutions are described below. Amino acid substitutions may be introduced into an antibody of interest and the products screened for a desired activity, *e.g.*, retained/improved antigen binding, decreased immunogenicity, or improved antibody-dependent cell mediated cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC). Both

conservative and non-conservative amino acid substitutions are contemplated for preparing the antibody variants.

[0092] In another example of a substitution to create a variant anti-BCMA antibody, one or more hypervariable region residues of a parent antibody are substituted. In general, variants are then selected based on improvements in desired properties compared to a parent antibody, for example, increased affinity, reduced affinity, reduced immunogenicity, increased pH dependence of binding. For example, an affinity matured variant antibody can be generated, *e.g.*, using phage display-based affinity maturation techniques such as those described herein and known in the field.

[0093] In some embodiments, the BCMA binding protein described herein is a single domain antibody such as a heavy chain variable domain (VH), a variable domain (VHH) of llama derived sdAb, peptide, ligand or a small molecule entity specific for BCMA. In some embodiments, the BCMA binding domain of the BCMA binding protein described herein is any domain that binds to BCMA including, but not limited to, domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody. In certain embodiments, the BCMA binding protein is a single-domain antibody. In other embodiments, the BCMA binding protein is a peptide. In further embodiments, the BCMA binding protein is a small molecule.

[0094] Generally, it should be noted that the term single domain antibody as used herein in its broadest sense is not limited to a specific biological source or to a specific method of preparation. Single domain antibodies are antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, goat, rabbit, and bovine. For example, in some embodiments, the single domain antibodies of the disclosure are obtained: (1) by isolating the VHH domain of a naturally occurring heavy chain antibody; (2) by expression of a nucleotide sequence encoding a naturally occurring VHH domain; (3) by "humanization" of a naturally occurring VHH domain or by expression of a nucleic acid encoding a such humanized VHH domain; (4) by "camelization" of a naturally occurring VH domain from any animal species, and in particular from a species of mammal, such as from a human being, or by expression of a nucleic acid encoding such a camelized VH domain; (5) by "camelisation" of a "domain

antibody" or "Dab", or by expression of a nucleic acid encoding such a camelized VH domain; (6) by using synthetic or semi-synthetic techniques for preparing proteins, polypeptides or other amino acid sequences; (7) by preparing a nucleic acid encoding a single domain antibody using techniques for nucleic acid synthesis known in the field, followed by expression of the nucleic acid thus obtained; and/or (8) by any combination of one or more of the foregoing.

[0095] In one embodiment, a single domain antibody corresponds to the VHH domains of naturally occurring heavy chain antibodies directed against BCMA. As further described herein, such VHH sequences can generally be generated or obtained by suitably immunizing a species of Llama with BCMA, (*i.e.*, so as to raise an immune response and/or heavy chain antibodies directed against BCMA), by obtaining a suitable biological sample from said Llama (such as a blood sample, serum sample or sample of B-cells), and by generating VHH sequences directed against BCMA, starting from said sample, using any suitable technique known in the field.

[0096] In another embodiment, such naturally occurring VHH domains against BCMA, are obtained from naïve libraries of Camelid VHH sequences, for example by screening such a library using BCMA, or at least one part, fragment, antigenic determinant or epitope thereof using one or more screening techniques known in the field. Such libraries and techniques are, for example, described in WO 99/37681, WO 01/90190, WO 03/025020 and WO 03/035694. Alternatively, improved synthetic or semi-synthetic libraries derived from naïve VHH libraries are used, such as VHH libraries obtained from naïve VHH libraries by techniques such as random mutagenesis and/or CDR shuffling, as for example, described in WO 00/43507.

[0097] In a further embodiment, yet another technique for obtaining VHH sequences directed against BCMA, involves suitably immunizing a transgenic mammal that is capable of expressing heavy chain antibodies (*i.e.*, so as to raise an immune response and/or heavy chain antibodies directed against BCMA), obtaining a suitable biological sample from said transgenic mammal (such as a blood sample, serum sample or sample of B-cells), and then generating VHH sequences directed against BCMA, starting from said sample, using any suitable technique known in the field. For example, for this purpose, the heavy chain antibody-expressing rats or mice and the further methods and techniques described in WO 02/085945 and in WO 04/049794 can be used.

[0098] In some embodiments, an anti-BCMA antibody, as described herein comprises single domain antibody with an amino acid sequence that corresponds to the amino acid sequence of a naturally occurring VHH domain, but that has been "humanized", *i.e.*, by replacing one or more amino acid residues in the amino acid sequence of said naturally occurring VHH sequence (and in particular in the framework sequences) by one or more of the amino acid residues that occur

at the corresponding position(s) in a VH domain from a conventional 4-chain antibody from a human being (*e.g.*, as indicated above). This can be performed in a manner known in the field, which will be clear to the skilled person, for example on the basis of the further description herein. Again, it should be noted that such humanized anti-BCMA single domain antibodies of the disclosure are obtained in any suitable manner known per se (*i.e.*, as indicated under points (1)-(8) above) and thus are not strictly limited to polypeptides that have been obtained using a polypeptide that comprises a naturally occurring VHH domain as a starting material. In some additional embodiments, a single domain BCMA antibody, as described herein, comprises a single domain antibody with an amino acid sequence that corresponds to the amino acid sequence of a naturally occurring VH domain, but that has been "camelized", *i.e.*, by replacing one or more amino acid residues in the amino acid sequence of a naturally occurring VH domain from a conventional 4-chain antibody by one or more of the amino acid residues that occur at the corresponding position(s) in a VHH domain of a heavy chain antibody. Such "camelizing" substitutions are preferably inserted at amino acid positions that form and/or are present at the VH-VL interface, and/or at the so-called Camelidae hallmark residues (see for example WO 94/04678 and Davies and Riechmann (1994 and 1996)). Preferably, the VH sequence that is used as a starting material or starting point for generating or designing the camelized single domain is preferably a VH sequence from a mammal, more preferably the VH sequence of a human being, such as a VH3 sequence. However, it should be noted that such camelized anti-BCMA single domain antibodies of the disclosure, in certain embodiments, are obtained in any suitable manner known in the field (*i.e.*, as indicated under points (1)-(8) above) and thus are not strictly limited to polypeptides that have been obtained using a polypeptide that comprises a naturally occurring VH domain as a starting material. For example, as further described herein, both "humanization" and "camelization" are performed by providing a nucleotide sequence that encodes a naturally occurring VHH domain or VH domain, respectively, and then changing, one or more codons in said nucleotide sequence in such a way that the new nucleotide sequence encodes a "humanized" or "camelized" single domain antibody, respectively. This nucleic acid can then be expressed, so as to provide the desired anti-BCMA single domain antibody of the disclosure. Alternatively, in other embodiments, based on the amino acid sequence of a naturally occurring VHH domain or VH domain, respectively, the amino acid sequence of the desired humanized or camelized anti-BCMA single domain antibody of the disclosure, respectively, are designed and then synthesized *de novo* using known techniques for peptide synthesis. In some embodiments, based on the amino acid sequence or nucleotide sequence of a naturally occurring VHH domain or VH domain, respectively, a nucleotide sequence encoding

the desired humanized or camelized anti-BCMA single domain antibody of the disclosure, respectively, is designed and then synthesized de novo using known techniques for nucleic acid synthesis, after which the nucleic acid thus obtained is expressed in using known expression techniques, so as to provide the desired anti-BCMA single domain antibody of the disclosure.

[0099] Other suitable methods and techniques for obtaining the anti-BCMA single domain antibody of the disclosure and/or nucleic acids encoding the same, starting from naturally occurring VH sequences or VHH sequences for example comprises combining one or more parts of one or more naturally occurring VH sequences (such as one or more framework (FR) sequences and/or complementarity determining region (CDR) sequences), one or more parts of one or more naturally occurring VHH sequences (such as one or more FR sequences or CDR sequences), and/or one or more synthetic or semi-synthetic sequences, in a suitable manner, so as to provide an anti-BCMA single domain antibody of the disclosure or a nucleotide sequence or nucleic acid encoding the same.

[00100] It is contemplated that in some embodiments the BCMA binding protein is fairly small and no more than 25 kD, no more than 20 kD, no more than 15 kD, or no more than 10 kD in some embodiments. In certain instances, the BCMA binding protein is 5 kD or less if it is a peptide or small molecule entity.

[00101] In some embodiments, the BCMA binding protein is an anti-BCMA specific antibody comprising a heavy chain variable complementarity determining region CDR1, a heavy chain variable CDR2, a heavy chain variable CDR3, a light chain variable CDR1, a light chain variable CDR2, and a light chain variable CDR3. In some embodiments, the BCMA binding protein comprises any domain that binds to BCMA including but not limited to domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, or antigen binding fragments such as single domain antibodies (sdAb), Fab, Fab', F(ab)2, and Fv fragments, fragments comprised of one or more CDRs, single-chain antibodies (*e.g.*, single chain Fv fragments (scFv)), disulfide stabilized (dsFv) Fv fragments, heteroconjugate antibodies (*e.g.*, bispecific antibodies), pFv fragments, heavy chain monomers or dimers, light chain monomers or dimers, and dimers consisting of one heavy chain and one light chain. In some embodiments, the BCMA binding protein is a single domain antibody. In some embodiments, the anti-BCMA single domain antibody comprises heavy chain variable complementarity determining regions (CDR), CDR1, CDR2, and CDR3.

[00102] In some embodiments, the BCMA binding protein of the present disclosure is a polypeptide comprising an amino acid sequence that is comprised of four framework regions/sequences (f1-f4) interrupted by three complementarity determining regions/sequences,

as represented by the formula: f1-r1-f2-r2-f3-r3-f4, wherein r1, r2, and r3 are complementarity determining regions CDR1, CDR2, and CDR3, respectively, and f1, f2, f3, and f4 are framework residues. The r1 residues of the BCMA binding protein of the present disclosure comprise, for example, amino acid residues 26, 27, 28, 29, 30, 31, 32, 33 and 34; the r2 residues of the BCMA binding protein of the present disclosure comprise, for example, amino acid residues, for example, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62 and 63; and the r3 residues of the BCMA binding protein of the present disclosure comprise, for example, amino acid residues, for example, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107 and 108. In some embodiments, the BCMA binding protein comprises an amino acid sequence selected from SEQ ID NOs: 346-460.

[00103] In one embodiment, the CDR1 does not comprise an amino acid sequence of SEQ ID NO: 473. In one embodiment, the CDR2 does not comprise an amino acid sequence of SEQ ID NO: 474. In one embodiment, the CDR3 does not comprise an amino acid sequence of SEQ ID NO: 475.

[00104] In some embodiments, the CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 1 or a variant thereof having one, two, three, four, five, six, seven, eight, nine, or ten amino acid substitutions. An exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 4. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 5. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 6. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 7. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 8. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 9. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 10. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 11. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 12. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 13. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 14. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 15. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 16. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 17. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 18. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 19. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 20. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 21. Another exemplary CDR1 comprises the amino acid sequence as set

[illegible]

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forth in SEQ ID NO: 90. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 91. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 92. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 93. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 94. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 95. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 96. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 97. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 98. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 99. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 100. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 101. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 102. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 103. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 104. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 105. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 106. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 107. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 108. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 109. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 110. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 111. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 112. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 113. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 114. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 115. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 116. Another exemplary CDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 117.

[00105] In some embodiments, the CDR2 comprises a sequence as set forth in SEQ ID NO: 2 or a variant having one, two, three, four, five, six, seven, eight, nine, or ten amino acid substitutions in SEQ ID NO: 2. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 118. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 119. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 120. Another exemplary CDR2 comprises the amino acid sequence as

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set forth in SEQ ID NO: 223. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 224. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 225. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 226. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 227. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 228. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 229. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 230. Another exemplary CDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 231.

[00106] In some embodiments, the CDR3 comprises a sequence as set forth in SEQ ID NO: 3 or a variant having one, two, three, four, five, six, seven, eight, nine, or ten amino acid substitutions in SEQ ID NO: 3. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 232. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 233. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 234. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 235. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 236. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 237. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 238. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 239. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 240. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 241. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 242. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 243. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 244. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 245. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 246. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 247. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 248. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 249. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 250. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 251. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 252. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 253. Another exemplary CDR3 comprises the amino acid sequence

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as set forth in SEQ ID NO: 322. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 323. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 324. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 325. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 326. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 327. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 328. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 329. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 330. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 331. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 332. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 333. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 334. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 335. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 336. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 337. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 338. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 339. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 340. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 341. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 342. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 343. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 344. Another exemplary CDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 345.

[00107] In various embodiments, the BCMA binding protein of the present disclosure has a CDR1 that has an amino acid sequence that is at least about 75%, about 76%, about 77%, about 78%, about 79%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to an amino acid sequence selected from SEQ ID NOs: 4-117.

[00108] In various embodiments, the BCMA binding protein of the present disclosure has a CDR2 that has an amino acid sequence that is at least about 75%, about 76%, about 77%, about 78%, about 79%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%,

about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to an amino acid sequence selected from SEQ ID NOs: 118-231.

[00109] In various embodiments, a complementarity determining region of the BCMA binding protein of the present disclosure has a CDR3 that has an amino acid sequence that is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to an amino acid sequence selected from SEQ ID NOs: 232-345.

[00110] In various embodiments, a BCMA binding protein of the present disclosure has an amino acid sequence that is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to an amino acid sequence selected from SEQ ID NOs: 346-460.

[00111] In various embodiments, a BCMA binding protein of the present disclosure has a framework 1 (f1) that has an amino acid sequence that is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in SEQ ID NO: 461 or SEQ ID NO: 462.

[00112] In various embodiments, a BCMA binding protein of the present disclosure has a framework 2 (f2) that has an amino acid sequence that is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in SEQ ID NO: 463.

[00113] In various embodiments, a BCMA binding protein of the present disclosure has a framework 3 (f3) that has an amino acid sequence that is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about

99%, or about 100% identical to the amino acid sequence set forth in SEQ ID NO: 464 or SEQ ID NO: 465.

[00114] In various embodiments, a BCMA binding protein of the present disclosure has a framework 4 (f4) that has an amino acid sequence that is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in SEQ ID NO: 466 or SEQ ID NO: 467.

[00115] In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 346. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 347. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 348. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 349. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 350. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 351. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 352. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 353. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 354. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 355. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 356. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 357. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 358. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 359.

[00116] In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 360. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 361. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 362. In some embodiments, the BCMA binding protein is a single domain

387. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 388. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 389.

[00119] In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 390. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 391. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 392. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 393. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 394. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 395. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 396. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 397. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 398. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 399.

[00120] In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 400. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 401. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 402. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 403. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 404. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 405. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 406. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 407. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 408. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 409.

[00121] In some embodiments, the BCMA binding protein is a humanized single domain antibody comprising the sequence of SEQ ID NO: 410. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO:

411. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 412. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 413. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 414. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 415. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 416. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 417. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 418. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 419.

[00122] In some embodiments, the BCMA binding protein is a humanized single domain antibody comprising the sequence of SEQ ID NO: 420. In some embodiments, the BCMA binding protein is a humanized single domain antibody comprising the sequence of SEQ ID NO: 421. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 422. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 423. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 424. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 425. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 426. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 427. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 428. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 429.

[00123] In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 430. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 431. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 432. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 433. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 434. In some embodiments, the BCMA binding protein is a single domain antibody comprising the

the sequence of SEQ ID NO: 459. In some embodiments, the BCMA binding protein is a single domain antibody comprising the sequence of SEQ ID NO: 460.

[00126] A BCMA binding protein described herein can bind to human BCMA with a Kd ranges from about 0.1 nM to about 500 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 450 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 400 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 350 nM. In some embodiments, the hKd and ranges from about 0.1 nM to about 300 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 250 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 200 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 150 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 100 nM. In some embodiments, the hKd ranges from about 0.1 nM to about 90 nM. In some embodiments, the hKd range from about 0.2 nM to about 80 nM. In some embodiments, the hKd ranges from about 0.3 nM to about 70 nM. In some embodiments, the hKd ranges from about 0.4 nM to about 50 nM. In some embodiments, the hKd ranges from about 0.5 nM to about 30 nM. In some embodiments, the hKd ranges from about 0.6 nM to about 10 nM. In some embodiments, the hKd ranges from about 0.7 nM to about 8 nM. In some embodiments, the hKd ranges from about 0.8 nM to about 6 nM. In some embodiments, the hKd ranges from about 0.9 nM to about 4 nM. In some embodiments, the hKd ranges from about 1 nM to about 2 nM.

[00127] In some embodiments, any of the foregoing BCMA binding proteins are affinity peptide tagged for ease of purification. In some embodiments, the affinity peptide tag is six consecutive histidine residues, also referred to as a His tag or a 6X-His tag (*e.g.*, SEQ ID NO: 471).

[00128] In certain embodiments, the BCMA binding proteins according to the present disclosure may be incorporated into BCMA targeting trispecific proteins. In some examples, the trispecific binding protein comprises a CD3 binding domain, a human serum albumin (HSA) binding domain and an anti-BCMA binding domain according to the present disclosure. In some instances, the trispecific binding protein comprises the domains described above in the following orientation: BCMA-HSA-CD3.

[00129] In certain embodiments, the BCMA binding proteins of the present disclosure preferentially bind membrane bound BCMA over soluble BCMA. Membrane bound BCMA refers to the presence of BCMA in or on the cell membrane surface of a cell that expresses BCMA. Soluble BCMA refers to BCMA that is no longer on in or on the cell membrane surface of a cell that expresses or expressed BCMA. In certain instances, the soluble BCMA is present

in the blood and/or lymphatic circulation in a subject. In one embodiment, the BCMA binding proteins bind membrane-bound BCMA at least 5 fold, 10 fold, 15 fold, 20 fold, 25 fold, 30 fold, 40 fold, 50 fold, 100 fold, 500 fold, or 1000 fold greater than soluble BCMA. In one embodiment, the antigen binding proteins of the present disclosure preferentially bind membrane-bound BCMA 30 fold greater than soluble BCMA. Determining the preferential binding of an antigen binding protein to membrane bound BCMA over soluble BCMA can be readily determined using assays well known in the art.

Integration into chimeric antigen receptors (CAR)

[00130] The BCMA binding proteins of the present disclosure, *e.g.*, an anti-BCMA single domain antibody, can, in certain examples, be incorporated into a chimeric antigen receptor (CAR). An engineered immune effector cell, *e.g.*, a T cell or NK cell, can be used to express a CAR that includes an anti-BCMA single domain antibody as described herein. In one embodiment, the CAR including an anti-BCMA single domain antibody as described herein is connected to a transmembrane domain via a hinge region, and further a costimulatory domain, *e.g.*, a functional signaling domain obtained from OX40, CD27, CD28, CD5, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), or 4-1BB. In some embodiments, the CAR further comprises a sequence encoding an intracellular signaling domain, such as 4-1BB and/or CD3 zeta.

Multispecific protein targeting BCMA

[00131] One embodiment provides a multispecific protein comprising a BCMA binding domain, wherein the BCMA binding domain is according to any one of above embodiments. In some embodiments, the multispecific protein comprises the BCMA binding domain according to any one of above embodiments (anti-BCMA domain), a CD3 binding domain (anti-CD3 domain), and an albumin binding domain (anti-ALB domain). In some embodiments, the BCMA targeting multispecific protein is a trispecific protein, wherein the trispecific protein has a domain order of H₂N-(C)-(A)-(B)-COOH. In some embodiments, the anti-BCMA domain (the anti-target domain, T), the anti-CD3 domain (C), and the anti-ALB domain (A) are in an anti-CD3: anti-ALB: anti-BCMA (CAT) orientation. In some embodiments, the anti-BCMA domain (the anti-target domain, T) the anti-CD3 domain (C), and the anti-ALB domain (A) are in an anti-BCMA: anti-ALB: anti-CD3 (TAC) orientation.

Tumor growth reduction properties

[00132] In certain embodiments, the BCMA binding proteins of the disclosure reduces the growth of tumor cells *in vivo* when administered to a subject who has tumor cells that express BCMA. Measurement of the reduction of the growth of tumor cells can be determined by multiple different methodologies well known in the art. Non-limiting examples include direct

measurement of tumor dimension, measurement of excised tumor mass and comparison to control subjects, measurement via imaging techniques (*e.g.*, CT or MRI) that may or may not use isotopes or luminescent molecules (*e.g.*, luciferase) for enhanced analysis, and the like. In specific embodiments, administration of the antigen binding agents of the disclosure results in a reduction of *in vivo* growth of tumor cells as compared to a control antigen binding agent by at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100%, with an about 100% reduction in tumor growth indicating a complete response and disappearance of the tumor. In further embodiments, administration of the antigen binding agents of the disclosure results in a reduction of *in vivo* growth of tumor cells as compared to a control antigen binding agent by about 50-100%, about 75-100% or about 90-100%. In further embodiments, administration of the antigen binding agents of the disclosure results in a reduction of *in vivo* growth of tumor cells as compared to a control antigen binding agent by about 50-60%, about 60-70%, about 70-80%, about 80-90%, or about 90-100%.

BCMA binding protein modifications

[00133] The BCMA binding proteins described herein encompass derivatives or analogs in which (i) an amino acid is substituted with an amino acid residue that is not one encoded by the genetic code, (ii) the mature polypeptide is fused with another compound such as polyethylene glycol, or (iii) additional amino acids are fused to the protein, such as a leader or secretory sequence or a sequence to block an immunogenic domain and/or for purification of the protein.

[00134] Typical modifications include, but are not limited to, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent crosslinks, formation of cystine, formation of pyroglutamate, formylation, gamma carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination.

[00135] Modifications are made anywhere in the BCMA binding proteins described herein, including the peptide backbone, the amino acid side-chains, and the amino or carboxyl termini. Certain common peptide modifications that are useful for modification of BCMA binding proteins include glycosylation, lipid attachment, sulfation, gamma-carboxylation of

glutamic acid residues, hydroxylation, blockage of the amino or carboxyl group in a polypeptide, or both, by a covalent modification, and ADP-ribosylation.

Polynucleotides encoding BCMA binding proteins

[00136] Also provided, in some embodiments, are polynucleotide molecules encoding a BCMA binding protein as described herein. In some embodiments, the polynucleotide molecules are provided as DNA constructs. In other embodiments, the polynucleotide molecules are provided as messenger RNA transcripts.

[00137] The polynucleotide molecules are constructed by known methods such as by combining the genes encoding the anti-BCMA binding protein, operably linked to a suitable promoter, and optionally a suitable transcription terminator, and expressing it in bacteria or other appropriate expression system such as, for example CHO cells.

[00138] In some embodiments, the polynucleotide is inserted into a vector, preferably an expression vector, which represents a further embodiment. This recombinant vector can be constructed according to known methods. Vectors of particular interest include plasmids, phagemids, phage derivatives, virii (*e.g.*, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, lentiviruses, and the like), and cosmids.

[00139] A variety of expression vector/host systems may be utilized to contain and express the polynucleotide encoding the polypeptide of the described BCMA binding protein. Examples of expression vectors for expression in *E.coli* are pSKK (Le Gall *et al.*, *J Immunol Methods*. (2004) 285(1):111-27), pcDNA5 (Invitrogen) for expression in mammalian cells, PICHIAPIK™ Yeast Expression Systems (Invitrogen), BACUVANCE™ Baculovirus Expression System (GenScript).

[00140] Thus, the BCMA binding proteins as described herein, in some embodiments, are produced by introducing a vector encoding the protein as described above into a host cell and culturing said host cell under conditions whereby the protein domains are expressed, may be isolated and, optionally, further purified.

Pharmaceutical compositions

[00141] Also provided, in some embodiments, are pharmaceutical compositions comprising a BCMA binding protein described herein, a vector comprising the polynucleotide encoding the polypeptide of the BCMA binding proteins or a host cell transformed by this vector and at least one pharmaceutically acceptable carrier. The term "pharmaceutically acceptable carrier" includes, but is not limited to, any carrier that does not interfere with the effectiveness of the biological activity of the ingredients and that is not toxic to the patient to whom it is administered. Examples of suitable pharmaceutical carriers are well known in the art and

include phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions etc. Such carriers can be formulated by conventional methods and can be administered to the subject at a suitable dose. Preferably, the compositions are sterile. These compositions may also contain adjuvants such as preservative, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents. A further embodiment provides one or more of the above described binding proteins, such as anti-BCMA single domain antibodies or antigen-binding fragments thereof packaged in lyophilized form, or packaged in an aqueous medium.

[00142] In some embodiments of the pharmaceutical compositions, the BCMA binding protein described herein is encapsulated in nanoparticles. In some embodiments, the nanoparticles are fullerenes, liquid crystals, liposome, quantum dots, superparamagnetic nanoparticles, dendrimers, or nanorods. In other embodiments of the pharmaceutical compositions, the BCMA binding protein is attached to liposomes. In some instances, the BCMA binding protein is conjugated to the surface of liposomes. In some instances, the BCMA binding protein is encapsulated within the shell of a liposome. In some instances, the liposome is a cationic liposome.

[00143] The BCMA binding proteins described herein are contemplated for use as a medicament. Administration is effected by different ways, *e.g.*, by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. In some embodiments, the route of administration depends on the kind of therapy and the kind of compound contained in the pharmaceutical composition. The dosage regimen will be determined by the attending physician and other clinical factors. Dosages for any one patient depends on many factors, including the patient's size, body surface area, age, sex, the particular compound to be administered, time and route of administration, the kind of therapy, general health and other drugs being administered concurrently. An "effective dose" refers to amounts of the active ingredient that are sufficient to affect the course and the severity of the disease, leading to the reduction or remission of such pathology and may be determined using known methods.

[00144] In some embodiments, the BCMA binding proteins of this disclosure are administered at a dosage of up to 10 mg/kg at a frequency of once a week. In some cases, the dosage ranges from about 1 ng/kg to about 10 mg/kg. In some embodiments, the dose is from about 1 ng/kg to about 10 ng/kg, about 5 ng/kg to about 15 ng/kg, about 12 ng/kg to about 20 ng/kg, about 18 ng/kg to about 30 ng/kg, about 25 ng/kg to about 50 ng/kg, about 35 ng/kg to about 60 ng/kg, about 45 ng/kg to about 70 ng/kg, about 65 ng/kg to about 85 ng/kg, about 80

ng/kg to about 1 µg/kg, about 0.5 µg/kg to about 5 µg/kg, about 2 µg/kg to about 10 µg/kg, about 7 µg/kg to about 15 µg/kg, about 12 µg/kg to about 25 µg/kg, about 20 µg/kg to about 50 µg/kg, about 35 µg/kg to about 70 µg/kg, about 45 µg/kg to about 80 µg/kg, about 65 µg/kg to about 90 µg/kg, about 85 µg/kg to about 0.1 mg/kg, about 0.095 mg/kg to about 10 mg/kg. In some cases, the dosage is about 0.1 mg/kg to about 0.2 mg/kg; about 0.25 mg/kg to about 0.5 mg/kg, about 0.45 mg/kg to about 1 mg/kg, about 0.75 mg/kg to about 3 mg/kg, about 2.5 mg/kg to about 4 mg/kg, about 3.5 mg/kg to about 5 mg/kg, about 4.5 mg/kg to about 6 mg/kg, about 5.5 mg/kg to about 7 mg/kg, about 6.5 mg/kg to about 8 mg/kg, about 7.5 mg/kg to about 9 mg/kg, or about 8.5 mg/kg to about 10 mg/kg. The frequency of administration, in some embodiments, is about less than daily, every other day, less than once a day, twice a week, weekly, once in 7 days, once in two weeks, once in two weeks, once in three weeks, once in four weeks, or once a month. In some cases, the frequency of administration is weekly. In some cases, the frequency of administration is weekly and the dosage is up to 10 mg/kg. In some cases, duration of administration is from about 1 day to about 4 weeks or longer.

Methods of treatment

[00145] Also provided herein, in some embodiments, are methods and uses for stimulating the immune system of an individual in need thereof comprising administration of a BCMA binding protein as described herein. In some instances, the administration of a BCMA binding protein described herein induces and/or sustains cytotoxicity towards a cell expressing a target antigen. In some instances, the cell expressing a target antigen is a terminally differentiated B cell that is a cancer or tumor cell, or a metastatic cancer or tumor cell.

[00146] Also provided herein are methods and uses for a treatment of a disease, disorder or condition associated with BCMA comprising administering to an individual in need thereof a BCMA binding protein or a multispecific binding protein comprising the BCMA binding protein described herein.

[00147] Diseases, disorders or conditions associated with BCMA include, but are not limited to, a cancer or a metastasis that is of a B cell lineage.

[00148] Cancers that can be treated, prevented, or managed by the BCMA binding proteins of the present disclosure, and methods of using them, include but are not limited to a primary cancer or a metastatic cancer.

[00149] Examples of such leukemias include, but are not limited to, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML), as well as a number of less common types such as, for example, Hairy cell leukemia (HCL), T-cell prolymphocytic leukemia (T-PLL), Large

granular lymphocytic leukemia and Adult T-cell leukemia, *etc.* Acute lymphoblastic leukemia (ALL) subtypes to be treated include, but are not limited to, precursor B acute lymphoblastic leukemia, precursor T acute lymphoblastic leukemia, Burkitt's leukemia, and acute biphenotypic leukemia. Chronic lymphocytic leukemia (CLL) subtypes to be treated include, but are not limited to, B-cell prolymphocytic leukemia. Acute myelogenous leukemia (AML) subtypes to be treated include, but are not limited to, acute promyelocytic leukemia, acute myeloblastic leukemia, and acute megakaryoblastic leukemia. Chronic myelogenous leukemia (CML) subtypes to be treated include, but are not limited to, chronic myelomonocytic leukemia.

[00150] Examples of a lymphoma to be treated with the subject methods include, but not limited to Hodgkin's disease, non-Hodgkin's disease, or any subtype of lymphoma.

[00151] Examples of such multiple myelomas include, but are not limited to, a multiple myeloma of the bone or other tissues including, for example, a smoldering multiple myeloma, a non-secretory myeloma, a osteosclerotic myeloma, *etc.*

[00152] For a review of such disorders, *see* Fishman *et al.*, 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia and Murphy *et al.*, 1997, Informed Decisions: The Complete Book of Cancer Diagnosis, Treatment, and Recovery, Viking Penguin, Penguin Books U.S.A., Inc., United States of America).

[00153] As used herein, in some embodiments, “treatment” or “treating” or “treated” refers to therapeutic treatment wherein the object is to slow (lessen) an undesired physiological condition, disorder or disease, or to obtain beneficial or desired clinical results. For the purposes described herein, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms; diminishment of the extent of the condition, disorder or disease; stabilization (*i.e.*, not worsening) of the state of the condition, disorder or disease; delay in onset or slowing of the progression of the condition, disorder or disease; amelioration of the condition, disorder or disease state; and remission (whether partial or total), whether detectable or undetectable, or enhancement or improvement of the condition, disorder or disease. Treatment includes eliciting a clinically significant response without excessive levels of side effects. Treatment also includes prolonging survival as compared to expected survival if not receiving treatment. In other embodiments, “treatment” or “treating” or “treated” refers to prophylactic measures, wherein the object is to delay onset of or reduce severity of an undesired physiological condition, disorder or disease, such as, for example is a person who is predisposed to a disease (*e.g.*, an individual who carries a genetic marker for a disease such as breast cancer).

[00154] In some embodiments of the methods described herein, the BCMA binding proteins as described herein are administered in combination with an agent for treatment of the

particular disease, disorder or condition. Agents include, but are not limited to, therapies involving antibodies, small molecules (*e.g.*, chemotherapeutics), hormones (steroidal, peptide, and the like), radiotherapies (γ -rays, X-rays, and/or the directed delivery of radioisotopes, microwaves, UV radiation and the like), gene therapies (*e.g.*, antisense, retroviral therapy and the like) and other immunotherapies. In some embodiments, a BCMA binding protein as described herein is administered in combination with anti-diarrheal agents, anti-emetic agents, analgesics, opioids and/or non-steroidal anti-inflammatory agents. In some embodiments, a BCMA binding protein as described herein is administered in combination with anti-cancer agents. Non-limiting examples of anti-cancer agents that can be used in the various embodiments of the disclosure, including pharmaceutical compositions and dosage forms and kits of the disclosure, include: acivicin; aclarubicin; acodazole hydrochloride; acronine; adozelesin; aldesleukin; altretamine; ambomycin; ametantrone acetate; aminoglutethimide; amsacrine; anastrozole; anthramycin; asparaginase; asperlin; azacitidine; azetepa; azotomycin; batimastat; benzodepa; bicalutamide; bisantrene hydrochloride; bisnafide dimesylate; bizelesin; bleomycin sulfate; brequinar sodium; bropiramine; busulfan; cactinomycin; calusterone; caracemide; carbetimer; carboplatin; carmustine; carubicin hydrochloride; carzelesin; cedefingol; chlorambucil; cirolemycin; cisplatin; cladribine; crisnatol mesylate; cyclophosphamide; cytarabine; dacarbazine; dactinomycin; daunorubicin hydrochloride; decitabine; dexormaplatin; dezaguanine; dezaguanine mesylate; diaziquone; docetaxel; doxorubicin; doxorubicin hydrochloride; droloxifene; droloxifene citrate; dromostanolone propionate; duazomycin; edatrexate; eflornithine hydrochloride; elsamitrucin; enloplatin; enpromate; epipropidine; epirubicin hydrochloride; erbulozole; esorubicin hydrochloride; estramustine; estramustine phosphate sodium; etanidazole; etoposide; etoposide phosphate; etoprine; fadrozole hydrochloride; fazarabine; fenretinide; floxuridine; fludarabine phosphate; fluorouracil; flurocitabine; fosquidone; fostriecin sodium; gemcitabine; gemcitabine hydrochloride; hydroxyurea; idarubicin hydrochloride; ifosfamide; ilmofosine; interleukin II (including recombinant interleukin II, or rIL2), interferon alpha-2a; interferon alpha-2b; interferon alpha-n1 interferon alpha-n3; interferon beta-I a; interferon gamma-I b; iproplatin; irinotecan hydrochloride; lanreotide acetate; letrozole; leuprolide acetate; liarozole hydrochloride; lometrexol sodium; lomustine; losoxantrone hydrochloride; masoprocol; maytansine; mechlorethamine hydrochloride; megestrol acetate; melengestrol acetate; melphalan; menogaril; mercaptopurine; methotrexate; methotrexate sodium; metoprine; meturedopa; mitindomide; mitocarcin; mitocromin; mitogillin; mitomalcin; mitomycin; mitosper; mitotane; mitoxantrone hydrochloride; mycophenolic acid; nocodazole; nogalamycin;

ormaplatin; oxisuran; paclitaxel; pegaspargase; peliomycin; pentamustine; peplomycin sulfate; perfosfamide; pipobroman; piposulfan; piroxantrone hydrochloride; plicamycin; plomestane; porfimer sodium; porfiromycin; prednimustine; procarbazine hydrochloride; puromycin; puromycin hydrochloride; pyrazofurin; riboprime; rogletimide; safingol; safingol hydrochloride; semustine; simtrazene; sparfosate sodium; sparsomycin; spirogermanium hydrochloride; spiromustine; spiroplatin; streptonigrin; streptozocin; sulofenur; talisomycin; tecogalan sodium; tegafur; teloxantrone hydrochloride; temoporfin; teniposide; teroxirone; testolactone; thiamiprine; thioguanine; thiotepa; tiazofurin; tirapazamine; toremifene citrate; trestolone acetate; triciribine phosphate; trimetrexate; trimetrexate glucuronate; triptorelin; tubulozole hydrochloride; uracil mustard; uredepa; vapreotide; verteporfin; vinblastine sulfate; vincristine sulfate; vindesine; vindesine sulfate; vinepidine sulfate; vinglycinate sulfate; vinleurosine sulfate; vinorelbine tartrate; vinzolidine sulfate; vinzolidine sulfate; vorozole; zeniplatin; zinostatin; zorubicin hydrochloride. Other examples of anti-cancer drugs include, but are not limited to: 20-epi-1,25 dihydroxyvitamin D3; 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin; ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; angiogenesis inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin glycinate; apoptosis gene modulators; apoptosis regulators; apurinic acid; ara-CDP-DL-PTBA; arginine deaminase; asulacrine; atamestane; atrimustine; axinastatin 1; axinastatin 2; axinastatin 3; azasetron; azatoxin; azatyrosine; baccatin III derivatives; balanol; batimastat; BCR/ABL antagonists; benzochlorins; benzoylstauosporine; beta lactam derivatives; beta-alethine; betaclamycin B; betulinic acid; bFGF inhibitor; bicalutamide; bisantrene; bisaziridinylspermine; bisnafide; bistratene A; bizelesin; breflate; bropirimine; budotitane; buthionine sulfoximine; calcipotriol; calphostin C; camptothecin derivatives; canarypox IL-2; capecitabine; carboxamide-amino-triazole; carboxyamidotriazole; CaRest M3; CARN 700; cartilage derived inhibitor; carzelesin; casein kinase inhibitors (ICOS); castanospermine; cecropin B; cetorelix; chlorins; chloroquinoxaline sulfonamide; cicaprost; cis-porphyrin; cladribine; clomifene analogues; clotrimazole; collismycin A; collismycin B; combretastatin A4; combretastatin analogue; conagenin; crambescidin 816; crisnatol; cryptophycin 8; cryptophycin A derivatives; curacin A; cyclopentantraquinones; cycloplatan; cypemycin; cytarabine ocfosfate; cytolytic factor; cytostatin; dacliximab; decitabine; dehydroadidemnin B; deslorelin; dexamethasone; dexifosfamide; dexrazoxane; dexverapamil; diaziquone; didemnin B; didox; diethylnorspermine;

dihydro-5-azacytidine; dihydrotaxol, 9-; dioxamycin; diphenyl spiromustine; docetaxel; docosanol; dolasetron; doxifluridine; droloxifene; dronabinol; duocarmycin SA; ebselen; ecomustine; edelfosine; edrecolomab; eflornithine; elemene; emitefur; epirubicin; epristeride; estramustine analogue; estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelandine; fluasterone; fludarabine; fluorodaunorubicin hydrochloride; forfenimex; formestane; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; idarubicin; idoxifene; idramantone; ilmofosine; ilomastat; imidazoacridones; imiquimod; immunostimulant peptides; insulin-like growth factor-I receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane; iododoxorubicin; ipomeanol, 4-; iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide+estrogen+progesterone; leuprorelin; levamisole; liarozole; linear polyamine analogue; lipophilic disaccharide peptide; lipophilic platinum compounds; lissoclinamide 7; lobaplatin; lombricine; lometrexol; lonidamine; losoxantrone; HMG-CoA reductase inhibitor (such as but not limited to, Lovastatin, Pravastatin, Fluvastatin, Statin, Simvastatin, and Atorvastatin); loxoribine; lurtotecan; lutetium texaphyrin; lysofylline; lytic peptides; maitansine; mannostatin A; marimastat; masoprocil; maspin; matrilysin inhibitors; matrix metalloproteinase inhibitors; menogaril; merbarone; meterelin; methioninase; metoclopramide; MIF inhibitor; mifepristone; miltefosine; mirimostim; mismatched double stranded RNA; mitoguazone; mitolactol; mitomycin analogues; mitonafide; mitotoxin fibroblast growth factor-saporin; mitoxantrone; mofarotene; molgramostim; monoclonal antibody, human chorionic gonadotrophin; monophosphoryl lipid A+myobacterium cell wall sk; mopidamol; multiple drug resistance gene inhibitor; multiple tumor suppressor 1-based therapy; mustard anticancer agent; mycaperoxide B; mycobacterial cell wall extract; myriaporone; N-acetyldinaline; N-substituted benzamides; nafarelin; nagrestip; naloxone+pentazocine; napavin; naphterpin; nartograstim; nedaplatin; nemorubicin; neridronic acid; neutral endopeptidase; nilutamide; nisamycin; nitric oxide modulators; nitroxide antioxidant; nitrullyn; O6-benzylguanine; octreotide; okicenone; oligonucleotides; onapristone; ondansetron; ondansetron; oracin; oral cytokine inducer; ormaplatin; osaterone; oxaliplatin; oxaunomycin; paclitaxel; paclitaxel analogues; paclitaxel derivatives; palauamine; palmitoylrhizoxin; pamidronic acid; panaxytriol; panomifene; parabactin; pazelliptine; pegaspargase; peldesine; pentosan polysulfate

sodium; pentostatin; pentozole; perflubron; perfosfamide; perillyl alcohol; phenazinomycin; phenylacetate; phosphatase inhibitors; picibanil; pilocarpine hydrochloride; pirarubicin; piritrexim; placetin A; placetin B; plasminogen activator inhibitor; platinum complex; platinum compounds; platinum-triamine complex; porfimer sodium; porfiromycin; prednisone; propyl bis-acridone; prostaglandin J2; proteasome inhibitors; protein A-based immune modulator; protein kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated hemoglobin polyoxyethylene conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate; rhizoxin; ribozymes; RII retinamide; rogletimide; rohitukine; romurtide; roquinimex; rubiginone B1; ruboxyl; safingol; saintopin; SarCNU; sarcophytol A; sargramostim; Sdi 1 mimetics; semustine; senescence derived inhibitor 1; sense oligonucleotides; signal transduction inhibitors; signal transduction modulators; single chain antigen binding protein; sizofiran; sobuzoxane; sodium borocaptate; sodium phenylacetate; solverol; somatomedin binding protein; sonermin; sparfosic acid; spicamycin D; spiromustine; splenopentin; spongistatin 1; squalamine; stem cell inhibitor; stem-cell division inhibitors; stipiamide; stromelysin inhibitors; sulfinosine; superactive vasoactive intestinal peptide antagonist; suradista; suramin; swainsonine; synthetic glycosaminoglycans; tallimustine; tamoxifen methiodide; tauromustine; tazarotene; tecogalan sodium; tegafur; tellurapyrylium; telomerase inhibitors; temoporfin; temozolomide; teniposide; tetrachlorodecaoxide; tetrazomine; thaliblastine; thiocoraline; thrombopoietin; thrombopoietin mimetic; thymalfasin; thymopoietin receptor agonist; thymotrinan; thyroid stimulating hormone; tin ethyl etiopurpurin; tirapazamine; titanocene bichloride; topsentin; toremifene; totipotent stem cell factor; translation inhibitors; tretinoin; triacetyluridine; tricinibine; trimetrexate; triptorelin; tropisetron; turosteride; tyrosine kinase inhibitors; tyrphostins; UBC inhibitors; ubenimex; urogenital sinus-derived growth inhibitory factor; urokinase receptor antagonists; vapreotide; variolin B; vector system, erythrocyte gene therapy; velaresol; veramine; verdins; verteporfin; vinorelbine; vinxaltine; VITAXIN®; vorozole; zanoterone; zeniplatin; zilascorb; and zinostatin stimalamer. Additional anti-cancer drugs are 5-fluorouracil and leucovorin. These two agents are particularly useful when used in methods employing thalidomide and a topoisomerase inhibitor. In some embodiments, the anti-BCMA single domain binding protein of the present disclosure is used in combination with gemcitabine.

[00155] In some embodiments, a BCMA binding proteins as described herein is administered before, during, or after surgery.

[00156] In some embodiments, the anti-cancer agent is conjugated via any suitable means to the trispecific protein.

Methods of detection of BCMA expression and diagnosis of BCMA associated cancer

[00157] According to another embodiment of the disclosure, kits for detecting expression of BCMA *in vitro* or *in vivo* are provided. The kits include the foregoing BCMA binding proteins (*e.g.*, a labeled anti-BCMA single domain antibody or antigen binding fragments thereof), and one or more compounds for detecting the label. In some embodiments, the label is selected from the group consisting of a fluorescent label, an enzyme label, a radioactive label, a nuclear magnetic resonance active label, a luminescent label, and a chromophore label.

[00158] In some cases, BCMA expression is detected in a biological sample. The sample can be any sample, including, but not limited to, tissue from biopsies, autopsies and pathology specimens. Biological samples also include sections of tissues, for example, frozen sections taken for histological purposes. Biological samples further include body fluids, such as blood, serum, plasma, sputum, spinal fluid or urine. A biological sample is typically obtained from a mammal, such as a human or non-human primate.

[00159] In one embodiment, provided is a method of determining if a subject has cancer by contacting a sample from the subject with an anti-BCMA single domain antibody as disclosed herein; and detecting binding of the single domain antibody to the sample. An increase in binding of the antibody to the sample as compared to binding of the antibody to a control sample identifies the subject as having cancer.

[00160] In another embodiment, provided is a method of confirming a diagnosis of cancer in a subject by contacting a sample from a subject diagnosed with cancer with an anti-BCMA single domain antibody as disclosed herein; and detecting binding of the antibody to the sample. An increase in binding of the antibody to the sample as compared to binding of the antibody to a control sample confirms the diagnosis of cancer in the subject.

[00161] In some examples of the disclosed methods, the single domain antibody is directly labeled.

[00162] In some examples, the methods further include contacting a second antibody that specifically binds the single domain antibody with the sample; and detecting the binding of the second antibody. An increase in binding of the second antibody to the sample as compared to binding of the second antibody to a control sample detects cancer in the subject or confirms the diagnosis of cancer in the subject.

[00163] In some cases, the cancer is a lymphoma, a leukemia or a multiple myeloma.

[00164] In some examples, the control sample is a sample from a subject without cancer. In particular examples, the sample is a blood or tissue sample.

[00165] In some cases, the antibody that binds (for example specifically binds) BCMA is directly labeled with a detectable label. In another embodiment, the antibody that binds (for example, specifically binds) BCMA (the first antibody) is unlabeled and a second antibody or other molecule that can bind the antibody that specifically binds BCMA is labeled. A second antibody is chosen such that it is able to specifically bind the specific species and class of the first antibody. For example, if the first antibody is a llama IgG, then the secondary antibody may be an anti-llama-IgG. Other molecules that can bind to antibodies include, without limitation, Protein A and Protein G, both of which are available commercially. Suitable labels for the antibody or secondary antibody are described above, and include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, magnetic agents and radioactive materials. Non-limiting examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase. Non-limiting examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin. Non-limiting examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin. A non-limiting exemplary luminescent material is luminol; a non-limiting exemplary magnetic agent is gadolinium, and non-limiting exemplary radioactive labels include ¹²⁵I, ¹³¹I, ³⁵S or ³H.

[00166] In an alternative embodiment, BCMA can be assayed in a biological sample by a competition immunoassay utilizing BCMA standards labeled with a detectable substance and an unlabeled antibody that specifically binds BCMA. In this assay, the biological sample, the labeled BCMA standards and the antibody that specifically bind BCMA are combined and the amount of labeled BCMA standard bound to the unlabeled antibody is determined. The amount of BCMA in the biological sample is inversely proportional to the amount of labeled BCMA standard bound to the antibody that specifically binds BCMA.

[00167] The immunoassays and method disclosed herein can be used for a number of purposes. In one embodiment, the antibody that specifically binds BCMA may be used to detect the production of BCMA in cells in cell culture. In another embodiment, the antibody can be used to detect the amount of BCMA in a biological sample, such as a tissue sample, or a blood or serum sample. In some examples, the BCMA is cell-surface BCMA. In other examples, the BCMA is soluble BCMA (*e.g.*, BCMA in a cell culture supernatant or soluble BCMA in a body fluid sample, such as a blood or serum sample).

[00168] In one embodiment, a kit is provided for detecting BCMA in a biological sample, such as a blood sample or tissue sample. For example, to confirm a cancer diagnosis in a subject, a biopsy can be performed to obtain a tissue sample for histological examination. Alternatively, a blood sample can be obtained to detect the presence of soluble BCMA protein or fragment. Kits for detecting a polypeptide will typically comprise a single domain antibody, according to the present disclosure, that specifically binds BCMA. In some embodiments, an antibody fragment, such as a scFv fragment, a VH domain, or a Fab is included in the kit. In a further embodiment, the antibody is labeled (for example, with a fluorescent, radioactive, or an enzymatic label).

[00169] In one embodiment, a kit includes instructional materials disclosing means of use of an antibody that binds BCMA. The instructional materials may be written, in an electronic form (such as a computer diskette or compact disk) or may be visual (such as video files), or provided through an electronic network, for example, over the internet, World Wide Web, an intranet, or other network. The kits may also include additional components to facilitate the particular application for which the kit is designed. Thus, for example, the kit may additionally contain means of detecting a label (such as enzyme substrates for enzymatic labels, filter sets to detect fluorescent labels, appropriate secondary labels such as a secondary antibody, or the like). The kits may additionally include buffers and other reagents routinely used for the practice of a particular method. Such kits and appropriate contents are well known to those of skill in the art.

[00170] In one embodiment, the diagnostic kit comprises an immunoassay. Although the details of the immunoassays may vary with the particular format employed, the method of detecting BCMA in a biological sample generally includes the steps of contacting the biological sample with an antibody which specifically reacts, under immunologically reactive conditions, to a BCMA polypeptide. The antibody is allowed to specifically bind under immunologically reactive conditions to form an immune complex, and the presence of the immune complex (bound antibody) is detected directly or indirectly.

[00171] Methods of determining the presence or absence of a cell surface marker are well known in the art. For example, the antibodies can be conjugated to other compounds including, but not limited to, enzymes, magnetic beads, colloidal magnetic beads, haptens, fluorochromes, metal compounds, radioactive compounds or drugs. The antibodies can also be utilized in immunoassays such as but not limited to radioimmunoassays (RIAs), ELISA, or immunohistochemical assays. The antibodies can also be used for fluorescence activated cell sorting (FACS). FACS employs a plurality of color channels, low angle and obtuse light-

scattering detection channels, and impedance channels, among other more sophisticated levels of detection, to separate or sort cells (see U.S. Patent No. 5, 061,620). Any of the single domain antibodies that bind BCMA, as disclosed herein, can be used in these assays. Thus, the antibodies can be used in a conventional immunoassay, including, without limitation, an ELISA, an RIA, FACS, tissue immunohistochemistry, Western blot or immunoprecipitation.

EXAMPLES

[00172] The application may be better understood by reference to the following non-limiting examples, which are provided as exemplary embodiments of the application. The following examples are presented in order to more fully illustrate embodiments and should in no way be construed, however, as limiting the broad scope of the application.

Example 1

Ability of an exemplar anti-BCMA trispecific domain antibody containing a BCMA binding protein of the present disclosure to mediate T cell killing of cancer cells expressing BCMA, in TDCC (T cell dependent cell cytotoxic) assays

[00173] Protein Production

[00174] Sequences of BCMA targeting trispecific molecules, containing a BCMA binding protein according to the present disclosure, were cloned into mammalian expression vector pcDNA 3.4 (Invitrogen) preceded by a leader sequence and followed by a 6x Histidine Tag (SEQ ID NO: 471). Expi293 cells (Life Technologies A14527) were maintained in suspension in Optimum Growth Flasks (Thomson) between 0.2 to 8 x 1e6 cells/mL in Expi293 media. Purified plasmid DNA was transfected into Expi293 cells in accordance with Expi293 Expression System Kit (Life Technologies, A14635) protocols, and maintained for 4-6 days post transfection. The amount of the exemplary trispecific proteins being tested, in the conditioned media, from the transfected Expi293 cells was quantitated using an Octet instrument with Protein A tips and using a control trispecific protein for a standard curve.

[00175] T cell dependent cellular cytotoxicity assays

[00176] Titrations of conditioned media was added to TDCC assays (T cell Dependent Cell Cytotoxicity assays) to assess whether the anti-BCMA single domain antibody is capable of forming a synapse between T cells and a BCMA-expressing cell line and direct the T cells to kill the BCMA-expressing cell line. In this assay (Nazarian *et al.*, 2015. *J. Biomol. Screen.*, 20:519-27), T cells and target cancer cell line cells were mixed together at a 10:1 ratio in a 384-well plate, and varying amounts of the trispecific proteins being tested were added. The tumor cell lines were engineered to express luciferase protein. After 48 hours, to quantitate the remaining viable tumor cells, STEADY-GLO® Luminescent Assay (Promega) was used.

[00177] In this example EJM cells were used, which is a cell line that serves as an *in vitro* model for multiple myeloma and plasma cell leukemia. Viability of the EJM cells is measured after 48 hours. It was seen that the trispecific proteins mediated T cell killing. **Fig. 1** shows an example cell viability assay with test proteins 01H08, 01F07, 02F02 and BH253 compared to a negative control. The EC₅₀ for the TDCC activity of several other test trispecific proteins are listed below in **Table 1**.

[00178] Binding affinity

[00179] In the instant study, the binding affinity to human BCMA protein of the BCMA targeting trispecific proteins containing a BCMA binding protein according to the present disclosure was determined. The affinity measurements are listed in **Table 1**.

[00180] **Table 1:** Binding affinity and TDCC Activity of several BCMA targeting trispecific proteins.

Construct Name	Human BCMA K _D (M)	TDCC EC50 (M)
253BH10	2.77E-08	5.29E-11
01H08	2.86E-09	3.41E-13
01F07	4.18E-09	7.02E-13
01H06	ND	1.00E-12
02G02	5.26E-09	1.08E-12
02B05	5.39E-09	1.22E-12
01C01	6.52E-09	1.33E-12
02F02	6.73E-09	1.36E-12
02E05	6.53E-09	1.37E-12
01E08	5.56E-09	1.50E-12
02C01	5.31E-09	1.55E-12
02E06	6.31E-09	1.57E-12
02B06	6.77E-09	1.65E-12
02F04	6.75E-09	1.72E-12
01G08	6.27E-09	1.91E-12
02C06	6.90E-09	1.95E-12
01H09	5.44E-09	2.21E-12
01F04	6.55E-09	2.21E-12

Construct Name	Human BCMA K_D (M)	TDCC EC50 (M)
01D02	7.35E-09	2.25E-12
02D11	6.71E-09	2.35E-12
01A07	6.95E-09	2.49E-12
02C03	7.09E-09	2.52E-12
02F07	7.06E-09	2.59E-12
01E04	7.29E-09	2.67E-12
02H09	6.83E-09	2.88E-12
01E03	6.36E-09	2.98E-12
02F05	7.15E-09	3.00E-12
01B05	6.52E-09	3.01E-12
01C05	6.09E-09	3.07E-12
02F12	7.76E-09	3.14E-12
01H11	7.06E-09	3.17E-12
02G06	7.50E-09	3.39E-12
01E06	8.91E-09	3.77E-12
01G11	9.70E-09	3.98E-12
02A05	7.06E-09	4.21E-12
01A08	1.17E-08	4.25E-12
02G05	7.12E-09	4.33E-12
01B09	1.12E-08	5.27E-12
01G01	1.46E-08	5.83E-12
01B06	9.10E-09	6.97E-12
01F10	1.44E-08	7.44E-12
01E05	1.17E-08	1.08E-11
02G01	1.63E-08	1.08E-11
01A06	1.58E-08	1.10E-11
02B04	1.52E-08	1.13E-11
01D06	1.49E-08	1.35E-11
02B07	1.58E-08	1.42E-11
02B11	1.33E-08	1.44E-11

Construct Name	Human BCMA K_D (M)	TDCC EC50 (M)
01H04	1.74E-08	1.47E-11
01D03	2.09E-08	1.49E-11
01A05	1.70E-08	1.51E-11
02F11	2.00E-08	1.52E-11
01D04	1.89E-08	1.60E-11
01B04	1.86E-08	1.61E-11
02C05	1.56E-08	1.62E-11
02E03	1.68E-08	1.65E-11
01D05	1.78E-08	1.66E-11
01C04	2.16E-08	1.75E-11
01E07	1.99E-08	1.92E-11
01G06	1.70E-08	1.92E-11
02F06	2.19E-08	1.93E-11
01B01	1.99E-08	1.95E-11
01D07	1.93E-08	1.96E-11
02A08	9.51E-09	2.01E-11
01A02	2.15E-08	2.18E-11
02G11	2.05E-08	2.38E-11
01G04	1.17E-08	2.41E-11
02F03	2.57E-08	2.45E-11
01C06	1.88E-08	2.51E-11
01A01	2.13E-08	2.64E-11
01B12	2.07E-08	2.73E-11
02A07	1.84E-08	2.79E-11
02G08	1.80E-08	2.86E-11
02E09	2.09E-08	3.11E-11
02H06	2.33E-08	3.19E-11
01H10	2.48E-08	3.52E-11
01F05	1.67E-08	3.72E-11
01C02	2.00E-08	3.73E-11

Construct Name	Human BCMA K_D (M)	TDCC EC50 (M)
02A04	1.76E-08	3.82E-11
02H05	1.96E-08	3.89E-11
02G09	3.44E-08	3.96E-11
02D06	2.33E-08	4.28E-11
02G07	1.93E-08	4.46E-11
01H05	2.74E-08	4.54E-11
01C08	2.83E-08	4.57E-11
01A03	3.08E-08	4.61E-11
01A09	2.39E-08	4.84E-11
02B01	2.14E-08	5.18E-11
02H01	3.56E-08	5.42E-11
02H04	3.11E-08	5.99E-11
02A11	2.52E-08	6.06E-11
01E10	1.85E-08	6.23E-11
02D09	2.89E-08	6.73E-11
01F08	2.14E-08	7.12E-11
01F03	1.50E-08	7.64E-11
02H11	2.75E-08	7.75E-11
01C07	1.98E-08	8.33E-11
01B08	2.56E-08	8.76E-11
01B03	2.62E-08	9.64E-11
01H01	3.59E-08	1.18E-10
02B12	2.52E-08	1.24E-10
01G10	4.19E-08	1.43E-10
01A04	3.75E-08	1.59E-10
01B07	4.39E-08	1.74E-10
01C10	4.64E-08	2.08E-10
01F02	4.13E-08	2.25E-10
01B02	1.88E-08	3.59E-10
01F12	4.05E-08	3.92E-10

Construct Name	Human BCMA K _D (M)	TDCC EC50 (M)
01G09	8.78E-08	4.41E-10
01D10	5.39E-08	4.53E-10
01F09	5.28E-08	9.45E-10

[00181] ND: Not determined.

[00182] Molecules 01H08, 01F07, 01H06, 02G02, 02B05, 01C01, 02F02, 02E05, 01E08, 02C01, 02E06, 02B06, 02F04, 01G08, 02C06, 01H09, 01F04, 01D02, 02D11, 01A07, 02C03, 02F07, 01E04, 02H09, 01E03, 02F05, 01B05, 01C05, 02F12, 01H11, 02G06, 01E06, 01G11, 02A05, 01A08, 02G05, 01B09, 01G01, 01B06, 01F10, 01E05, 02G01, 01A06, 02B04, 01D06, 02B07, 02B11, 01H04, 01D03, 01A05, 02F11, 01D04, 01B04, 02C05, 02E03, 01D05, 01C04, 01E07, 01G06, 02F06, 01B01, 01D07, 02A08, 01A02, 02G11, 01G04, 02F03, 01C06, 01A01 have at least two fold increase TDCC potency and also show increase affinity compared to a molecule with the parental CDRs, 253BH10.

[00183] Molecules 01H08, 01F07, 01H06, 02G02, 02B05, 01C01, 02F02, 02E05, 01E08, 02C01, 02E06, 02B06, 02F04, 01G08, 02C06, 01H09, 01F04, 01D02, 02D11, 01A07, 02C03, 02F07, 01E04, 02H09, 01E03, 02F05, 01B05, 01C05, 02F12, 01H11, 02G06, 01E06, 01G11, 02A05, 01A08, 02G05, 01B09 have at least ten-fold increase TDCC potency and also show increase affinity compared to a molecule with the parental CDRs, 253BH10.

[00184] An anti-GFP trispecific molecule, included in these assays as a negative control, had no detectable BCMA binding and no effect on cell viability in the TDCC assay (data not shown).

Example 2

Methods to assess binding and cytotoxic activities of exemplary purified trispecific antigen binding proteins containing a BCMA binding domain according to the present disclosure against Jeko1, MOLP8 and OPM2 cells

[00185] *Protein Production*

[00186] Sequences of BCMA targeting trispecific molecules, containing a BCMA binding protein according to the present disclosure, preceded by a leader sequence and followed by a 6x Histidine Tag (SEQ ID NO: 471), were expressed using the vectors and methods previously described (Running Deer and Allison, 2004. *Biotechnol Prog.* 20:880-9) except lipid

based reagents and non-linearized plasmid DNA were used for cell transfection. Recombinant trispecific proteins were purified using affinity chromatography, ion exchange, and/or size exclusion chromatography. Purified protein was quantitated using theoretical extinction coefficients and absorption spectroscopy. An image of a Coomassie stained SDS-PAGE demonstrates the purity of the proteins (**Fig. 2**).

[00187] Cytotoxicity assays

[00188] A human T-cell dependent cellular cytotoxicity (TDCC) assay was used to measure the ability of T cell engagers, including trispecific molecules, to direct T cells to kill tumor cells (Nazarian *et al.*, 2015. *J. Biomol. Screen.*, 20:519-27). In this assay, T cells and target cancer cell line cells are mixed together at a 10:1 ratio in a 384-well plate, and varying amounts of the trispecific proteins being tested are added. The tumor cell lines are engineered to express luciferase protein. After 48 hours, to quantitate the remaining viable tumor cells, STEADY-GLO® Luminescent Assay (Promega) was used.

[00189] In the instant study, titrations of purified protein were added to TDCC assays (T cell Dependent Cell Cytotoxicity assays) to assess whether the anti-BCMA single domain antibody was capable of forming a synapse between T cells and BCMA-expressing Jeko1, MOLP8 and OPM2 cancer cell lines. Jeko1 is a B cell lymphoma cell line. MOLP-8 is a myeloma cell line. OPM-2 is a human myeloma cell line.

[00190] Viability of the cells was measured after 48 hours. It was seen that the trispecific proteins mediated T cell killing. **Fig. 3** shows an example cell viability assay with test proteins compared to a negative control. The EC₅₀ for the TDCC activity of several other test trispecific proteins are listed below in **Table 2**. An anti-GFP trispecific molecule, included in these assays as a negative control, had no effect on cell viability (data not shown).

[00191] **Table 2:** TDCC EC₅₀ Values for 3 Cell Lines for Select Binder Sequences in TriTAC format

Construct name	Jeko1 EC50 (M)	MOLP-8 EC50 (M)	OPM-2 EC50 (M)
BH2T TriTAC	3.2E-10	2.0E-10	1.6E-10
01F07 TriTAC	5.3E-12	1.5E-12	4.4E-12
01F07-M34Y TriTAC	5.6E-12	1.5E-12	3.6E-12
01F07-M34G TriTAC	9.0E-12	2.2E-12	5.6E-12
01G08 TriTAC	1.5E-11	2.5E-12	6.9E-12
01H08 TriTAC	4.0E-12	9.4E-13	3.1E-12
02B05 TriTAC	8.3E-12	2.5E-12	6.5E-12

02B06 TriTAC	1.1E-11	2.8E-12	9.7E-12
02E05 TriTAC	1.1E-11	3.3E-12	1.2E-11
02E06 TriTAC	9.1E-12	2.4E-12	7.4E-12
02F02 TriTAC	8.2E-12	3.5E-12	1.0E-11
02F04 TriTAC	1.0E-11	2.5E-12	7.3E-12
02G02 TriTAC	1.1E-11	2.8E-12	6.6E-12
02G02-M34Y TriTAC	1.1E-11	5.6E-12	6.2E-12
02G02-M34G TriTAC	1.2E-11	4.0E-12	7.1E-12

[00192] *Binding affinity*

[00193] In the instant study, the binding affinity to human BCMA protein of the BCMA targeting trispecific proteins containing a BCMA binding protein according to the present disclosure was determined.

[00194] **Table 3:** Binding affinity of purified targeting trispecific proteins containing a BCMA binding protein according to the present disclosure.

Construct name	Human BCMA KD (M)
01F07-M34Y TriTAC	3.0E-09
01F07-M34G TriTAC	6.0E-09
02B05 TriTAC	6.0E-09
02G02-M34Y TriTAC	5.0E-09
02G02-M34G TriTAC	7.0E-09

Example 3

ADCC activity of an exemplar anti-BCMA multidomain antibody of the present disclosure

[00195] This study is directed to determining the ability of an exemplary anti-BCMA multidomain antibody of the present disclosure to mediate ADCC as compared to a parental llama anti-BCMA antibody which does not have sequence modifications or substitutions as the exemplary antibody of the disclosure. Both antibodies are expressed as multidomain proteins which include an additional immunoglobulin Fc domain.

[00196] *Materials*

[00197] Donors are leukaphoresed, and NK cells are isolated from the leukopack by the Cell Purification Group using the Milteni AUTOMACS® Pro negative selection system. NK

cells are held overnight at 4° C on a rocker, then washed, counted and resuspended at 4×10^6 cells/mL in complete RPMI for use in the ADCC assay.

[00198] Targets: Tumor cell targets are selected based on BCMA expression. Targets are washed and counted. 6×10^6 targets are resuspended in complete RPMI and labeled in a final concentration of 10 μ M calcein (Sigma #C1359-00UL calcein am 4 mm in anhydrous DMSO) for 40 minutes at 37 °C, 5% CO₂. Cells are washed twice in PBS, resuspended in complete RPMI and incubated at 37 °C, 5% CO₂ for 2 hrs. After labeling, target cells are washed, recounted and resuspended at 0.2×10^6 cells/mL in complete RPMI for use in the ADCC assay.

[00199] Methods

[00200] The ADCC assay is performed in a 96-well round bottom tissue culture plate (Corning 3799). The test proteins are titrated from 20 μ g/mL to 0.0002 μ g/mL by carrying 10 μ L in 1000 μ L of complete RPMI containing 10% FCS (a 1:10 dilution). Calcein labeled targets are added, 50 μ L to contain 10,000 cells. Target cells and various concentrations of the multidomain proteins containing either the exemplar anti-BCMA single domain antibody or the comparator antibody are incubated for 40 minutes at 4 °C, then NK cell effectors added, 50 μ L to contain 100,000 cells (10:1 E:T ratio). Cultures are incubated for 4 hrs at 37 °C then supernatants pulled and assayed for calcein release by measuring fluorescence at 485-535 nm on a Wallac Victor II 1420 Multilable HTS counter. 100% lysis values are determined by lysing six wells of labeled targets with IGEPAL® 630 detergent (3 μ L per well) and spontaneous lysis values determined by measuring the fluorescence in supernatants from targets alone.

[00201] Statistical Analysis

[00202] Percent (%) specific lysis is defined as (sample fluorescence) – (spontaneous lysis fluorescence) / (100% lysis – spontaneous lysis fluorescence). Spontaneous lysis is determined by wells containing only targets and 100% lysis is determined by wells where targets are lysed with IGEPAL CA 630 detergent. Raw data is entered in an Excel spreadsheet with embedded formulae to calculate % specific lysis and resultant values transferred to graphic program (GraphPad Prism) where the data is transformed in a curve fit graph. Subsequent analyses (linear regression calculations) are done in GraphPad to generate EC₅₀ values.

Example 4

CDC activity of an exemplar anti-BCMA single domain antibody of the present disclosure

[00203] To evaluate the anti-tumor activity of exemplar anti-BCMA single domain antibody, according to the present disclosure, against cancer cells, the cytotoxic activity in A431/H9 and NCI-H226 cell models in the presence of human serum as a source of complement

is tested. The exemplar anti-BCMA single domain antibody is expressed as a multidomain protein containing a Fc domain.

[00204] A multidomain protein containing the exemplar anti-BCMA single domain antibody of the present disclosure exerts potent CDC activity by killing cancer cell lines, and shows no activity on a BCMA-negative cell line.

Example 5

Xenograft tumor model

[00205] An exemplary BCMA targeting trispecific protein containing an exemplary BCMA binding protein of this disclosure, 02B05 (SEQ ID NO: 383), was evaluated in a xenograft model.

[00206] On day 0, NCG mice were subcutaneously inoculated with RPMI-8226 cells, and also intraperitoneally implanted with normal human peripheral blood mononuclear cells (PBMCs). Treatment with the exemplary BCMA targeting trispecific protein was also started on day 0 (qdx10) (once daily for 10 days). The dosage of administration was 5 µg/kg, 50 µg/kg, or 500 µg/kg of the BCMA targeting trispecific protein 02B05, or a vehicle as control. Tumor volumes were determined for 25 days. As shown in **Fig. 29**, the mean tumor volumes were significantly lower in mice treated with the exemplary BCMA targeting trispecific protein (02B05) (at 50 µg/kg, or 500 µg/kg), as compared to the mice treated with the vehicle or the lower dose of BCMA targeting trispecific protein (02B05) (at 5 µg/kg).

[00207] On day 0, NCG mice were subcutaneously inoculated with Jeko 1 cells, and also intraperitoneally implanted with normal human peripheral blood mononuclear cells (PBMCs). Treatment with the exemplary BCMA targeting trispecific protein was started on day 3 (qdx10) (once daily for 10 days). The dosage of administration was 5 µg/kg, 50 µg/kg, or 500 µg/kg of the BCMA targeting trispecific protein 02B05, or a vehicle as control. Tumor volumes were determined for 25 days. As shown in **Fig. 30**, the mean tumor volumes were significantly lower in mice treated with the exemplary BCMA targeting trispecific protein (02B05) (at 500 µg/kg), as compared to the mice treated with the vehicle or the lower doses of BCMA targeting trispecific protein (02B05) (at 5 µg/kg or 50 µg/kg).

Example 6

Affinity Measurements for human and cynomolgus BCMA, CD3ε, and albumin, using an exemplar BCMA targeting trispecific containing a BCMA binding protein of this disclosure protein of this disclosure

[00208] The aim of this study was to assess the affinity of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) (SEQ ID NO: 383), toward human BCMA, cynomolgus BCMA, human CD3 ϵ , cynomolgus CD3 ϵ , human albumin, cynomolgus albumin, and mouse albumin. The affinities were measured using an Octet instrument. For these measurements, streptavidin tips were first loaded with 2.5 nM human BCMA-Fc, 2.5 nM cynomolgus BCMA-Fc, 2.5 nM human CD3 ϵ -Fc, 2.5 nM cynomolgus CD3 ϵ -Fc, 50 nM human serum albumin (HSA), 50 nM cynomolgus serum albumin, or 50 nM mouse serum albumin. Subsequently, the exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 was incubated with the tips, and following an association period, the tips were moved to a buffer solution to allow the exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) to disassociate. The affinities for binding to human and cynomolgus BCMA and CD3 ϵ were measured in the presence of 15 mg/ml human serum albumin. Average calculated K_D values from these studies are provided in **Table 4** (n indicates the number of independent measurements, n/d indicates no binding detected under the conditions tested). Binding was detected to human BCMA, human CD3 ϵ , cynomolgus CD3 ϵ , human serum albumin, cynomolgus serum albumin, and mouse serum albumin. Under the conditions tested, no binding was detected to cynomolgus BCMA.

[00209] **Table 4.** Measured K_D values for exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure, 02B05, to protein ligands.

Protein ligand	Species	K_D (nM)	n
BCMA	human	2.4 ± 0.2	2
	cynomolgus	n/d	2
CD3 ϵ	human	8 ± 1	2
	cynomolgus	7.8 ± 0.4	2
Albumin	human	6 ± 1	3
	cynomolgus	7.5	1
	mouse	76	1

Example 7**Human T cell binding ability of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure of this disclosure**

[00210] Exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure, 02B05 (SEQ ID NO: 383) was tested for its ability to bind to purified T cells. Briefly, the BCMA trispecific protein or phosphate buffered saline (PBS) were incubated with purified T cells from 4 different anonymous human donors. After washing unbound protein, the T cells were then incubated with an Alexa Fluor 647 conjugated antibody that recognizes the anti-albumin domain in the 02B05 BCMA trispecific antigen-binding protein. The T cells were then analyzed by flow cytometry. It was observed that human T cells incubated with the 02B05 BCMA trispecific antigen-binding protein had notable shifts associated with Alexa Fluor 647 staining compared to cells that were incubated with PBS. The results are shown in Figs. 4A, 4B, 4C, and 4D. In conclusion, this study indicated that the exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure was able to bind human T cells.

Example 8**Ability of an exemplary BCMA targeting trispecific protein of this disclosure to bind BCMA expressing cells**

[00211] Exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) was tested for its ability to bind to BCMA expressing cells. Briefly, the 02B05 BCMA trispecific antigen-binding protein was incubated with cell lines expressing BCMA (NCI-H929; EJM; RPMI-8226; OPM2) or lacking BCMA (NCI-H510A; DMS-153). Expression of BCMA RNA in these cells is indicated by the FPKM (fragments per kilobase million) values listed in **Figs. 5A-F**: the RNA FPKM values are from the Cancer Cell Line Encyclopedia (Broad Institute, Cambridge, MA USA). After washing unbound protein, the cells were then incubated with an Alexa Fluor 647 conjugated antibody that recognizes the anti-albumin domain in the 02B05 BCMA trispecific antigen-binding protein. The cells were then analyzed by flow cytometry. As a negative control, cells were incubated with a trispecific protein targeting GFP. Cells expressing BCMA RNA and incubated with the BCMA trispecific protein had notable shifts associated with Alexa Fluor 647 staining compared to cells that were incubated with GFP trispecific protein (as in **Figs. 5A, 5B, 5D, and 5E**). Whereas, cells lacking BCMA RNA produced equivalent Alexa Fluor 647 staining with

the BCMA trispecific protein and the GFP trispecific protein (as seen in **Figs. 5C**, and **5F**). Thus, this study indicated that the exemplary BCMA trispecific antigen-binding was able to selectively bind to cells expressing BCMA.

Example 9

Ability of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure to mediate T cell killing of cancer cells expressing BCMA

[00212] Exemplary BCMA trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) was tested for its ability to direct T cells to kill BCMA expressing cells in the presence and absence of human serum albumin (HSA) using a standard TDCC assay as described in **Example 1**. Because the exemplary BCMA trispecific protein contains an anti-albumin domain, this experiment was performed to confirm that binding to albumin would not prevent the BCMA trispecific antigen-binding protein from directing T cells to kill BCMA expressing cells. Five BCMA expressing cell lines were tested: EJM, Jeko, OPM2, MOLP8, and NCI-H929. Representative data for an experiment with the EJM cells are shown in **Fig. 6**. It was observed that viability of the EJM cells decreased with increasing amount of the exemplary 02B05 BCMA trispecific antigen-binding protein in the presence or absence of human serum albumin (HSA), whereas a control GFP targeting trispecific protein did not affect cell viability. In the presence of albumin, higher concentrations of BCMA trispecific protein were needed to reduce viability of the EJM cells. The EC₅₀ values for cell killing by BCMA trispecific protein for the EJM cells as well as the Jeko, OPM2, MOL8, and NCI-H929 cells in the absence or presence of HSA are provided in **Table 5**. With all five cell lines, the exemplary 02B05 BCMA trispecific antigen-binding protein directed T cells to kill target cells in the presence of HSA.

[00213] **Table 5** TDCC EC₅₀ Values for an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure in the presence or absence of human serum albumin with five different BCMA expressing cell lines

Cell Line	EC₅₀ without HSA (pM)	EC₅₀ with HSA (pM)
EJM	1.0	53
Jeko	8.3	662
OPM2	6.5	328
MOLP8	2.5	388
NCI-H929	6.7	194

Example 10**Ability of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure to mediate T cell killing of cancer cells expressing BCMA, using a smaller target cell to effector cell ratio**

[00214] In the standard TDCC assay (as described in **Example 1**), a ratio 1 target cell (EJM cells or OPM2 cells) per 10 effector cells (T cells) is used in a 48 hour assay. In this experiment, the ability of exemplary BCMA targeting trispecific protein containing an exemplary BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) to direct T cells to kill target cells with smaller target cell to effector ratios was tested. The expectation was that less killing would be observed when fewer effector cells were used. Two BCMA expressing cell lines were tested, EJMs and OPM2, using target to effector cell ratios of 1:1, 1:3, and 1:10, and the experiment was performed in the presence of 15 mg/ml HSA. A GFP targeting trispecific protein was used as a negative control. Data from this experiment is shown in **Fig. 7** (TDCC assay with EJMs cells) and **Fig. 8** (TDCC assay with OPM2 cells). As expected, near complete killing of the target cells was observed with a 1:10 target to effector cell ratio. The amount of killing was reduced with decreasing effector cells. The EC₅₀ values for cell killing with each ratio are listed in **Table 6** (n/d indicates insufficient killing was observed to calculate an EC₅₀ value). The EC₅₀ values increased when fewer effector cells were present. Thus, as expected, reducing the number of effector cells to target cells reduced TDCC activity of the BCMA trispecific protein.

[00215] **Table 6** TDCC EC₅₀ values for an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) with varied target cell (EJM cells) to effector cell (T cells) ratios (tested in presence of 15 mg/ml HSA)

Target cell:		OPM2 EC ₅₀
T Cell ratio	EJM EC ₅₀ (pM)	(pM)
1:10	154	371
1:3	523	1896
1:1	1147	n/d

Example 11**Ability of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure to mediate T cell killing of cancer cells expressing BCMA, in a time course study, using a smaller target cell to effector cell ratio**

[00216] In the standard TDCC assay (**Example 1**), a ratio 1 target cell per 10 effector cells (T cells) is used in a 48 hour assay. In this experiment, a time course was performed using a 1 to 1 ratio of target cells (EJM cells) to effector cells (T cells). The expectation was that with increased time, a 1 to 1 ratio would result in target cell killing. The TDCC assay was performed using EJMs and a 1:1 target to effector cell ratio, and the experiment was performed in the presence of 15 mg/ml HSA. A GFP targeting trispecific protein was used as a negative control. Target cell viability was measured on days 1, 2, 3, and 4 following incubation of the target cells and effector cells, at a 1:1 ratio, in presence of the exemplary 02B05 BCMA trispecific antigen-binding protein and 15 mg/ml HSA, or the GFP targeting trispecific protein and 15 mg/ml HSA. While no target cell killing was observed on day 1, killing was observed at all other time points with the 02B05 BCMA trispecific-antigen-binding protein, with the amount of killing increasing with time (**Fig. 9**). No target cell killing was observed with the GFP targeting trispecific protein. The EC₅₀ values calculated for cell killing on each day are provided in **Table 7** (n/d indicates insufficient killing to determine an EC₅₀ value). From this study it was concluded that the exemplary 02B05 BCMA trispecific protein was able to direct T cell killing with lower numbers of effector cells, but more time was needed to achieve more complete killing.

[00217] **Table 7** TDCC EC₅₀ values for an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) with a 1 to 1 target cell (EJM cells) to effector cell (T cells) ratios (tested in presence of 15 mg/ml HSA), at varied time points

	EC ₅₀ (pM)
Day 1	n/d
Day 2	1859
Day 3	1420
Day 4	1012

Example 12

Ability of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure to direct human T cells to kill BCMA expressing cells

[00218] Exemplary BCMA trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) was tested for its ability to direct T cells from four different anonymous human donors to kill four different BCMA expressing cells in the presence of 15 mg/ml human serum albumin (HSA) using a standard TDCC assay as described in **Example 1**. The BCMA expressing cell lines were EJMs, NCI-H929, OPM2, and RPMI8226.

As negative controls, two cell lines that lack BCMA expression, OVCAR8 and NCI-H510A, were also tested in the TDCC assays. A control GFP targeting trispecific protein was also used as a negative control. With the four BCMA expressing cell lines and all four T cell donors, cell viability decreased with increasing amounts of the BCMA trispecific protein but not with the GFP trispecific protein (**Figs. 10, 11, 12, and 13**). The EC₅₀ values for cell killing are provided in **Table 8**. The exemplary 02B05 BCMA trispecific antigen-binding protein did not direct killing of the cell lines lacking BCMA expression (**Figs. 14 and 15**). Thus, it was inferred that the exemplary 02B05 BCMA trispecific antigen-binding protein was able to direct T cells from multiple donors to kill a spectrum of BCMA expressing cell lines.

[00219] **Table 8** Exemplary BCMA trispecific protein EC₅₀ values from TDCC assays with four BCMA expressing cell lines and four T cell donors in presence of 15 mg/ml HSA

	EC50 (pM)			
	H929	OPM2	RPMI8226	EJM
Donor 02	169	250	275	151
Donor 35	113	199	371	121
Donor 81	124	265	211	143
Donor 86	239	416	543	191

Example 13

Ability of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure to direct cynomolgus T cells to kill BCMA expressing cells

[00220] Exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) was tested for its ability to direct T cells from cynomolgus monkeys to kill BCMA expressing cells in the presence of 15 mg/ml human serum albumin (HSA). The experimental conditions were the same as described in **Example 1** except peripheral blood mononuclear cells (PBMC) from cynomolgus monkeys were used as a source of T cells. Two BCMA expressing cell lines were tested, RPMI8226 and NCI-H929. As shown in **Figs. 16 and 17**, the BCMA trispecific protein was able to direct T cells present in the cynomolgus PBMCs to kill the two BCMA expressing cell lines. The EC₅₀ values for the cell killing are listed in **Table 9**. A GFP trispecific protein did not affect viability of the BCMA expressing cells. Thus, the BCMA expressing trispecific protein, which can bind cynomolgus CD3ε (as shown in **Example 6**), can direct cynomolgus T cells to kill cells expressing human BCMA.

[00221] **Table 9** BCMA trispecific protein EC₅₀ values from TDCC Assays with two cell lines and two cynomolgus PMBC donors in the presence of 15 mg/ml HSA

	EC ₅₀ (pM)	
	RPMI8226	NCI-H929
Donor G322	3654	1258
Donor GA33	1003	288

Example 14

Exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure in mediating induction of T cell activation

[00222] Exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) was tested for its ability to activate T cells in the presence of BCMA expressing cells. The BCMA expressing cell lines were EJM, OPM2, and RPMI8226. As negative controls, two cells lines that lack BCMA expression were also included, OVCAR8 and NCI-H510A. T cells were obtained from four different anonymous human donors. The assays were set up using the conditions of a standard TDCC assay as described in **Example 1** except the assay was adapted to 96-well format and the assay was carried out in the presence of 15 mg/ml HSA. After the 48 hour assay, T cell activation was assessed by using flow cytometry to measure expression of T cell activation biomarkers CD25 and CD69 on the surface of the T cells. With increasing concentrations of the exemplary 02B05 BCMA trispecific antigen-binding protein increased expression of CD69 and CD25 was observed on T cells when co-cultured with the BCMA expressing cells (as shown in **Figs. 18-23**). Thus, the observed interaction was dependent on interaction of the BCMA binding sequence within the exemplary BCMA targeting trispecific protein, as little to no activation was observed with a control GFP trispecific protein (as shown in **Figs. 18-23**) or with target cells with no BCMA expression (as shown in **Figs. 24-27**). Therefore the exemplary BCMA targeting trispecific protein activated T cells in co-cultures containing BCMA expressing cells. This conclusion is bolstered by additional data. For instance, expression of a cytokine, TNF α , was measured in the medium collected from a co-culture of T cells and BCMA expressing target cells treated with increasing concentrations of the exemplary BCMA targeting trispecific protein or with the negative control GFP trispecific protein. The co-cultures were set up using the conditions of a standard TDCC assay (as described in Example 1) supplemented with 15 mg/ml HSA. TNF α was measured using an electrochemiluminescent assay (Meso Scale Discovery).

Robust induction of TNF α expression was observed with the exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) and not the GFP trispecific protein (**Fig. 28**). This result further supports that the exemplary BCMA targeting trispecific protein activated T cells in co-cultures containing BCMA expressing cells.

Example 15

Pharmacokinetics of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure

[00223] Cynomolgus monkeys were administered single intravenous doses of an exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (02B05) (SEQ ID NO: 383), at 0.01 mg/kg, 0.1 mg/kg, or 1 mg/kg. Two animals were included per dose group. Following the administration, serum samples were collected and analyzed by two different electrochemiluminescent assays. One assay used biotinylated CD3 ϵ as a capture reagent and detected with sulfo tagged BCMA (termed the functional assay). Another assay used as a capture reagent a biotinylated antibody recognizing the anti-albumin domain in the exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) and used as a detection reagent a sulfo tagged antibody recognizing the anti-CD3 binding domain in the exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure (*i.e.*, an anti-idiotypic antibody). The results from the electrochemiluminescent assays are plotted in **Fig. 31**. As seen in **Fig. 31**, the exemplary BCMA targeting trispecific protein was detected in the cynomolgus serum samples, even after 504 hours after the administration. The exemplary BCMA targeting trispecific protein was identified using both the sulfo-tagged BCMA (lines labeled using the term “functional” in **Fig. 31**) and by the anti-idiotypic antibody (lines labeled using the term “anti-idiotypic” in **Fig. 31**).

[00224] To confirm that the exemplary BCMA targeting trispecific protein retained the ability to direct T cells to kill BCMA expressing EJM cells, after in vivo administration, serum samples from the 168 hour time point were tested in a TDCC assay (as described in Example 1) in the presence of 16.7% serum from a cynomolgus monkey that has not been exposed to a BCMA targeting trispecific protein, titrating the exemplary BCMA targeting trispecific protein using the protein concentrations determined using the electrochemiluminescent assays (shown in **Fig. 32**). Fresh diluted exemplary BCMA targeting trispecific protein containing a BCMA binding protein of this disclosure 02B05 (SEQ ID NO: 383) was compared to the BCMA

trisppecific protein collected from the test cynomolgus monkeys at 168 h. A GFP trisppecific protein was included as a negative control. This study demonstrated that the exemplary BCMA targeting trisppecific protein collected from the test cynomolgus monkeys' serum had identical activity as freshly diluted protein, and that the protein in the serum samples retained the ability to direct T cells to kill BCMA expressing EJM cells.

[00225] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

Sequence Table

SEQ ID NO:	Description	Sequence
1.	Exemplary CDR1	X ₁ X ₂ X ₃ X ₄ X ₅ X ₆ X ₇ PX ₈ G where X ₁ is T or S; X ₂ is N, D, or S; X ₃ is I, D, Q, H, V, or E; X ₄ is F, S, E, A, T, M, V, I, D, Q, P, R, or G; X ₅ is S, M, R, or N; X ₆ is I, K, S, T, R, E, D, N, V, H, L, A, Q, or G; X ₇ is S, T, Y, R, or N; and X ₈ is M, G, or Y
2.	Exemplary CDR2	AIX ₉ GX ₁₀ X ₁₁ TX ₁₂ YADSVK where X ₉ is H, N, or S; X ₁₀ is F, G, K, R, P, D, Q, H, E, N, T, S, A, I, L, or V; X ₁₁ is S, Q, E, T, K, or D; and X ₁₂ is L, V, I, F, Y, or W
3.	Exemplary CDR3	VPWGX ₁₃ YHPX ₁₄ X ₁₅ VX ₁₆ where X ₁₃ is D, I, T, K, R, A, E, S, or Y; X ₁₄ is R, G, L, K, T, Q, S, or N; X ₁₅ is N, K, E, V, R, M, or D; and X ₁₆ is Y, A, V, K, H, L, M, T, R, Q, C, S, or N
SEQ ID NO:	Name	HCDR1
4.	01A01	TDIFSISPMG
5.	01A02	TNIFSSSPMG
6.	01A03	TNIFSISPGG
7.	01A04	TNIFMISPMG
8.	01A05	TNIFSSSPMG
9.	01A06	TNIFSIRPMG
10.	01A07	TNISSISPMG
11.	01A08	TNIFSSSPMG
12.	01A09	TNIFSITPMG
13.	01B01	TNIPSISPMG
14.	01B02	TNITSISPMG
15.	01B03	TNIFSKSPMG

16.	01B04	TNDFSISPMG
17.	01B05	TNITSISPMG
18.	01B06	TNIFSISPMG
19.	01B07	TNIFSRSPMG
20.	01B08	TNIESISPMG
21.	01B09	SNIFSISPMG
22.	01B12	TNIFSTSPMG
23.	01C01	TNIVSISPMG
24.	01C02	TNIESISPMG
25.	01C04	TNIPSISPMG
26.	01C05	TNIFSSSPMG
27.	01C06	TNIFSISPMG
28.	01C07	TNIFSIYPMG
29.	01C08	TNIFSNSPMG
30.	01C10	TNISSISPMG
31.	01D02	TNIVSISPMG
32.	01D03	TNIFSNSPMG
33.	01D04	TNITSISPMG
34.	01D05	TNIFSDSPMG
35.	01D06	TNIFSRSPMG
36.	01D07	TNIFSASPMG
37.	01D10	TNIFSASPMG
38.	01E03	TNITSISPMG
39.	01E04	TNIASISPMG
40.	01E05	TNIFSRSPMG
41.	01E06	TNIFSLSPMG
42.	01E07	TNIPSISPMG
43.	01E08	TNIFSQSPMG
44.	01E10	TNIESISPMG
45.	01F02	TNIFSHSPMG
46.	01F03	TNIFSESPMG
47.	01F04	TNIDSISPMG
48.	01F05	TNIFSSSPMG
49.	01F07	TNIFSTSPMG
50.	01F08	TNITSVSPMG
51.	01F09	TNISSISPMG
52.	01F10	SNIFSISPMG
53.	01F12	TNIFRISPMG
54.	01G01	TNIVSISPMG
55.	01G04	TNIDSISPMG

56.	01G06	TNIFSRSPMG
57.	01G08	TNIQSISPMG
58.	01G09	TNIFNISPMG
59.	01G10	TNEFSISPMG
60.	01G11	TNIPSISPMG
61.	01H01	TNIGSISPMG
62.	01H04	TNIFSKSPMG
63.	01H05	TNIFSITPMG
64.	01H06	TSDFSISPMG
65.	01H08	TNIMSISPMG
66.	01H09	TNIMSISPMG
67.	01H10	TNIPSISPMG
68.	01H11	TNIFSTSPMG
69.	02A04	TNIFSQSPMG
70.	02A05	TNIASISPMG
71.	02A07	TNIFSKSPMG
72.	02A08	TNIFSRSPMG
73.	02A11	TNHFSISPMG
74.	02B01	TNIFSNSPMG
75.	02B04	TNIFSTSPMG
76.	02B05	TNIFSISPYG
77.	02B06	TNIFSNSPMG
78.	02B07	TNIFSSSPMG
79.	02B11	TNIVSISPMG
80.	02B12	TNISSISPMG
81.	02C01	TNIISISPMG
82.	02C03	TNIASISPMG
83.	02C05	TNIFSESPMG
84.	02C06	TNIFSTSPMG
85.	02D06	TNISSISPMG
86.	02D09	TNVVSISPMG
87.	02D11	TNEFSISPMG
88.	02E03	TNIFSNSPMG
89.	02E05	TNIFSRSPMG
90.	02E06	TNIFSDSPMG
91.	02E09	TNDFSISPMG
92.	02F02	TNIFSKSPMG
93.	02F03	TNIFSIYPMG
94.	02F04	TNIFSSSPMG
95.	02F05	TNIFSVSPMG

96.	02F06	TNIFSITPMG
97.	02F07	TNIESISPMG
98.	02F11	TNIFSTSPMG
99.	02F12	TNIESISPMG
100.	02G01	TNIFSINPMG
101.	02G02	TNIFSITPMG
102.	02G05	TNITSISPMG
103.	02G06	TNIFSGSPMG
104.	02G07	TNIFSITPMG
105.	02G08	TNIDSISPMG
106.	02G09	TNIFSDSPMG
107.	02G11	TNIDSISPMG
108.	02H01	TNIFSKSPMG
109.	02H04	TNIFSVSPMG
110.	02H05	TNQFSISPMG
111.	02H06	TNIRSISPMG
112.	02H09	TNIFSRSPMG
113.	02H11	TNITSISPMG
114.	01F07-M34Y	TNIFSTSPYG
115.	01F01-M34G	TNIFSTSPGG
116.	02G02-M34Y	TNIFSITPYG
117.	02G02-M34G	TNIFSITPGG
SEQ ID NO:	Name	CDR2
118.	01A01	AIHGGSTLYADSVK
119.	01A02	AINGFSTLYADSVK
120.	01A03	AIHGSSTLYADSVK
121.	01A04	AIHGDSTLYADSVK
122.	01A05	AIHGFSTLYADSVK
123.	01A06	AIHGFSTVYADSVK
124.	01A07	AIHGTSTLYADSVK
125.	01A08	AIHGESTLYADSVK
126.	01A09	AIHGRSTLYADSVK
127.	01B01	AIHGESTLYADSVK
128.	01B02	AISGFSTLYADSVK
129.	01B03	AIHGKSTLYADSVK
130.	01B04	AIHGKSTLYADSVK
131.	01B05	AIHGFETLYADSVK
132.	01B06	AIHGDSTLYADSVK
133.	01B07	AIHGNSTLYADSVK
134.	01B08	AIHGSSTLYADSVK

135.	01B09	AIHGSSTLYADSVK
136.	01B12	AIHGFQTLYADSVK
137.	01C01	AIHGHSTLYADSVK
138.	01C02	AIHGNSTLYADSVK
139.	01C04	AIHGDSTLYADSVK
140.	01C05	AIHGFKTLYADSVK
141.	01C06	AIHGDSTLYADSVK
142.	01C07	AIHGFSTYYADSVK
143.	01C08	AIHGGSTLYADSVK
144.	01C10	AIHGFSTLYADSVK
145.	01D02	AIHGKSTLYADSVK
146.	01D03	AIHGDSTLYADSVK
147.	01D04	AIHGVSTLYADSVK
148.	01D05	AIHGTSTLYADSVK
149.	01D06	AIHGDSTLYADSVK
150.	01D07	AIHGSSTLYADSVK
151.	01D10	AIHGSSTLYADSVK
152.	01E03	AIHGDSTLYADSVK
153.	01E04	AIHGTSTLYADSVK
154.	01E05	AIHGTSTLYADSVK
155.	01E06	AIHGDSTLYADSVK
156.	01E07	AIHQSTLYADSVK
157.	01E08	AIHGDSTLYADSVK
158.	01E10	AIHGKSTLYADSVK
159.	01F02	AIHGTSTLYADSVK
160.	01F03	AIHGNSTLYADSVK
161.	01F04	AIHGFQTLYADSVK
162.	01F05	AIHGFSTWYADSVK
163.	01F07	AIHGFSTIYADSVK
164.	01F08	AIHGPSTLYADSVK
165.	01F09	AIHGHSTLYADSVK
166.	01F10	AIHGESTLYADSVK
167.	01F12	AIHGDSTLYADSVK
168.	01G01	AIHGDSTLYADSVK
169.	01G04	AIHGNSTLYADSVK
170.	01G06	AIHGFETLYADSVK
171.	01G08	AIHGFETLYADSVK
172.	01G09	AIHGFSTYYADSVK
173.	01G10	AIHGLSTLYADSVK
174.	01G11	AIHGASTLYADSVK

175.	01H01	AIHGQSTLYADSVK
176.	01H04	AIHGQSTLYADSVK
177.	01H05	AIHGTSTLYADSVK
178.	01H06	AIHGFETLYADSVK
179.	01H08	AIHGFSTVYADSVK
180.	01H09	AIHGNSTLYADSVK
181.	01H10	AIHGESTLYADSVK
182.	01H11	AIHGFSTLYADSVK
183.	02A04	AIHGKSTLYADSVK
184.	02A05	AIHGKSTLYADSVK
185.	02A07	AIHGNSTLYADSVK
186.	02A08	AIHGESTLYADSVK
187.	02A11	AIHGSSTLYADSVK
188.	02B01	AIHGRSTLYADSVK
189.	02B04	AIHGFSTIYADSVK
190.	02B05	AIHGTSTLYADSVK
191.	02B06	AIHGFSTLYADSVK
192.	02B07	AIHGHSTLYADSVK
193.	02B11	AIHGDSTLYADSVK
194.	02B12	AIHGFDTLYADSVK
195.	02C01	AIHGASTLYADSVK
196.	02C03	AIHGSSTLYADSVK
197.	02C05	AIHGFTTLYADSVK
198.	02C06	AIHGTSTLYADSVK
199.	02D06	AIHGFSTVYADSVK
200.	02D09	AIHGKSTLYADSVK
201.	02D11	AIHGESTLYADSVK
202.	02E03	AIHGPSTLYADSVK
203.	02E05	AIHGISTLYADSVK
204.	02E06	AIHGFSTFYADSVK
205.	02E09	AIHGGSTLYADSVK
206.	02F02	AIHGSSTLYADSVK
207.	02F03	AIHGSSTLYADSVK
208.	02F04	AIHGFSTLYADSVK
209.	02F05	AIHGNSTLYADSVK
210.	02F06	AIHGESTLYADSVK
211.	02F07	AIHGFSTLYADSVK
212.	02F11	AIHGTSTLYADSVK
213.	02F12	AIHGTSTLYADSVK
214.	02G01	AIHGFDTLYADSVK

215.	02G02	AIHGASTLYADSVK
216.	02G05	AIHGNSTLYADSVK
217.	02G06	AIHGNSTLYADSVK
218.	02G07	AIHGESTLYADSVK
219.	02G08	AIHGESTLYADSVK
220.	02G09	AIHGFSTLYADSVK
221.	02G11	AIHGSSTLYADSVK
222.	02H01	AIHGSSTLYADSVK
223.	02H04	AIHGNSTLYADSVK
224.	02H05	AIHGKSTLYADSVK
225.	02H06	AIHGSSTLYADSVK
226.	02H09	AIHGSSTLYADSVK
227.	02H11	AIHGESTLYADSVK
228.	01F07-M34Y	AIHGFSTLYADSVK
229.	01F01-M34G	AIHGFSTLYADSVK
230.	02G02-M34Y	AIHGASTLYADSVK
231.	02G02-M34G	AIHGASTLYADSVK
SEQ ID NO:	Name	CDR3
232.	01A01	VPWGDYHPRNVA
233.	01A02	VPWGDYHPRNVH
234.	01A03	VPWGDYHPRNVY
235.	01A04	VPWGRYHPRNVY
236.	01A05	VPWGDYHPRNVY
237.	01A06	VPWGDYHPRNVY
238.	01A07	VPWGDYHPGNVY
239.	01A08	VPWGDYHPRKVY
240.	01A09	VPWGSYHPRNVY
241.	01B01	VPWGDYHPRNVA
242.	01B02	VPWGDYHPRNVY
243.	01B03	VPWGDYHPRNVV
244.	01B04	VPWGDYHPRNVK
245.	01B05	VPWGDYHPGNVY
246.	01B06	VPWGEYHPRNVY
247.	01B07	VPWGIYHPRNVY
248.	01B08	VPWGRYHPRNVY
249.	01B09	VPWGDYHPGNVY
250.	01B12	VPWGDYHPRNVV
251.	01C01	VPWGDYHPGNVY
252.	01C02	VPWGRYHPRNVY
253.	01C04	VPWGDYHPRNVY

254.	01C05	VPWGDYHPGNVY
255.	01C06	VPWGKYHPRNVY
256.	01C07	VPWGSYHPRNVY
257.	01C08	VPWGDYHPRNVH
258.	01C10	VPWGYYHPRNVY
259.	01D02	VPWGDYHPGNVY
260.	01D03	VPWGDYHPRNVR
261.	01D04	VPWGDYHPRNVQ
262.	01D05	VPWGDYHPRNVY
263.	01D06	VPWGDYHPRNVT
264.	01D07	VPWGDYHPRNVN
265.	01D10	VPWGRYHPRNVY
266.	01E03	VPWGDYHPGNVY
267.	01E04	VPWGDYHPGNVY
268.	01E05	VPWGKYHPRNVY
269.	01E06	VPWGDYHPRNVY
270.	01E07	VPWGDYHPRNVQ
271.	01E08	VPWGDYHPGNVC
272.	01E10	VPWGDYHPRRVY
273.	01F02	VPWGRYHPRNVY
274.	01F03	VPWGTYHPRNVY
275.	01F04	VPWGDYHPGNVY
276.	01F05	VPWGRYHPRNVY
277.	01F07	VPWGDYHPGNVY
278.	01F08	VPWGDYHPTNVY
279.	01F09	VPWGRYHPRNVY
280.	01F10	VPWGDYHPRNVT
281.	01F12	VPWGRYHPRNVY
282.	01G01	VPWGDYHPRRVY
283.	01G04	VPWGDYHPRMVY
284.	01G06	VPWGDYHPRNVL
285.	01G08	VPWGDYHPGNVY
286.	01G09	VPWGRYHPRNVY
287.	01G10	VPWGAYHPRNVY
288.	01G11	VPWGDYHPRNVA
289.	01H01	VPWGDYHPQNVY
290.	01H04	VPWGDYHPRNVT
291.	01H05	VPWGRYHPRNVY
292.	01H06	VPWGDYHPGNVY
293.	01H08	VPWGDYHPGNVY

294.	01H09	VPWGDYHPGNVY
295.	01H10	VPWGDYHPRNVY
296.	01H11	VPWGDYHPGNVY
297.	02A04	VPWGDYHPSNVY
298.	02A05	VPWGDYHPGNVY
299.	02A07	VPWGDYHPREVY
300.	02A08	VPWGRYHPGNVY
301.	02A11	VPWGDYHPRVVY
302.	02B01	VPWGDYHPRNVM
303.	02B04	VPWGDYHPLNVY
304.	02B05	VPWGDYHPGNVY
305.	02B06	VPWGDYHPGNVY
306.	02B07	VPWGDYHPRNVT
307.	02B11	VPWGDYHPRNVS
308.	02B12	VPWGDYHPRNVY
309.	02C01	VPWGDYHPGNVY
310.	02C03	VPWGDYHPGNVY
311.	02C05	VPWGDYHPRNVT
312.	02C06	VPWGDYHPGNVY
313.	02D06	VPWGRYHPRNVY
314.	02D09	VPWGDYHPNNVY
315.	02D11	VPWGDYHPGNVY
316.	02E03	VPWGDYHPRNVT
317.	02E05	VPWGDYHPGNVY
318.	02E06	VPWGDYHPGNVY
319.	02E09	VPWGDYHPRNVA
320.	02F02	VPWGDYHPGNVY
321.	02F03	VPWGDYHPKNVY
322.	02F04	VPWGDYHPGNVY
323.	02F05	VPWGKYHPRNVY
324.	02F06	VPWGRYHPRNVY
325.	02F07	VPWGDYHPGNVY
326.	02F11	VPWGDYHPRNVQ
327.	02F12	VPWGDYHPGNVY
328.	02G01	VPWGDYHPRNVS
329.	02G02	VPWGDYHPGNVY
330.	02G05	VPWGDYHPGNVY
331.	02G06	VPWGDYHPGNVY
332.	02G07	VPWGDYHPRDVY
333.	02G08	VPWGDYHPRNVT

334.	02G09	VPWGDYHPRNVA
335.	02G11	VPWGDYHPRNVT
336.	02H01	VPWGDYHPRNVY
337.	02H04	VPWGDYHPRNVY
338.	02H05	VPWGDYHPRNVV
339.	02H06	VPWGDYHPRNVV
340.	02H09	VPWGDYHPGNVY
341.	02H11	VPWGDYHPRNVY
342.	01F07-M34Y	VPWGDYHPGNVY
343.	01F01-M34G	VPWGDYHPGNVY
344.	02G02-M34Y	VPWGDYHPGNVY
345.	02G02-M34G	VPWGDYHPGNVY

SEQ ID NO	Construct Name	VHH Sequences
346.	BH2T	EVQLVESGGGLVQPGRSLTLSCAASTNIFSI SPMGWYRQAPGKQRELVAAIHGFS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
347.	01A01	EVQLVESGGGLVQPGRSLTLSCAASTDIFSI SPMGWYRQAPGKQRELVAAIHGGS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVAWG QGTQVTVSS
348.	02E09	EVQLVESGGGLVQPGRSLTLSCAASTNDFSISPMGWYRQAPGKQRELVAAIHGGS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVAWG QGTQVTVSS
349.	01B03	EVQLVESGGGLVQPGRSLTLSCAASTNIFSKSPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVVWG QGTQVTVSS
350.	01B04	EVQLVESGGGLVQPGRSLTLSCAASTNDFSISPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVKKG QGTQVTVSS
351.	02H05	EVQLVESGGGLVQPGRSLTLSCAASTNQFSISPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVVWG QGTQVTVSS
352.	01A02	EVQLVESGGGLVQPGRSLTLSCAASTNIFSSSPMGWYRQAPGKQRELVAAIHGFS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVHWG QGTQVTVSS
353.	01A05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSSSPMGWYRQAPGKQRELVAAIHGFS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
354.	01B12	EVQLVESGGGLVQPGRSLTLSCAASTNIFSTSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVVWG QGTQVTVSS
355.	01G06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSRSPMGWYRQAPGKQRELVAAIHGFE TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVLWG QGTQVTVSS
356.	02C05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSESPMGWYRQAPGKQRELVAAIHGFT TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVTWG QGTQVTVSS
357.	02G09	EVQLVESGGGLVQPGRSLTLSCAASTNIFSDSPMGWYRQAPGKQRELVAAIHGFS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVAWG QGTQVTVSS
358.	01C08	EVQLVESGGGLVQPGRSLTLSCAASTNIFSNSPMGWYRQAPGKQRELVAAIHGGS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVHWG

SEQ ID NO	Construct Name	VHH Sequences
		QGTQVTVSS
359.	02B01	EVQLVESGGGLVQPGRSLTLSCAASNIFSNSPMGWYRQAPGKQRELVAAIHGSR TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV MWG QGTQVTVSS
360.	02E03	EVQLVESGGGLVQPGRSLTLSCAASNIFSNSPMGWYRQAPGKQRELVAAIHGSR TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV TWG QGTQVTVSS
361.	01D03	EVQLVESGGGLVQPGRSLTLSCAASNIFSNSPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV RWG QGTQVTVSS
362.	01D06	EVQLVESGGGLVQPGRSLTLSCAASNIFSRSPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV TWG QGTQVTVSS
363.	01H04	EVQLVESGGGLVQPGRSLTLSCAASNIFSKSPMGWYRQAPGKQRELVAAIHGQS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV TWG QGTQVTVSS
364.	02B07	EVQLVESGGGLVQPGRSLTLSCAASNIFSSSPMGWYRQAPGKQRELVAAIHGHS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV TWG QGTQVTVSS
365.	01A08	EVQLVESGGGLVQPGRSLTLSCAASNIFSSSPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS
366.	01B07	EVQLVESGGGLVQPGRSLTLSCAASNIFSRSPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG IYHPRNV YWG QGTQVTVSS
367.	01F03	EVQLVESGGGLVQPGRSLTLSCAASNIFSESPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG TYHPRNV YWG QGTQVTVSS
368.	02F05	EVQLVESGGGLVQPGRSLTLSCAASNIFSVSPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG KYHPRNV YWG QGTQVTVSS
369.	02H04	EVQLVESGGGLVQPGRSLTLSCAASNIFSVSPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS
370.	02A07	EVQLVESGGGLVQPGRSLTLSCAASNIFSKSPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS
371.	01D05	EVQLVESGGGLVQPGRSLTLSCAASNIFSDSPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS
372.	01E05	EVQLVESGGGLVQPGRSLTLSCAASNIFSRSPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG KYHPRNV YWG QGTQVTVSS
373.	01F02	EVQLVESGGGLVQPGRSLTLSCAASNIFSHSPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG RYHPRNV YWG QGTQVTVSS
374.	02C06	EVQLVESGGGLVQPGRSLTLSCAASNIFSTSPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS
375.	02F11	EVQLVESGGGLVQPGRSLTLSCAASNIFSTSPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV QWG QGTQVTVSS
376.	01E06	EVQLVESGGGLVQPGRSLTLSCAASNIFSLSPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS
377.	01A03	EVQLVESGGGLVQPGRSLTLSCAASNIFSI SPGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYMQNSLRPEDTALYYCNKVPWG DYHPRNV YWG QGTQVTVSS

SEQ ID NO	Construct Name	VHH Sequences
378.	02A11	EVQLVESGGGLVQPGRSLTLSCAASTNHFSISPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRVYWG QGTQVTVSS
379.	01D07	EVQLVESGGGLVQPGRSLTLSCAASTNIFASPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVNWG QGTQVTVSS
380.	01D10	EVQLVESGGGLVQPGRSLTLSCAASTNIFASPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
381.	01A07	EVQLVESGGGLVQPGRSLTLSCAASTNISSISPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
382.	02F12	EVQLVESGGGLVQPGRSLTLSCAASTNIESISPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
383.	02B05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSISPYGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
384.	01E04	EVQLVESGGGLVQPGRSLTLSCAASTNIASISPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
385.	02A05	EVQLVESGGGLVQPGRSLTLSCAASTNIASISPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
386.	02C03	EVQLVESGGGLVQPGRSLTLSCAASTNIASISPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
387.	01E03	EVQLVESGGGLVQPGRSLTLSCAASTNITSISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
388.	01H09	EVQLVESGGGLVQPGRSLTLSCAASTNIMSISPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
389.	02G05	EVQLVESGGGLVQPGRSLTLSCAASTNITSISPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
390.	01C01	EVQLVESGGGLVQPGRSLTLSCAASTNIVSISPMGWYRQAPGKQRELVAAIHGHS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
391.	01D02	EVQLVESGGGLVQPGRSLTLSCAASTNIVSISPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
392.	02D09	EVQLVESGGGLVQPGRSLTLSCAASTNVVSISPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPNNVYWG QGTQVTVSS
393.	02C01	EVQLVESGGGLVQPGRSLTLSCAASTNIISISPMGWYRQAPGKQRELVAAIHGAS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
394.	02G02	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPMGWYRQAPGKQRELVAAIHGAS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
395.	01B05	EVQLVESGGGLVQPGRSLTLSCAASTNITSISPMGWYRQAPGKQRELVAAIHGFE TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
396.	01G08	EVQLVESGGGLVQPGRSLTLSCAASTNIQSISPMGWYRQAPGKQRELVAAIHGFE TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
397.	01H06	EVQLVESGGGLVQPGRSLTLSCAASTSDFSISPMGWYRQAPGKQRELVAAIHGFE

SEQ ID NO	Construct Name	VHH Sequences
		TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
398.	01F04	EVQLVESGGGLVQPGRSLTLSCAASTNIDSISPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
399.	01H08	EVQLVESGGGLVQPGRSLTLSCAASTNIMSISPMGWYRQAPGKQRELVAAIHGFQ TVYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
400.	02F07	EVQLVESGGGLVQPGRSLTLSCAASTNIESISPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
401.	01C05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSSSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTARYYCNKVPWGDYHPGNVYWG QGTQVTVSS
402.	02F04	EVQLVESGGGLVQPGRSLTLSCAASTNIFSSSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
403.	02B06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSNSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
404.	01F07	EVQLVESGGGLVQPGRSLTLSCAASTNIFSTSPMGWYRQAPGKQRELVAAIHGFQ TIYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
405.	02B04	EVQLVESGGGLVQPGRSLTLSCAASTNIFSTSPMGWYRQAPGKQRELVAAIHGFQ TIYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
406.	01H11	EVQLVESGGGLVQPGRSLTLSCAASTNIFSTSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
407.	02E06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSDSPMGWYRQAPGKQRELVAAIHGFQ TFYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
408.	01E08	EVQLVESGGGLVQPGRSLTLSCAASTNIFSQSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVCWG QGTQVTVSS
409.	02A04	EVQLVESGGGLVQPGRSLTLSCAASTNIFSQSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG KGTQVTVSS
410.	02A08	EVQLVESGGGLVQPGRSLTLSCAASTNIFSRSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPGNVYWG QGTQVTVSS
411.	02E05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSRSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
412.	02H09	EVQLVESGGGLVQPGRSLTLSCAASTNIFSRSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
413.	02G06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSGSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
414.	01B09	EVQLVESGGGLVQPGRSLTLSCAASTNIFSIYPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
415.	02F03	EVQLVESGGGLVQPGRSLTLSCAASTNIFSIYPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
416.	02F02	EVQLVESGGGLVQPGRSLTLSCAASTNIFSKSPMGWYRQAPGKQRELVAAIHGFQ TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS

SEQ ID NO	Construct Name	VHH Sequences
		QGTQVTVSS
417.	02H01	EVQLVESGGGLVQPGRSLTLSCAASTNIFSKSPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
418.	01G10	EVQLVESGGGLVQPGRSLTLSCAASTNEFSISPMGWYRQAPGKQRELVAAIHGSL TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGAYHPRNVYWG QGTQVTVSS
419.	02D11	EVQLVESGGGLVQPGRSLTLSCAASTNEFSISPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
420.	01B01	EVQLVESGGGLVQPGRSLTLSCAASTNIPISPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVAWG QGTQVTVSS
421.	01G11	EVQLVESGGGLVQPGRSLTLSCAASTNIPISPMGWYRQAPGKQRELVAAIHGAS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVAWG QGTQVTVSS
422.	01H10	EVQLVESGGGLVQPGRSLTLSCAASTNIPISPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
423.	01C04	EVQLVESGGGLVQPGRSLTLSCAASTNIPISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
424.	01D04	EVQLVESGGGLVQPGRSLTLSCAASTNITSISPMGWYRQAPGKQRELVAAIHGV TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVQWG QGTQVTVSS
425.	01E07	EVQLVESGGGLVQPGRSLTLSCAASTNIPISPMGWYRQAPGKQRELVAAIHQGS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVQWG QGTQVTVSS
426.	02B11	EVQLVESGGGLVQPGRSLTLSCAASTNIVSISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVSWG QGTQVTVSS
427.	01F10	EVQLVESGGGLVQPGRSLTLSCAASTNIFSIISPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVTWG QGTQVTVSS
428.	02G08	EVQLVESGGGLVQPGRSLTLSCAASTNIDSISPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVTWG QGTQVTVSS
429.	02G11	EVQLVESGGGLVQPGRSLTLSCAASTNIDSISPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVTWG QGTQVTVSS
430.	02H06	EVQLVESGGGLVQPGRSLTLSCAASTNIRSISPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVVWG QGTQVTVSS
431.	01B02	EVQLVESGGGLVQPGRSLTLSCAASTNITSISPMGWYRQAPGKQRELVAAIISGFS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNEVPWGDYHPRNVYWG QGTQVTVSS
432.	02H11	EVQLVESGGGLVQPGRSLTLSCAASTNITSISPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
433.	01F08	EVQLVESGGGLVQPGRSLTLSCAASTNITSVSPMGWYRQAPGKQRELVAAIHGPS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPTNVYWG QGTQVTVSS
434.	01H01	EVQLVESGGGLVQPGRSLTLSCAASTNIGSISPMGWYRQAPGKQRELVAAIHQGS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPQNVYWG QGTQVTVSS
435.	01E10	EVQLVESGGGLVQPGRSLTLSCAASTNIESISPMGWYRQAPGKQRELVAAIHGKS TLYADSVKGRFTISRDNAKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRRVYWG

SEQ ID NO	Construct Name	VHH Sequences
		QGTQVTVSS
436.	01G01	EVQLVESGGGLVQPGRSLTLSCAASTNIVSISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPRRVYWG QGTQVTVSS
437.	01G04	EVQLVESGGGLVQPGRSLTLSCAASTNIDSISPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPRMVYWG QGTQVTVSS
438.	01A04	EVQLVESGGGLVQPGRSLTLSCAASTNIFMISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
439.	01F12	EVQLVESGGGLVQPGRSLTLSCAASTNIFRISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
440.	01B06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGEYHPRNVYWG QGTQVTVSS
441.	01C06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSISPMGWYRQAPGKQRELVAAIHGDS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWKGYHPRNVYWG QGTQVTVSS
442.	01B08	EVQLVESGGGLVQPGRSLTLSCAASTNIESISPMGWYRQAPGKQRELVAAIHGSS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
443.	01C02	EVQLVESGGGLVQPGRSLTLSCAASTNIESISPMGWYRQAPGKQRELVAAIHGNS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
444.	01C10	EVQLVESGGGLVQPGRSLTLSCAASTNISSISPMGWYRQAPGKQRELVAAIHGFS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGYHYHPRNVYWG QGTQVTVSS
445.	01F09	EVQLVESGGGLVQPGRSLTLSCAASTNISSISPMGWYRQAPGKQRELVAAIHGHS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
446.	02D06	EVQLVESGGGLVQPGRSLTLSCAASTNISSISPMGWYRQAPGKQRELVAAIHGFS TVYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
447.	01A06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSIRPMGWYRQAPGKQRELVAAIHGFS TVYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
448.	01C07	EVQLVESGGGLVQPGRSLTLSCAASTNIFSIPMGWYRQAPGKQRELVAAIHGFS TYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGSYHPRNVYWG QGTQVTVSS
449.	01G09	EVQLVESGGGLVQPGRSLTLSCAASTNIFNISPMGWYRQAPGKQRELVAAIHGFS TYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
450.	01F05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSSSPMGWYRQAPGKQRELVAAIHGFS TWYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
451.	02B12	EVQLVESGGGLVQPGRSLTLSCAASTNISSISPMGWYRQAPGKQRELVAAIHGFD TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPRNVYWG QGTQVTVSS
452.	02G01	EVQLVESGGGLVQPGRSLTLSCAASTNIFSINPMGWYRQAPGKQRELVAAIHGFD TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGDYHPRNVSWG QGTQVTVSS
453.	01A09	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPMGWYRQAPGKQRELVAAIHGSR TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGSYHPRNVYWG QGTQVTVSS
454.	01H05	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPMGWYRQAPGKQRELVAAIHGTS TLYADSVKGRFTISRDNAKNSIYLMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS

SEQ ID NO	Construct Name	VHH Sequences
455.	02F06	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNANKNSIYLQMNSLRPEDTALYYCNKVPWGRYHPRNVYWG QGTQVTVSS
456.	02G07	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPMGWYRQAPGKQRELVAAIHGES TLYADSVKGRFTISRDNANKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPRDVIYWG QGTQVTVSS
457.	01F07- M34Y	EVQLVESGGGLVQPGRSLTLSCAASTNIFSTSPYGWYRQAPGKQRELVAAIHGFS TIYADSVKGRFTISRDNANKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
458.	01F01- M34G	EVQLVESGGGLVQPGRSLTLSCAASTNIFSTSPGGWYRQAPGKQRELVAAIHGFS TIYADSVKGRFTISRDNANKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
459.	02G02- M34Y	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPYGWYRQAPGKQRELVAAIHGAS TLYADSVKGRFTISRDNANKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
460.	02G02- M34G	EVQLVESGGGLVQPGRSLTLSCAASTNIFSITPGGWYRQAPGKQRELVAAIHGAS TLYADSVKGRFTISRDNANKNSIYLQMNSLRPEDTALYYCNKVPWGDYHPGNVYWG QGTQVTVSS
461.	F1	EVQLVESGGGLVQPGRSLTLSCAAS
462.	F1	EVQLVESGGGLVQPGRSLTLSCVAS
463.	F2	WYRQAPGKQRELVA
464.	F3	GRFTISRDNANKNSIYLQMNSLRPEDTALYYCNK
465.	F3	GRFTISRDNANKNSIYLQMNSLRPEDTALYYCNE
466.	F4	WGQGTQVTVSS
467.	F4	WGKGTQVTVSS
468.	Human BCMA	MLQMAGQCSQNEYFDSLHACIPCLRCSSNTPPLTCQRYCNASVTNSVKGTNAI LWTCLGLSLIISLAVFVLMFLLRKINSEPLKDEFKNTGSGLLGMANIDLEKSRGTG DEIILPRGLEYTVEECTCEDCIKSKPKVDSDFCFPLPAMEEGATILVTTKTNDYCN KSLPAALSATEIEKSISAR
469.	Murine BCMA	MAQQCFHSEYFDSLHACKPCHLRCSNPPATCQPYCDPSVTSSVKGTYYTLWIFL GLTLVLSLALFTISFLLRKMNPEALKDEPQSPGQLDGSQALDKADTELTRIRAGD DRIFPRSLLEYTVEECTCEDCVKSKPKGSDHFFPLPAMEEGATILVTTKTGDYGN SSVPTALQSVGMGEKPTHTR
470.	Cynomolgus BCMA	MLQMARQCSQNEYFDSLHDCCKPCQLRCSSTPPLTCQRYCNASMTNSVKGMNAIL WTCLGLSLIISLAVFVLTFLLRKMSSEPLKDEFKNTGSGLLGMANIDLEKGRGTG EIVLPRGLEYTVEECTCEDCIKNKPKVDSDFCFPLPAMEEGATILVTTKTNDYCN SLSAALSVTEIEKSISAR
471.	6x His tag	His-His-His-His-His-His
472.	253BH10 (llama anti-BCMA antibody)	QVQLVESGGGLVQPGESLRSLSCAASTNIFSISPMGWYRQAPGKQRELVAAIHGFS TLYADSVKGRFTISRDNANKNTIYLQMNSLKPEDTAVYYCNKVPWGDYHPRNVYWG QGTQVTVSS
473.	253BH10 CDR1	TNIFSISPMG
474.	253BH10 CDR2	AIHGFSTLYADSVK
475.	253BH10	VPWGDYHPRNVY

SEQ ID NO	Construct Name	VHH Sequences
	CDR3	

CLAIMS

What is claimed:

1. A single domain B cell maturation agent (BCMA) binding protein, wherein the single domain BCMA binding protein comprises a complementarity determining region 1 (CDR1), a CDR2, and a CDR3, and wherein:

- (a) the CDR1 has the amino acid sequence of SEQ ID NO: 11, the CDR2 has the amino acid sequence of SEQ ID NO: 125, and the CDR3 has the amino acid sequence of SEQ ID NO: 239;
- (b) the CDR1 has the amino acid sequence of SEQ ID NO: 95, the CDR2 has the amino acid sequence of SEQ ID NO: 209, and the CDR3 has the amino acid sequence of SEQ ID NO: 323;
- (c) the CDR1 has the amino acid sequence of SEQ ID NO: 84, the CDR2 has the amino acid sequence of SEQ ID NO: 198, and the CDR3 has the amino acid sequence of SEQ ID NO: 312;
- (d) the CDR1 has the amino acid sequence of SEQ ID NO: 41, the CDR2 has the amino acid sequence of SEQ ID NO: 155, and the CDR3 has the amino acid sequence of SEQ ID NO: 269;
- (e) the CDR1 has the amino acid sequence of SEQ ID NO: 10, the CDR2 has the amino acid sequence of SEQ ID NO: 124, and the CDR3 has the amino acid sequence of SEQ ID NO: 238;
- (f) the CDR1 has the amino acid sequence of SEQ ID NO: 99, the CDR2 has the amino acid sequence of SEQ ID NO: 213, and the CDR3 has the amino acid sequence of SEQ ID NO: 327;
- (g) the CDR1 has the amino acid sequence of SEQ ID NO: 76, the CDR2 has the amino acid sequence of SEQ ID NO: 190, and the CDR3 has the amino acid sequence of SEQ ID NO: 304;
- (h) the CDR1 has the amino acid sequence of SEQ ID NO: 39, the CDR2 has the amino acid sequence of SEQ ID NO: 153, and the CDR3 has the amino acid sequence of SEQ ID NO: 267;
- (i) the CDR1 has the amino acid sequence of SEQ ID NO: 70, the CDR2 has the amino acid sequence of SEQ ID NO: 184, and the CDR3 has the amino acid sequence of SEQ ID NO: 298;
- (j) the CDR1 has the amino acid sequence of SEQ ID NO: 82, the CDR2 has the amino acid sequence of SEQ ID NO: 196, and the CDR3 has the amino acid sequence of SEQ ID NO: 310;

- (k) the CDR1 has the amino acid sequence of SEQ ID NO: 38, the CDR2 has the amino acid sequence of SEQ ID NO: 152, and the CDR3 has the amino acid sequence of SEQ ID NO: 266;
- (l) the CDR1 has the amino acid sequence of SEQ ID NO: 66, the CDR2 has the amino acid sequence of SEQ ID NO: 180, and the CDR3 has the amino acid sequence of SEQ ID NO: 294;
- (m) the CDR1 has the amino acid sequence of SEQ ID NO: 102, the CDR2 has the amino acid sequence of SEQ ID NO: 216, and the CDR3 has the amino acid sequence of SEQ ID NO: 330;
- (n) the CDR1 has the amino acid sequence of SEQ ID NO: 34, the CDR2 has the amino acid sequence of SEQ ID NO: 137, and the CDR3 has the amino acid sequence of SEQ ID NO: 251;
- (o) the CDR1 has the amino acid sequence of SEQ ID NO: 42, the CDR2 has the amino acid sequence of SEQ ID NO: 145, and the CDR3 has the amino acid sequence of SEQ ID NO: 259;
- (p) the CDR1 has the amino acid sequence of SEQ ID NO: 81, the CDR2 has the amino acid sequence of SEQ ID NO: 195, and the CDR3 has the amino acid sequence of SEQ ID NO: 309;
- (q) the CDR1 has the amino acid sequence of SEQ ID NO: 101, the CDR2 has the amino acid sequence of SEQ ID NO: 215, and the CDR3 has the amino acid sequence of SEQ ID NO: 329;
- (r) the CDR1 has the amino acid sequence of SEQ ID NO: 17, the CDR2 has the amino acid sequence of SEQ ID NO: 131, and the CDR3 has the amino acid sequence of SEQ ID NO: 245;
- (s) the CDR1 has the amino acid sequence of SEQ ID NO: 57, the CDR2 has the amino acid sequence of SEQ ID NO: 171, and the CDR3 has the amino acid sequence of SEQ ID NO: 285;
- (t) the CDR1 has the amino acid sequence of SEQ ID NO: 64, the CDR2 has the amino acid sequence of SEQ ID NO: 178, and the CDR3 has the amino acid sequence of SEQ ID NO: 292;
- (u) the CDR1 has the amino acid sequence of SEQ ID NO: 47, the CDR2 has the amino acid sequence of SEQ ID NO: 161, and the CDR3 has the amino acid sequence of SEQ ID NO: 275;
- (v) the CDR1 has the amino acid sequence of SEQ ID NO: 65, the CDR2 has the amino acid sequence of SEQ ID NO: 179, and the CDR3 has the amino acid sequence of SEQ ID NO: 293;

- (w) the CDR1 has the amino acid sequence of SEQ ID NO: 97, the CDR2 has the amino acid sequence of SEQ ID NO: 211, and the CDR3 has the amino acid sequence of SEQ ID NO: 325;
- (x) the CDR1 has the amino acid sequence of SEQ ID NO: 26, the CDR2 has the amino acid sequence of SEQ ID NO: 140, and the CDR3 has the amino acid sequence of SEQ ID NO: 254;
- (y) the CDR1 has the amino acid sequence of SEQ ID NO: 94, the CDR2 has the amino acid sequence of SEQ ID NO: 208, and the CDR3 has the amino acid sequence of SEQ ID NO: 322;
- (z) the CDR1 has the amino acid sequence of SEQ ID NO: 77, the CDR2 has the amino acid sequence of SEQ ID NO: 191, and the CDR3 has the amino acid sequence of SEQ ID NO: 305;
- (aa) the CDR1 has the amino acid sequence of SEQ ID NO: 49, the CDR2 has the amino acid sequence of SEQ ID NO: 163, and the CDR3 has the amino acid sequence of SEQ ID NO: 277;
- (bb) the CDR1 has the amino acid sequence of SEQ ID NO: 68, the CDR2 has the amino acid sequence of SEQ ID NO: 182, and the CDR3 has the amino acid sequence of SEQ ID NO: 296;
- (cc) the CDR1 has the amino acid sequence of SEQ ID NO: 90, the CDR2 has the amino acid sequence of SEQ ID NO: 204, and the CDR3 has the amino acid sequence of SEQ ID NO: 318;
- (dd) the CDR1 has the amino acid sequence of SEQ ID NO: 43, the CDR2 has the amino acid sequence of SEQ ID NO: 157, and the CDR3 has the amino acid sequence of SEQ ID NO: 271;
- (ee) the CDR1 has the amino acid sequence of SEQ ID NO: 89, the CDR2 has the amino acid sequence of SEQ ID NO: 203, and the CDR3 has the amino acid sequence of SEQ ID NO: 317;
- (ff) the CDR1 has the amino acid sequence of SEQ ID NO: 112, the CDR2 has the amino acid sequence of SEQ ID NO: 226, and the CDR3 has the amino acid sequence of SEQ ID NO: 340;
- (gg) the CDR1 has the amino acid sequence of SEQ ID NO: 103, the CDR2 has the amino acid sequence of SEQ ID NO: 217, and the CDR3 has the amino acid sequence of SEQ ID NO: 331;
- (hh) the CDR1 has the amino acid sequence of SEQ ID NO: 21, the CDR2 has the amino acid sequence of SEQ ID NO: 135, and the CDR3 has the amino acid sequence of SEQ ID NO: 249;

(ii) the CDR1 has the amino acid sequence of SEQ ID NO: 92, the CDR2 has the amino acid sequence of SEQ ID NO: 206, and the CDR3 has the amino acid sequence of SEQ ID NO: 320;

(jj) the CDR1 has the amino acid sequence of SEQ ID NO: 87, the CDR2 has the amino acid sequence of SEQ ID NO: 201, and the CDR3 has the amino acid sequence of SEQ ID NO: 315; or

(kk) the CDR1 has the amino acid sequence of SEQ ID NO: 60, the CDR2 has the amino acid sequence of SEQ ID NO: 174, and the CDR3 has the amino acid sequence of SEQ ID NO: 288.

2. The single domain B cell maturation agent (BCMA) binding protein of claim 1, wherein the single domain BCMA binding protein comprises a sequence of SEQ ID NO: 365, 368, 374, 376, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 406, 407, 408, 411, 412, 413, 414, 416, 419, or 421.

3. The single domain B cell maturation agent (BCMA) binding protein of claim 2, wherein the single domain BCMA binding protein comprises the sequence of SEQ ID NO: 383.

4. The single domain BCMA binding protein of any one of claims 1-3, that is human, humanized, affinity matured, or a combination thereof.

5. The single domain BCMA binding protein of any one of claims 1-4, wherein the single domain BCMA binding protein further comprises a Fc domain.

6. The single domain BCMA binding protein of any one of claims 1-5, wherein the single domain BCMA binding protein further comprises an anti-cancer agent.

7. The single domain BCMA binding protein of claim 6, wherein the anti-cancer agent is conjugated to the single domain BCMA binding protein.

8. A multispecific binding protein comprising the single domain BCMA binding protein according to any one of claims 1-7, a human serum albumin binding domain, and a CD3 binding domain.

9. The multispecific binding protein of claim 8, comprising a domain order of H2N-(C)-(A)-(B)-COOH, wherein (C) is the CD3 binding domain, (A) is the human serum albumin binding domain, and (B) is the single domain BCMA binding protein.

10. A method for treating or ameliorating a B cell lineage cancer expressing BCMA in a subject in need thereof, comprising administering to the subject a single domain BCMA binding protein of any one of claims 1-7 or a multispecific binding protein according to claim 8 or 9.

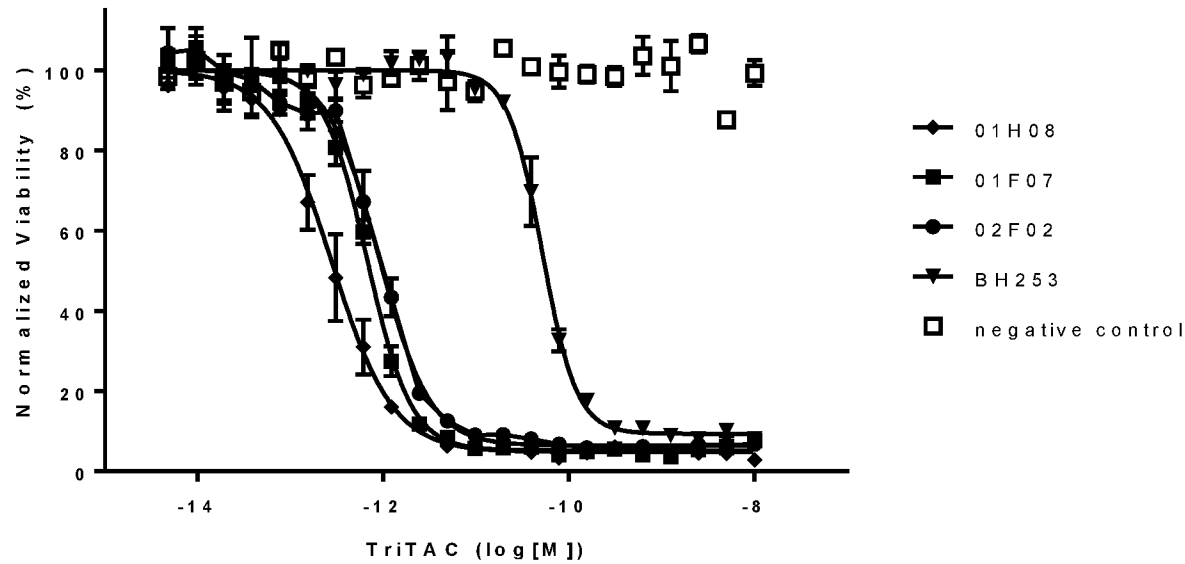
11. Use of a single domain BCMA binding protein of any one of claims 1-7 or a multispecific binding protein according to claim 8 or 9, in the manufacture of a medicament for treating or ameliorating a B cell lineage cancer expressing BCMA in a subject in need thereof.

12. The method of claim 10, or the use of claim 11, wherein the B cell lineage cancer is a primary cancer or a metastatic cancer.

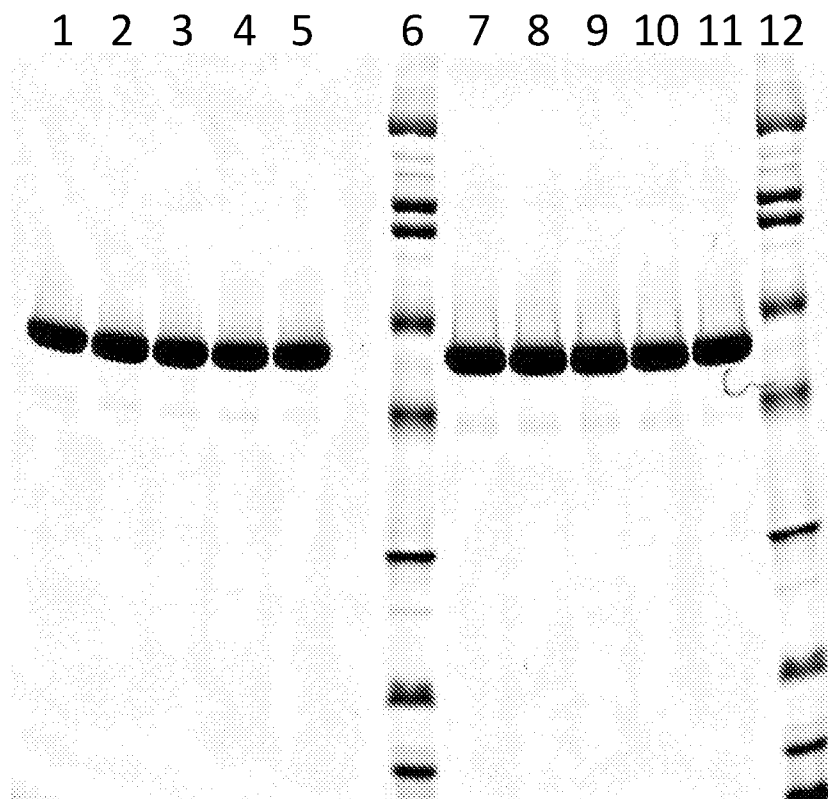
13. The method or use of any one of claims 10 to 12, wherein the B cell lineage cancer is a multiple myeloma, a leukemia, or a lymphoma.

FIG. 1

Redirected Killing of EJM Cells by Purified Human T Cells



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FIG. 2**SDS-PAGE OF PURIFIED BCMA TARGETING TRISPECIFIC PROTEINS**

Lane 1: 01F07-M34Y TriTAC non-reduced
Lane 2: 01F07-M34G-TriTAC non-reduced
Lane 3: 02B05 TriTAC non-reduced
Lane 4: 02G02-M34Y TriTAC non-reduced
Lane 5: 02G02 M34G TriTAC non-reduced
Lane 6: Broad Range SDS-PAGE Standard (Bio-Rad #1610317)
Lane 7: 01F07-M34Y TriTAC non-reduced
Lane 8: 01F07-M34G-TriTAC non-reduced
Lane 9: 02B05 TriTAC non-reduced
Lane 10: 02G02-M34Y TriTAC non-reduced
Lane 11: 02G02 M34G TriTAC non-reduced
Lane 12: Broad Range SDS-PAGE Standard (Bio-Rad #1610317)

FIG. 3A

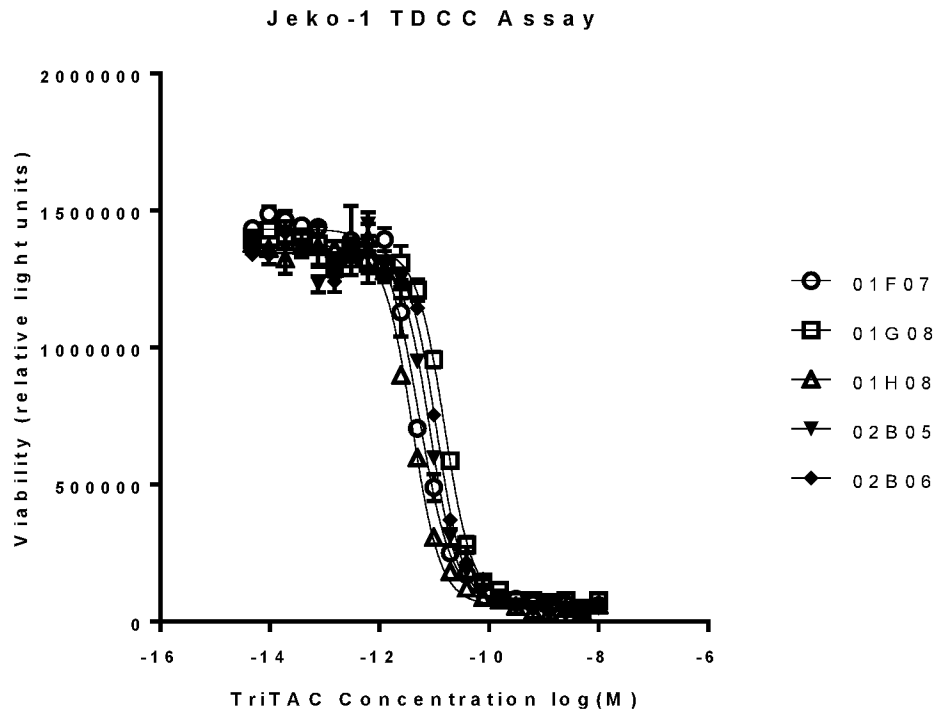


FIG. 3B

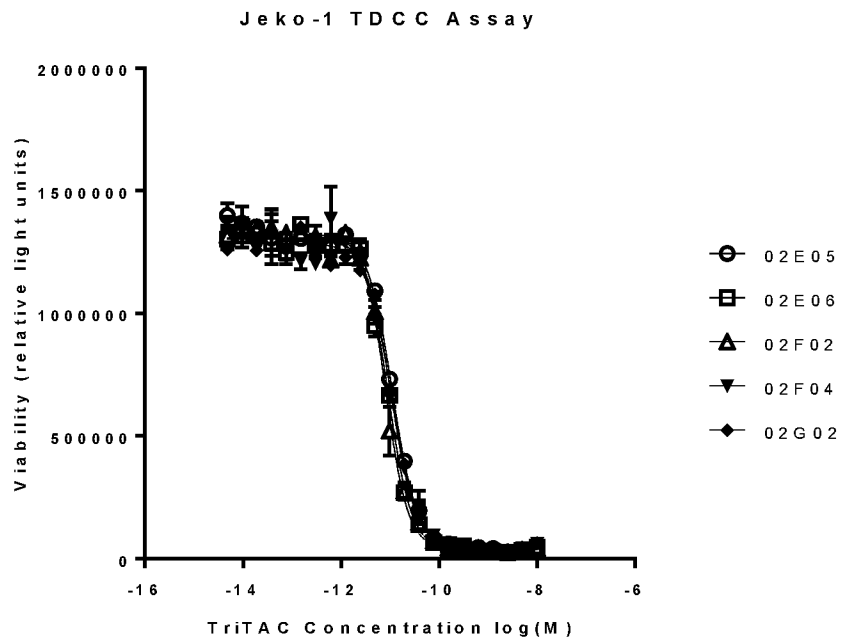


FIG. 3C

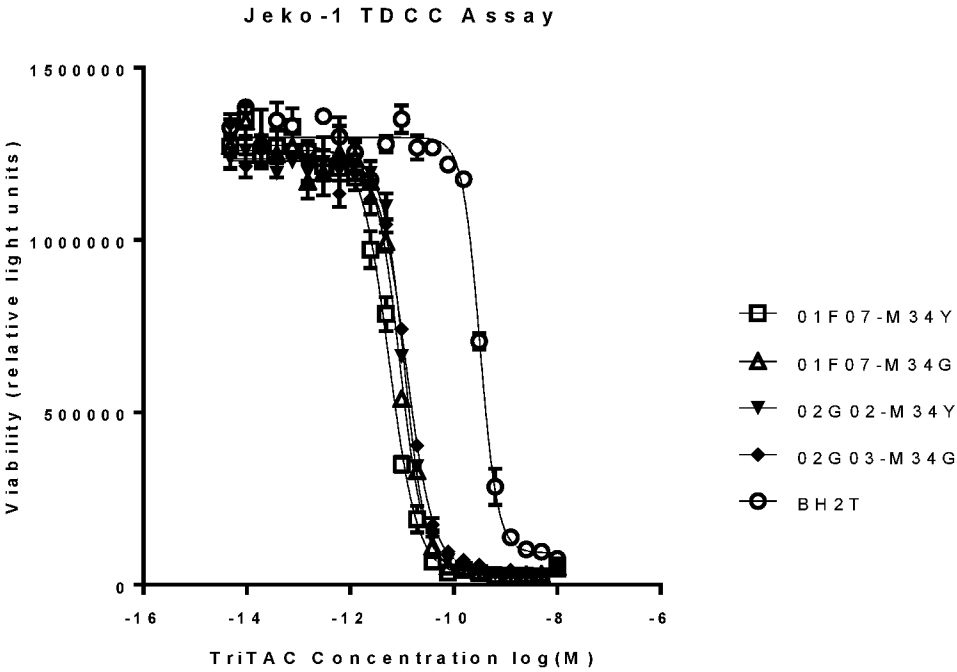


FIG. 3D

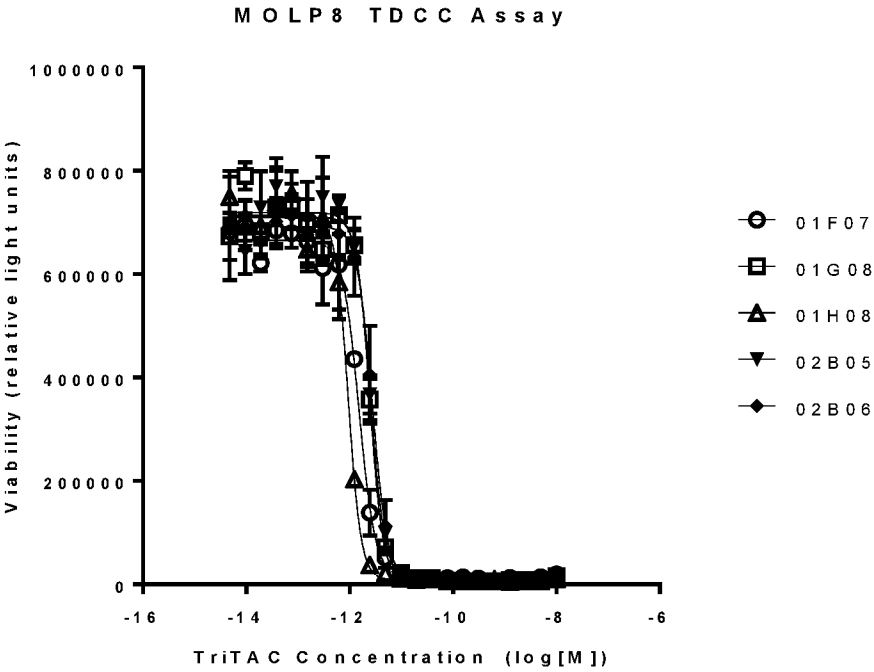


FIG. 3E

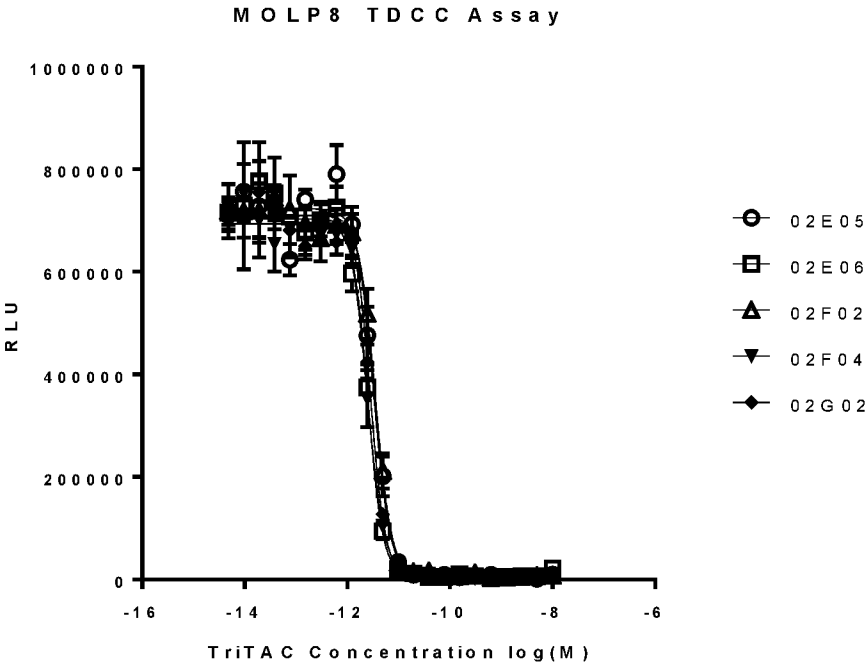


FIG. 3F

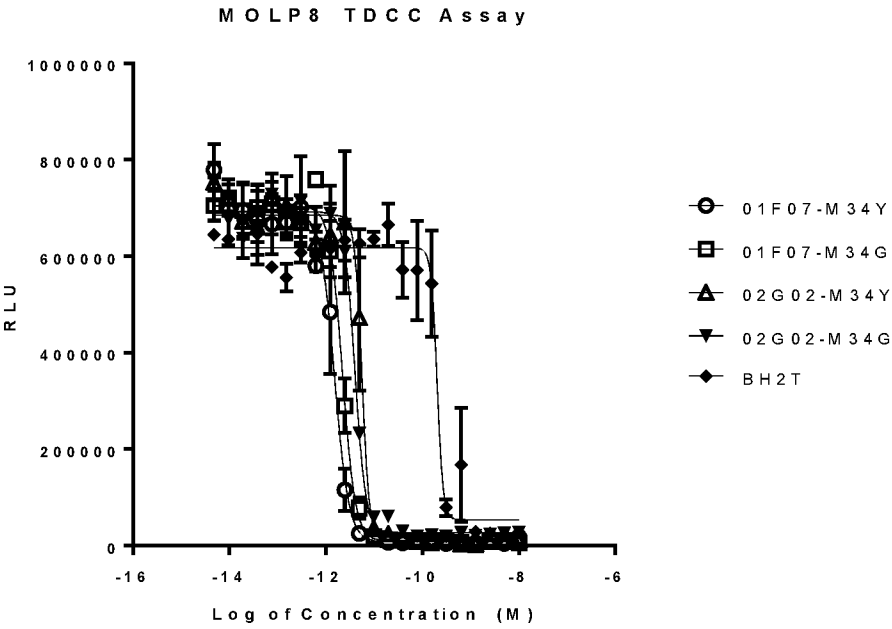


FIG. 3G

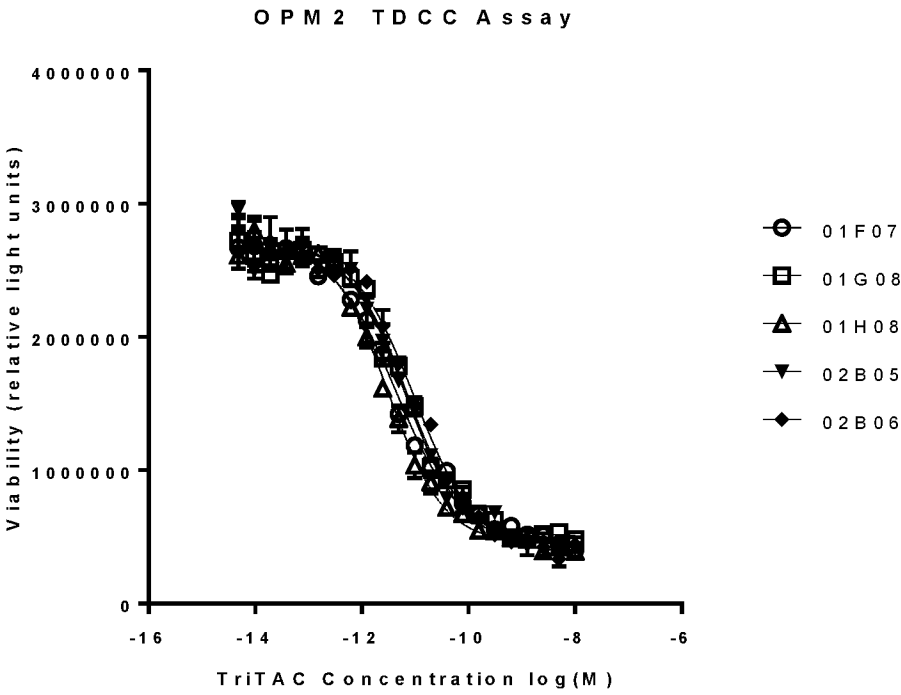


FIG. 3H

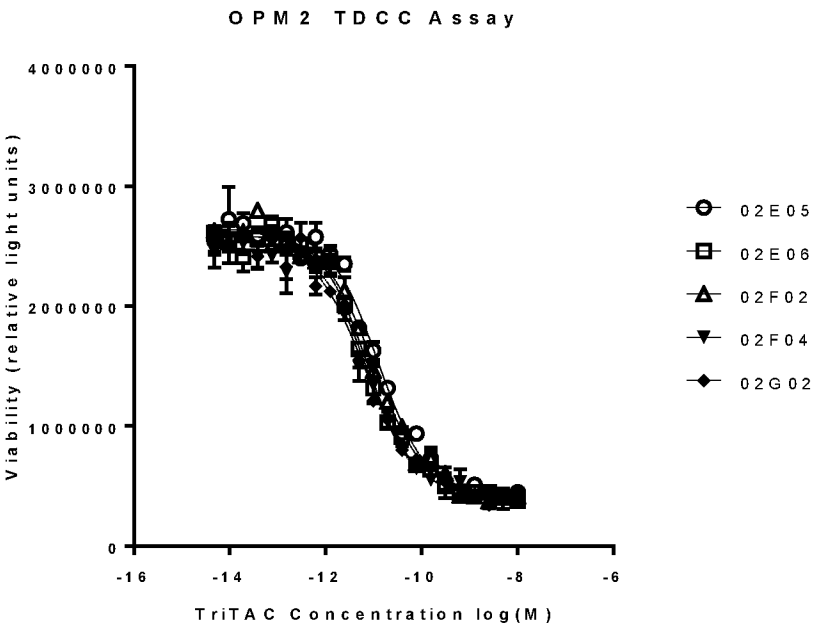


FIG. 3I

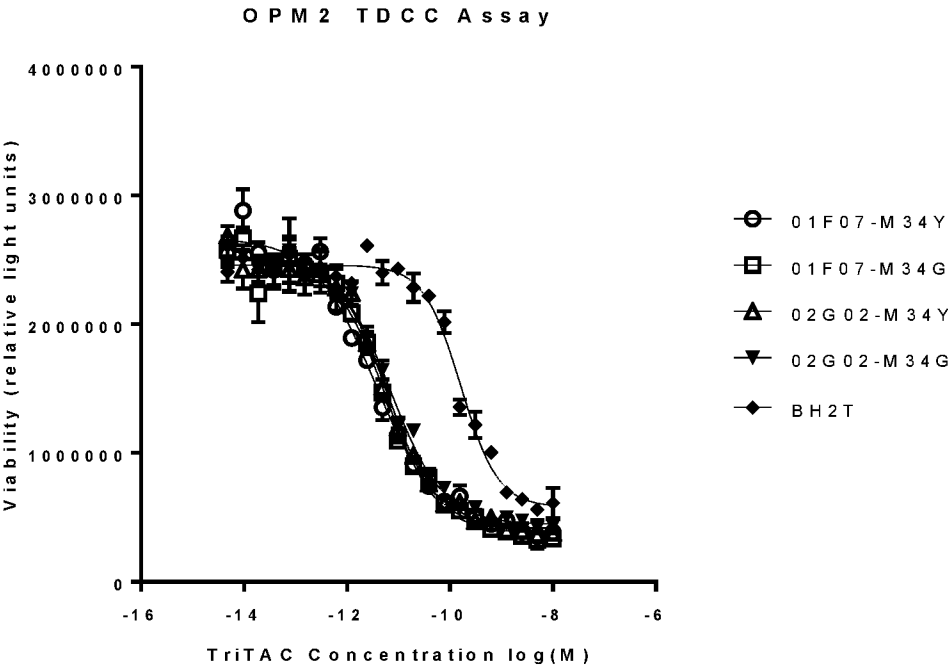


FIG. 4A

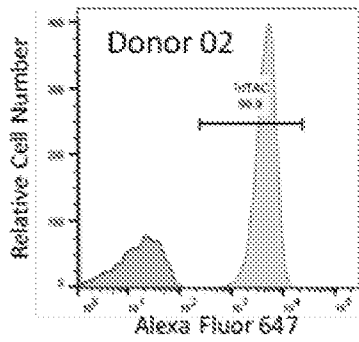
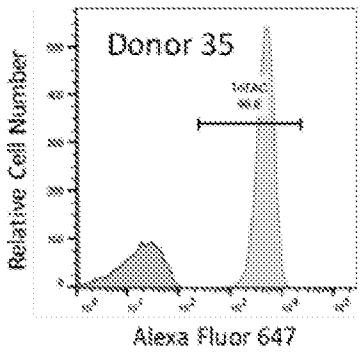


FIG. 4B



BCMA Trispecific Protein
Secondary Control

FIG. 4C

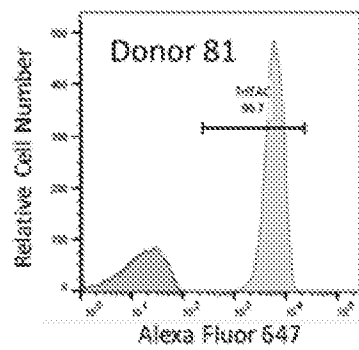
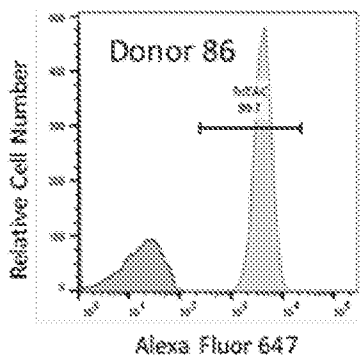


FIG. 4D



BCMA Trispecific Protein
Secondary Control

FIG. 5A

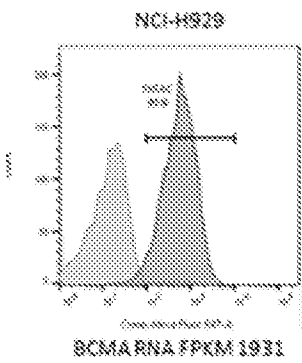


FIG. 5B

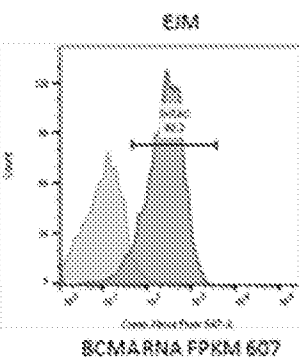
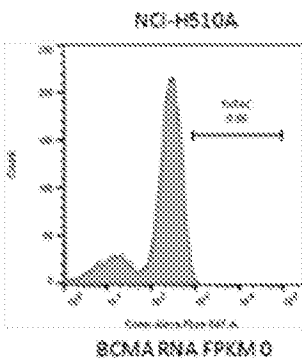


FIG. 5C



BCMA Trispecific Protein
GFP Trispecific Protein

FIG. 5D

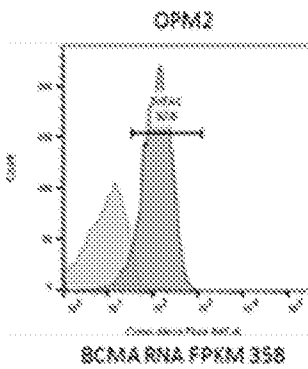


FIG. 5E

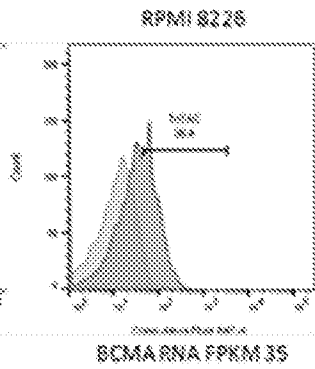
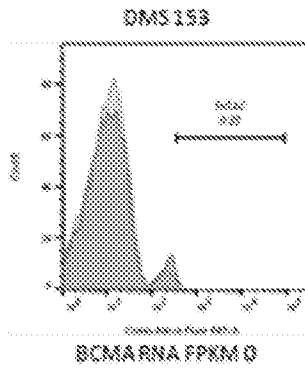
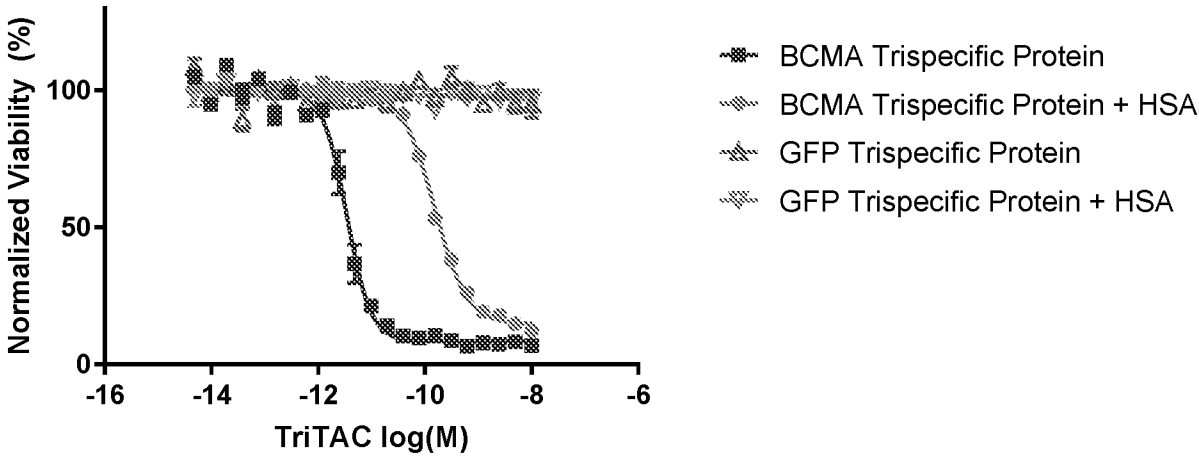


FIG. 5F



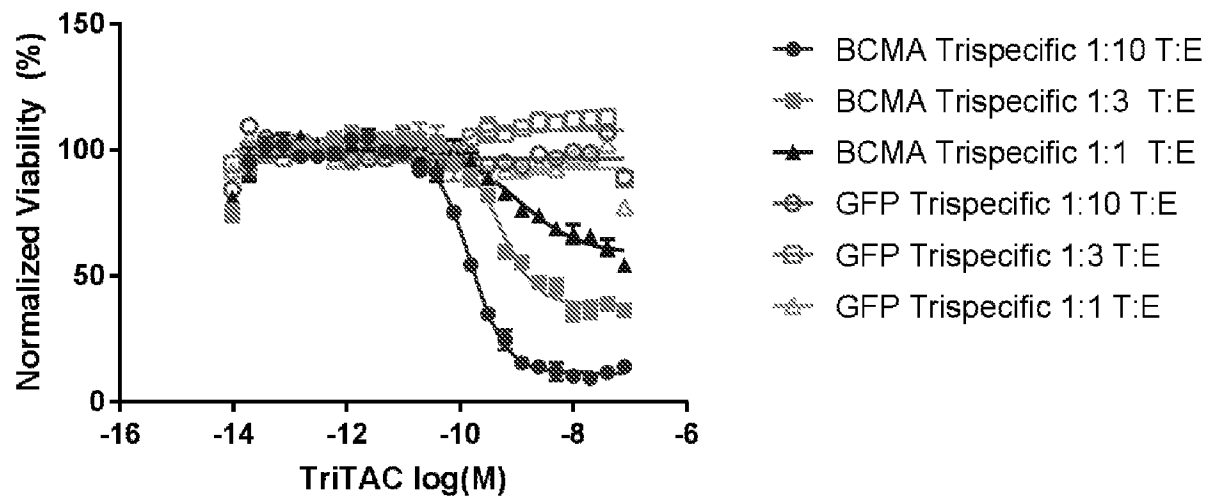
BCMA Trispecific Protein
GFP Trispecific Protein

FIG. 6



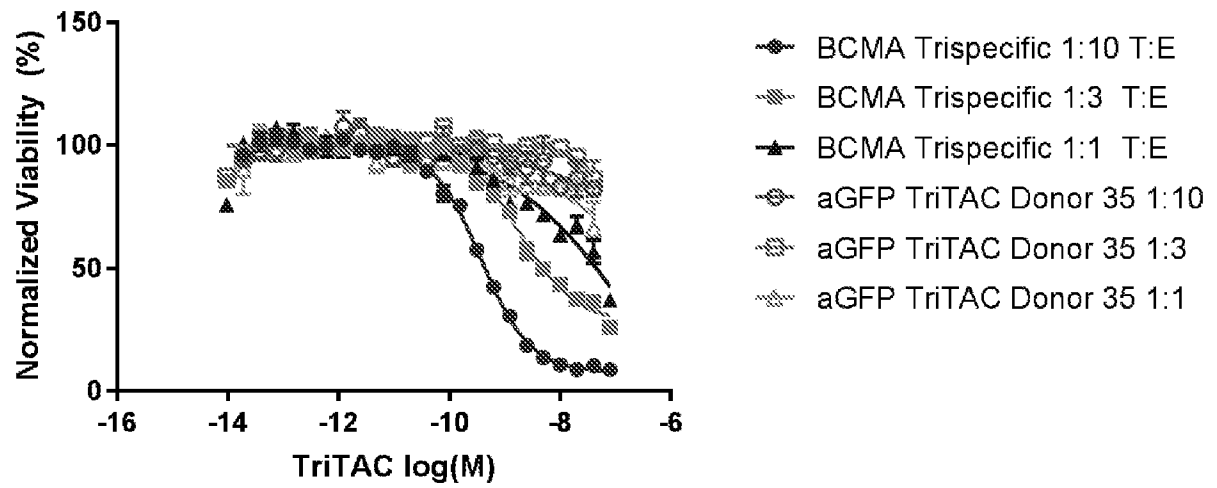
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FIG. 7



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FIG. 8



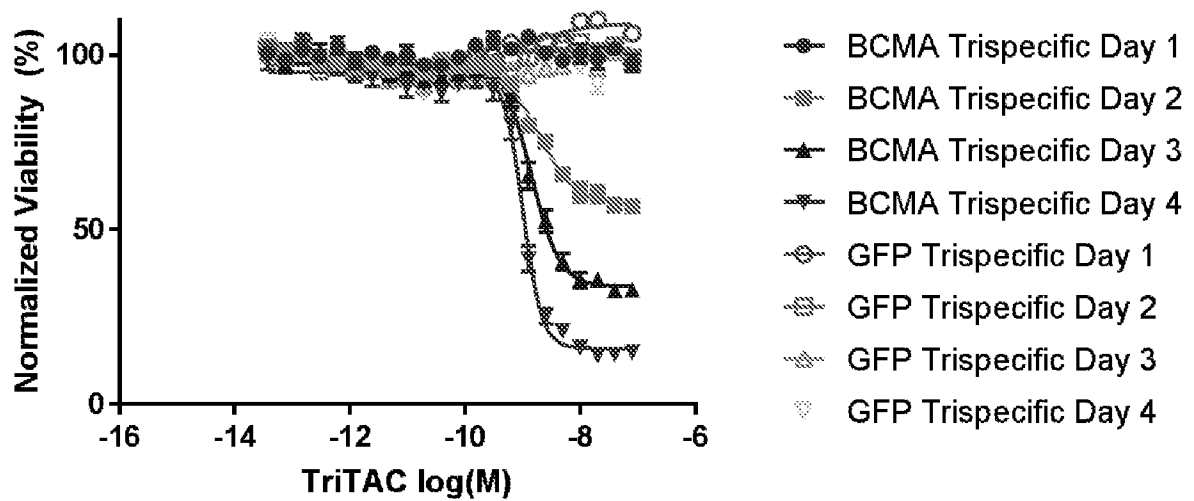


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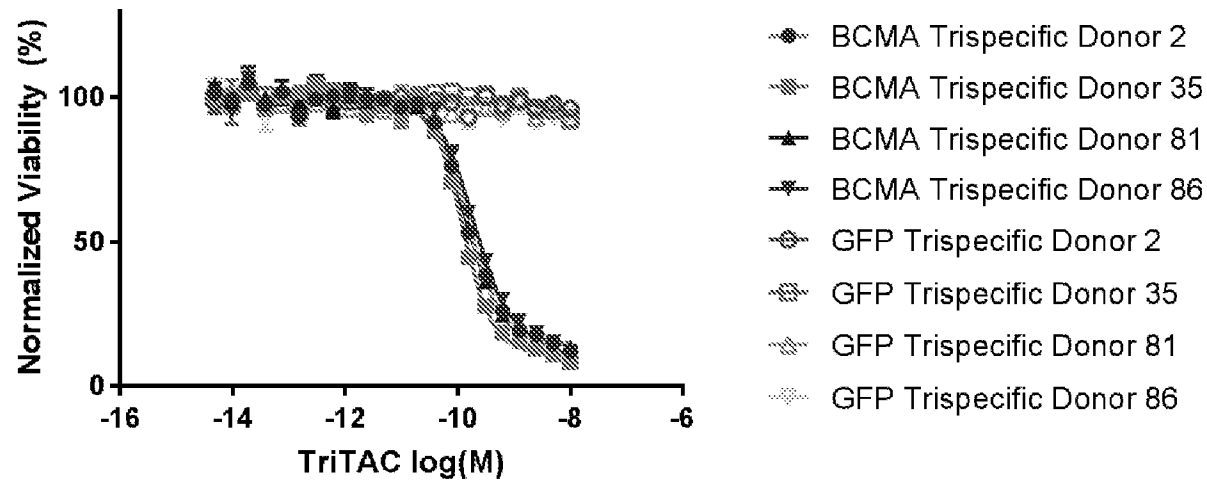
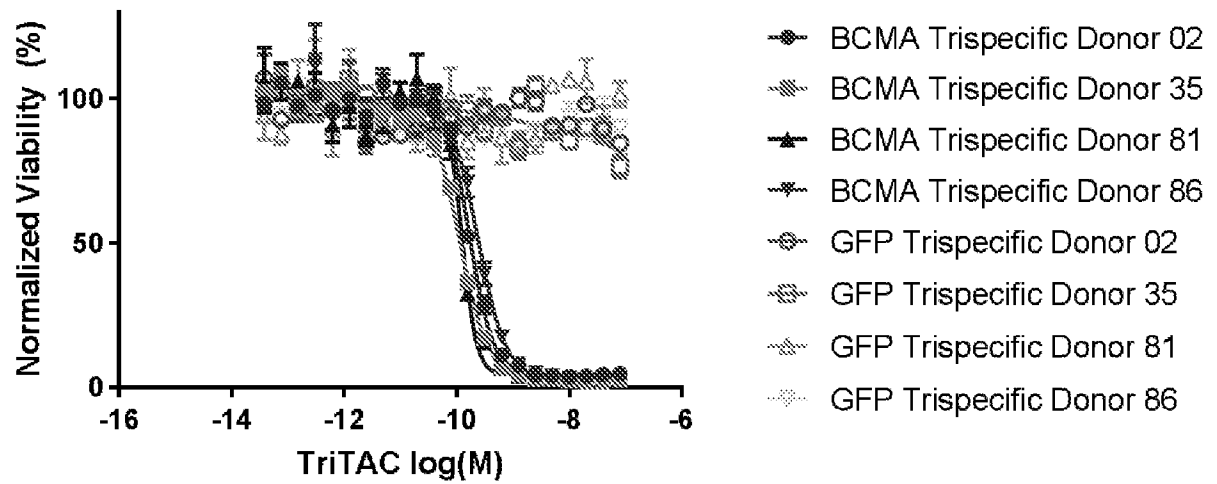
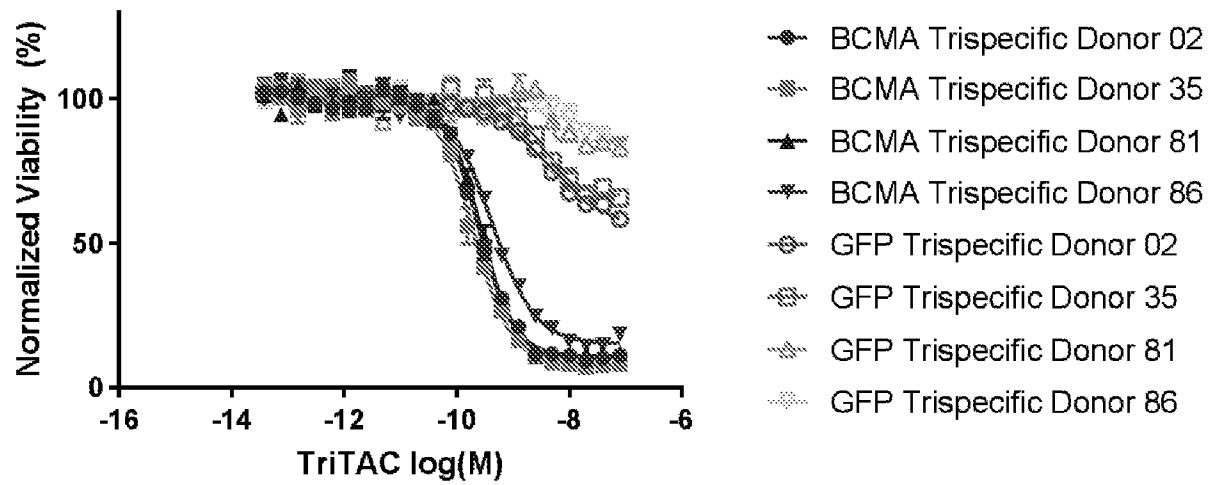


FIG. 11



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FIG. 12



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FIG. 13

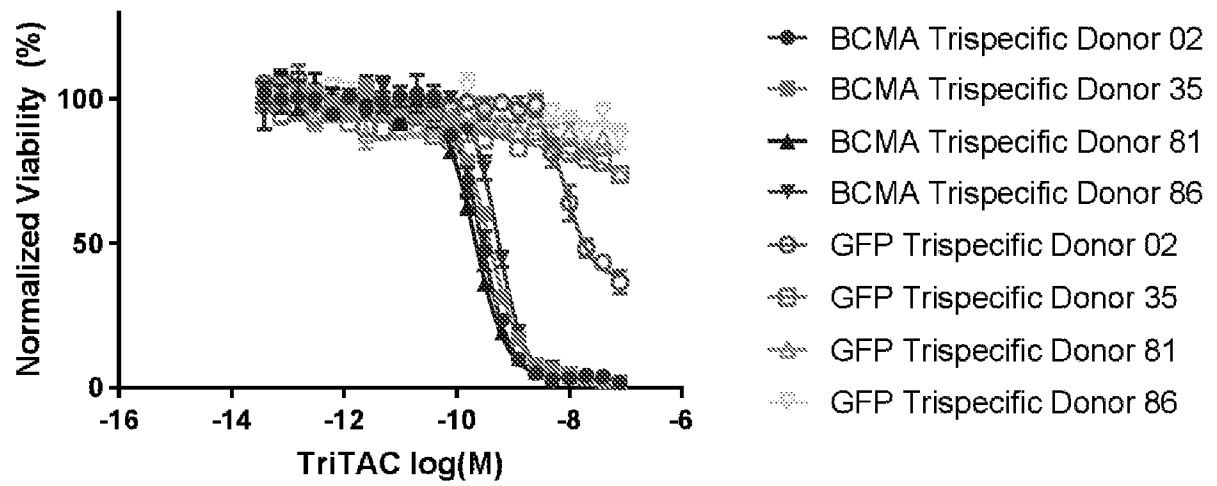


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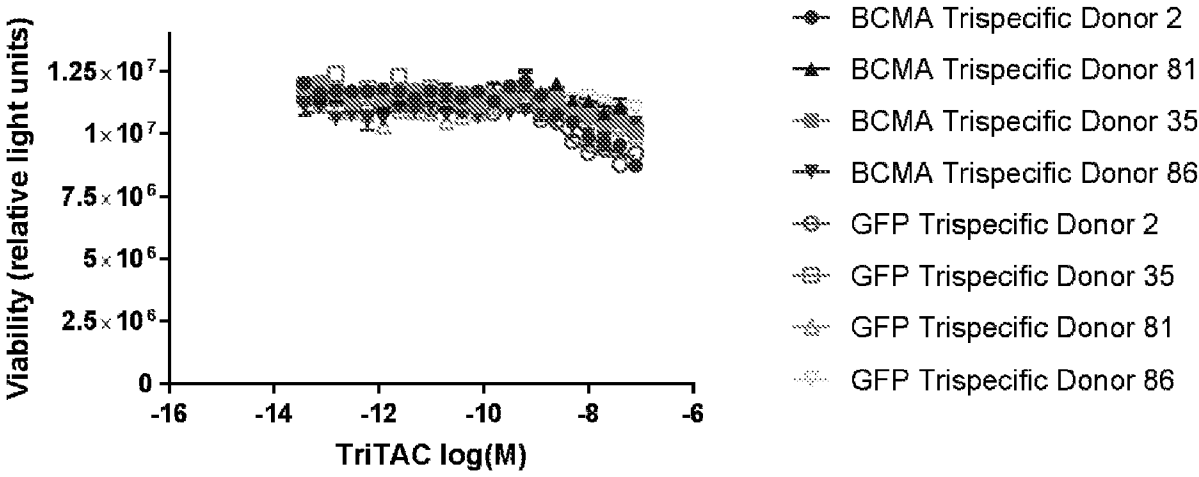
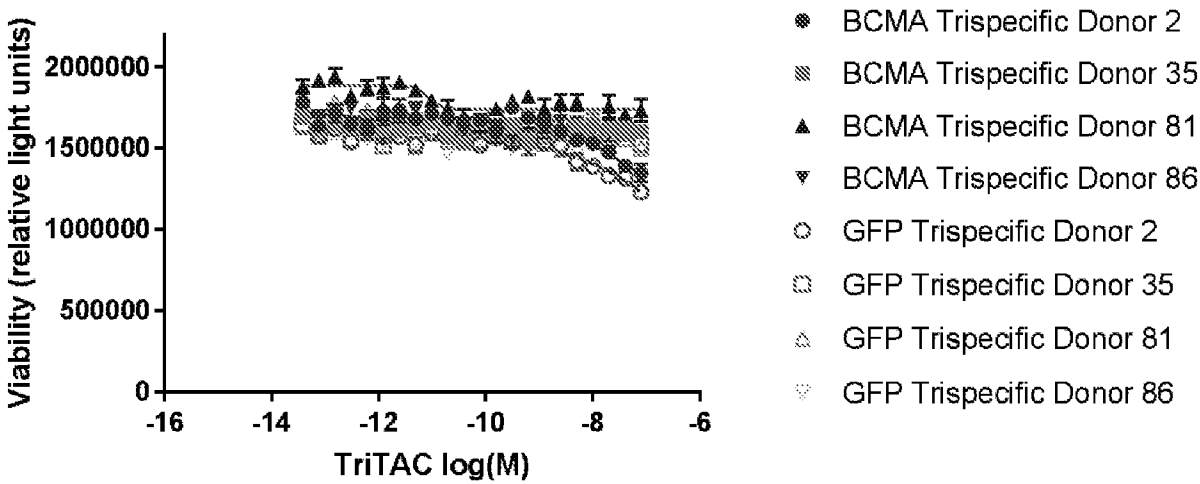


FIG. 15



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FIG. 16

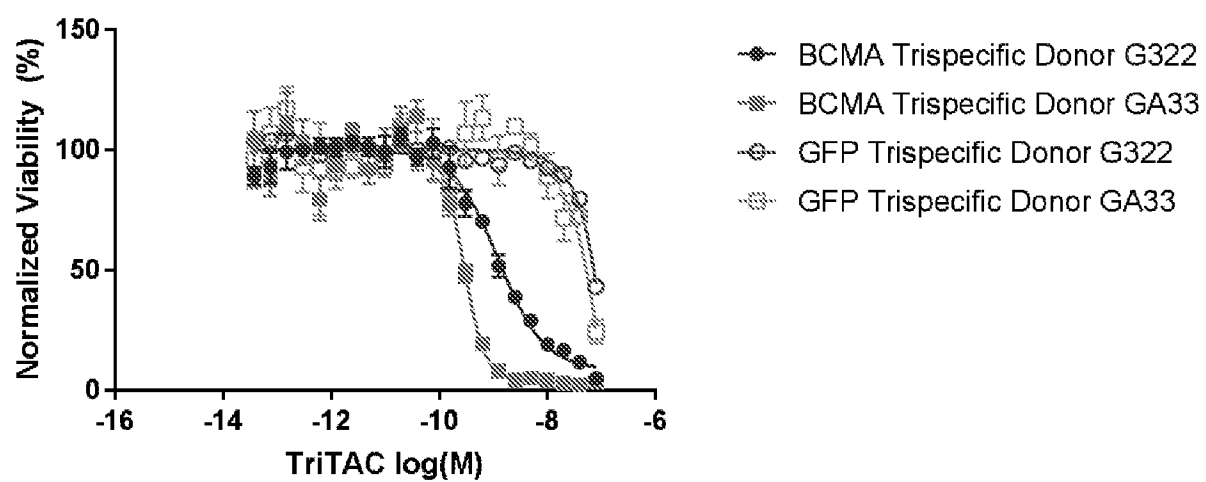


FIG. 17

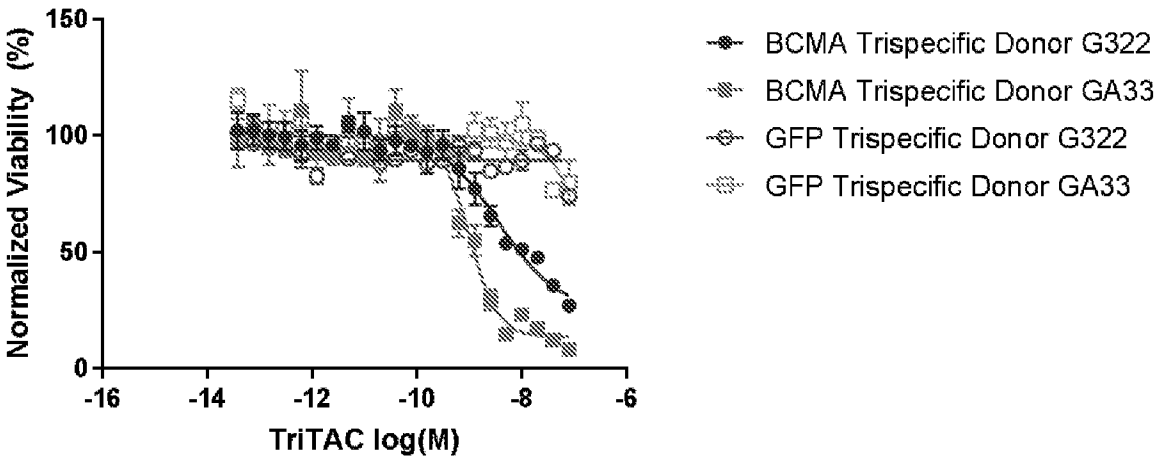


FIG. 18

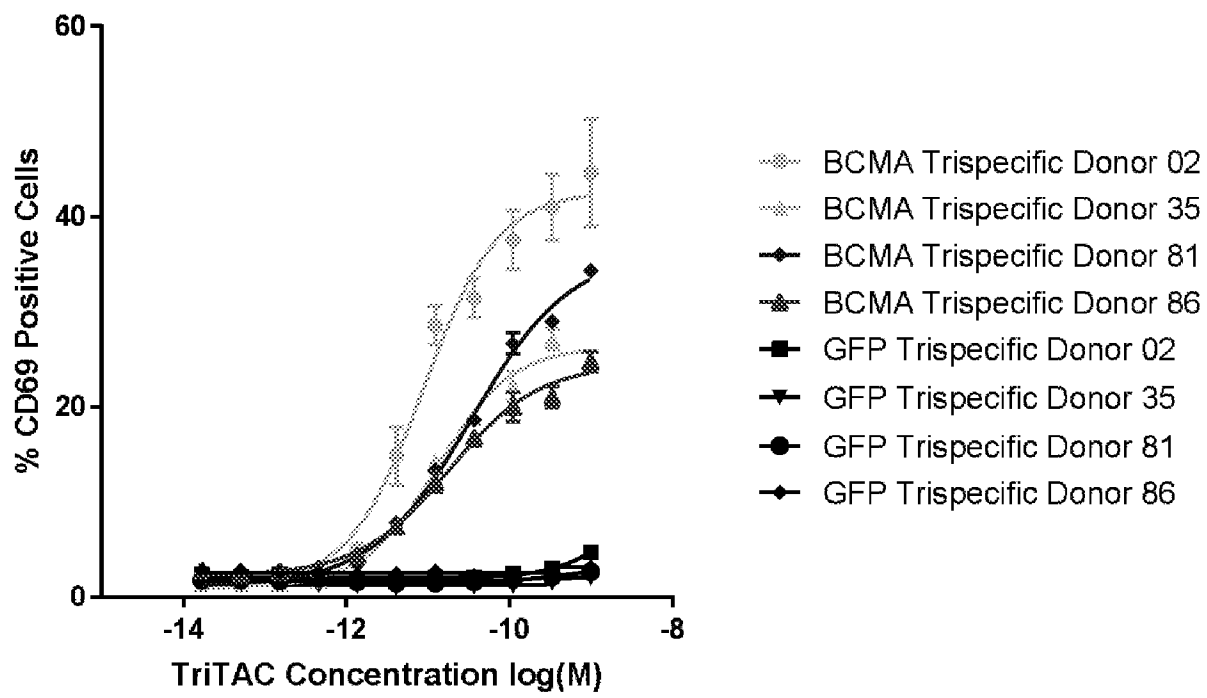


FIG. 19

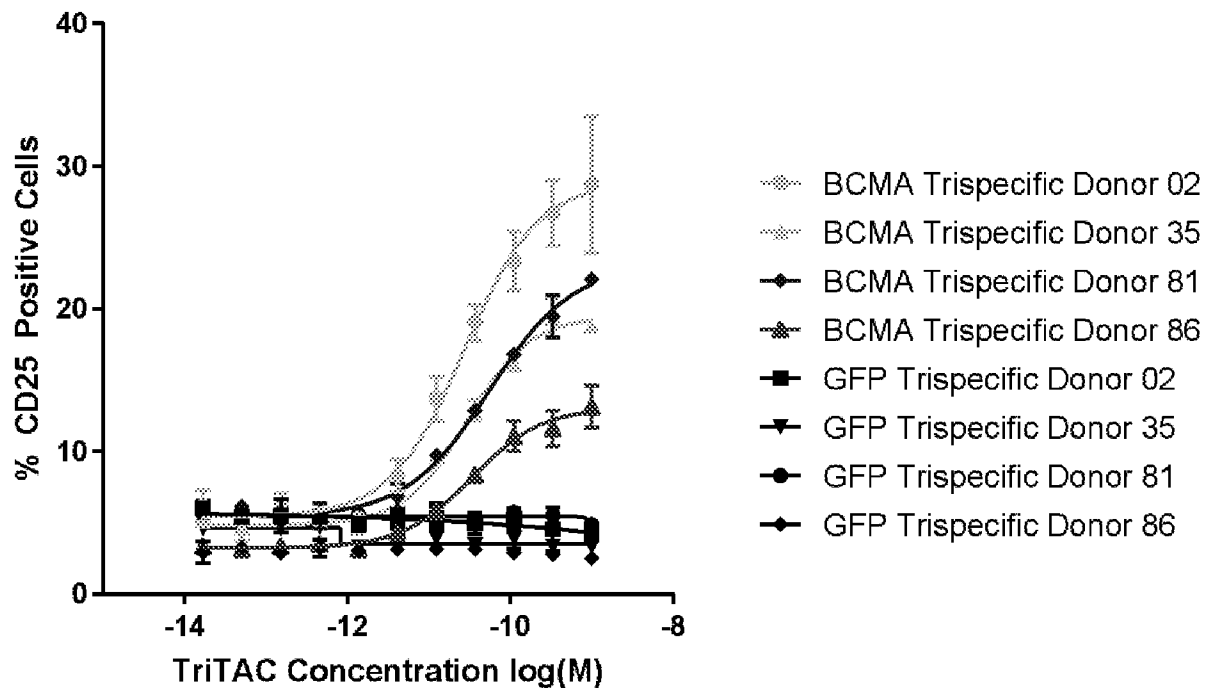


FIG. 20

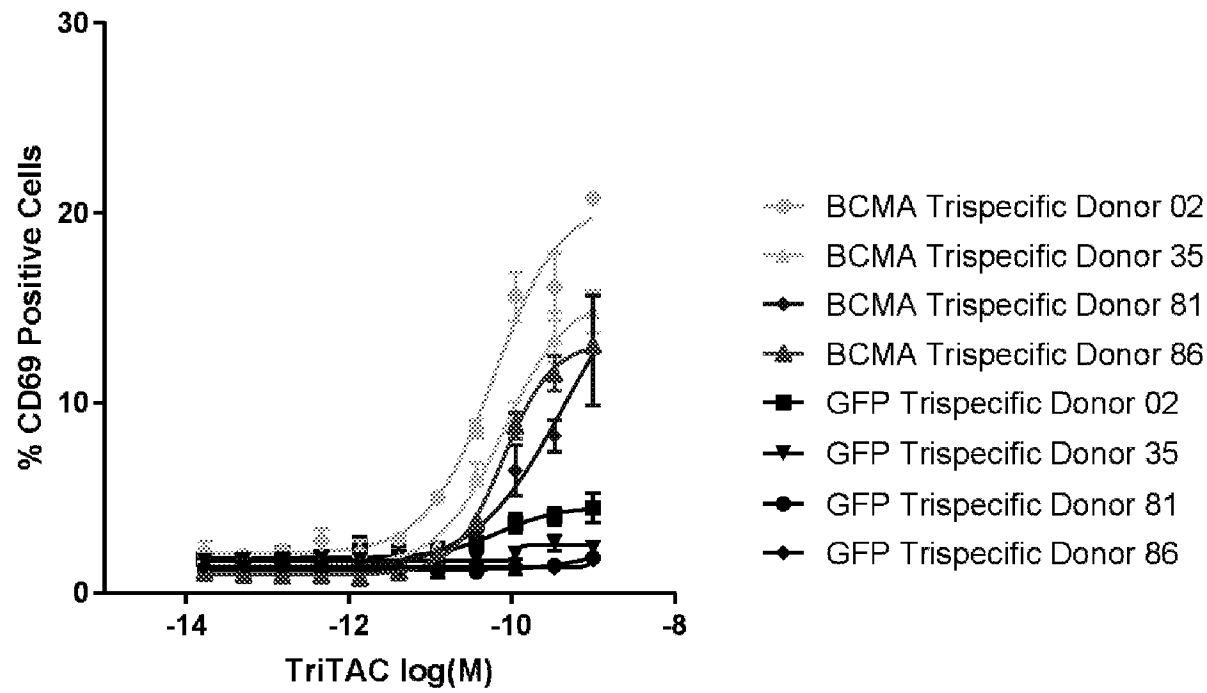


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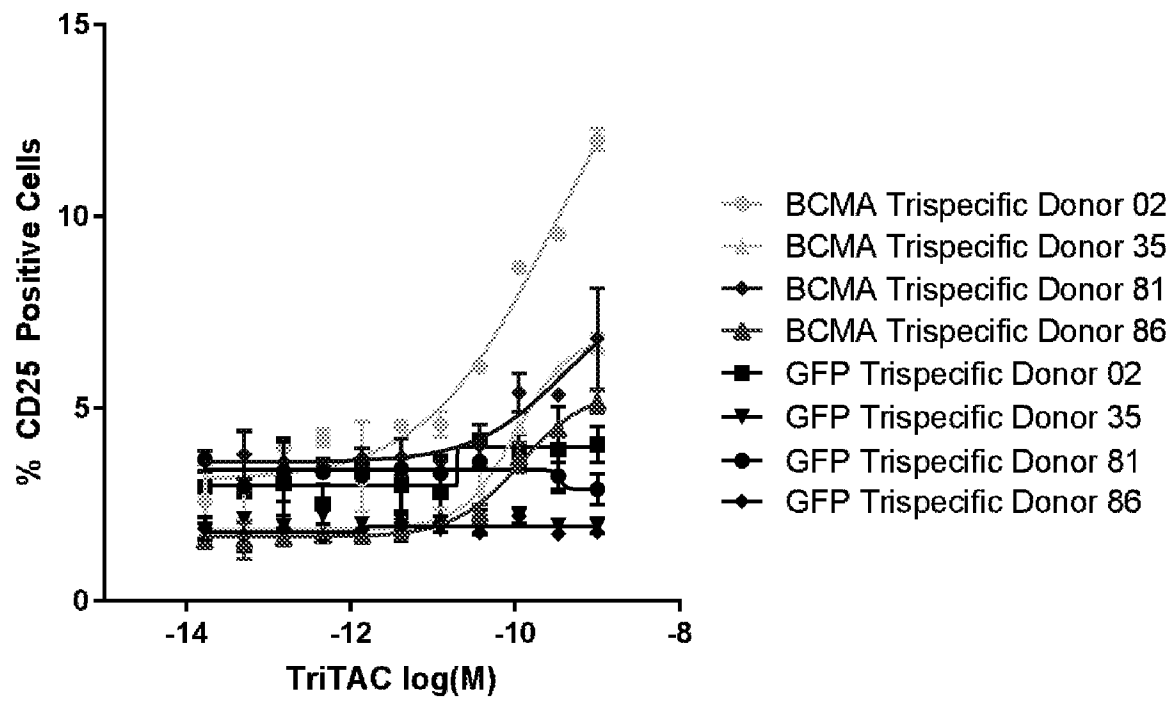


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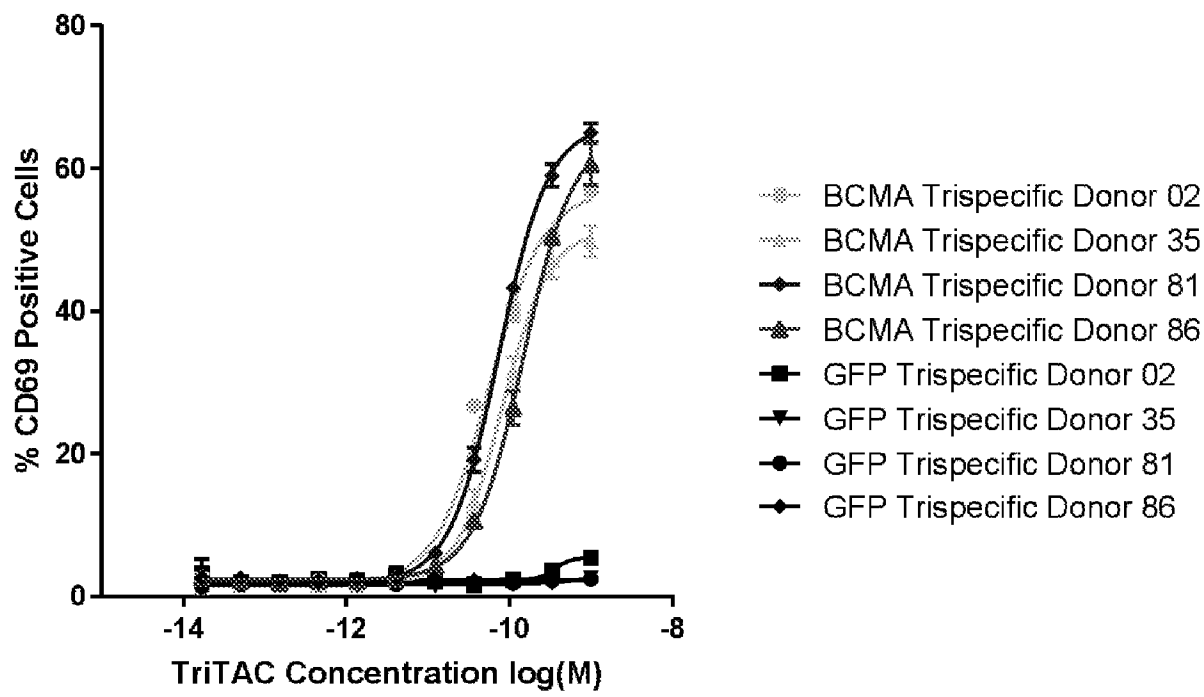


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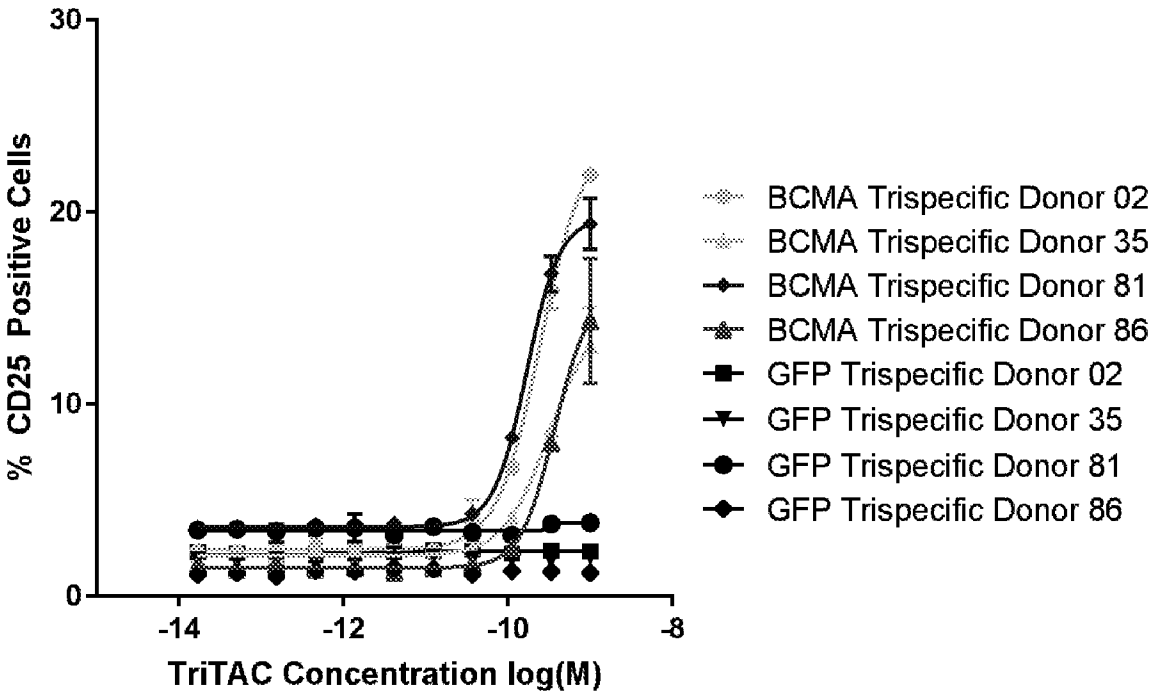
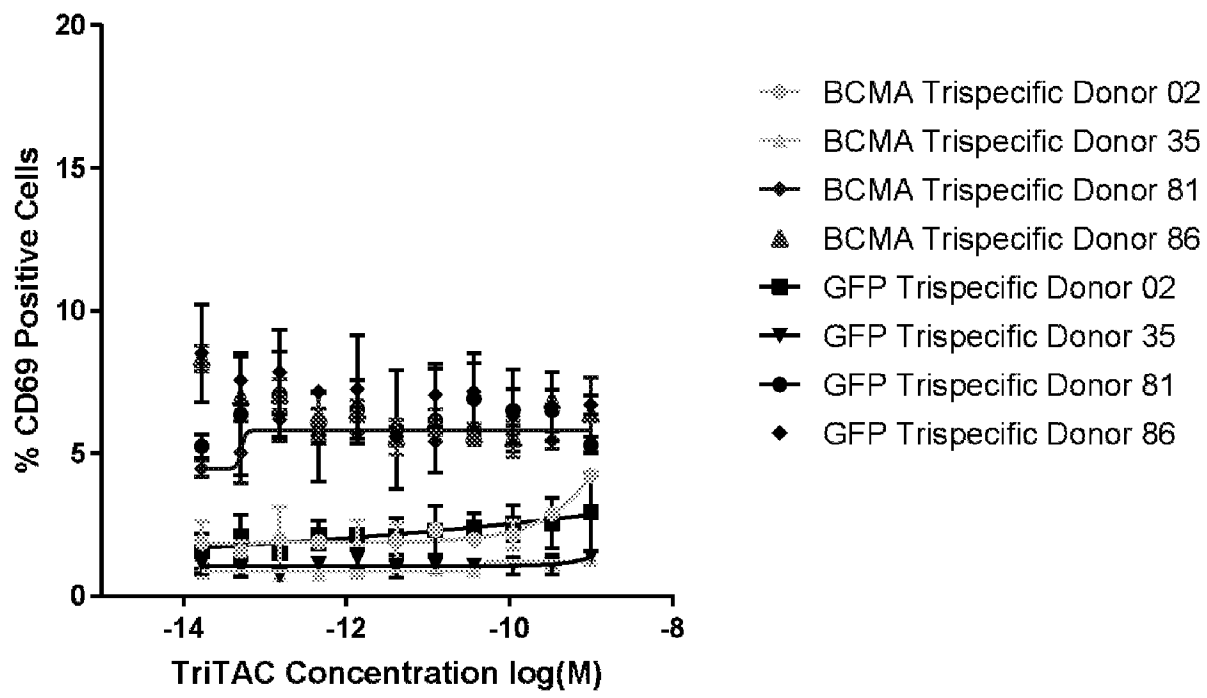


FIG. 24



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FIG. 25

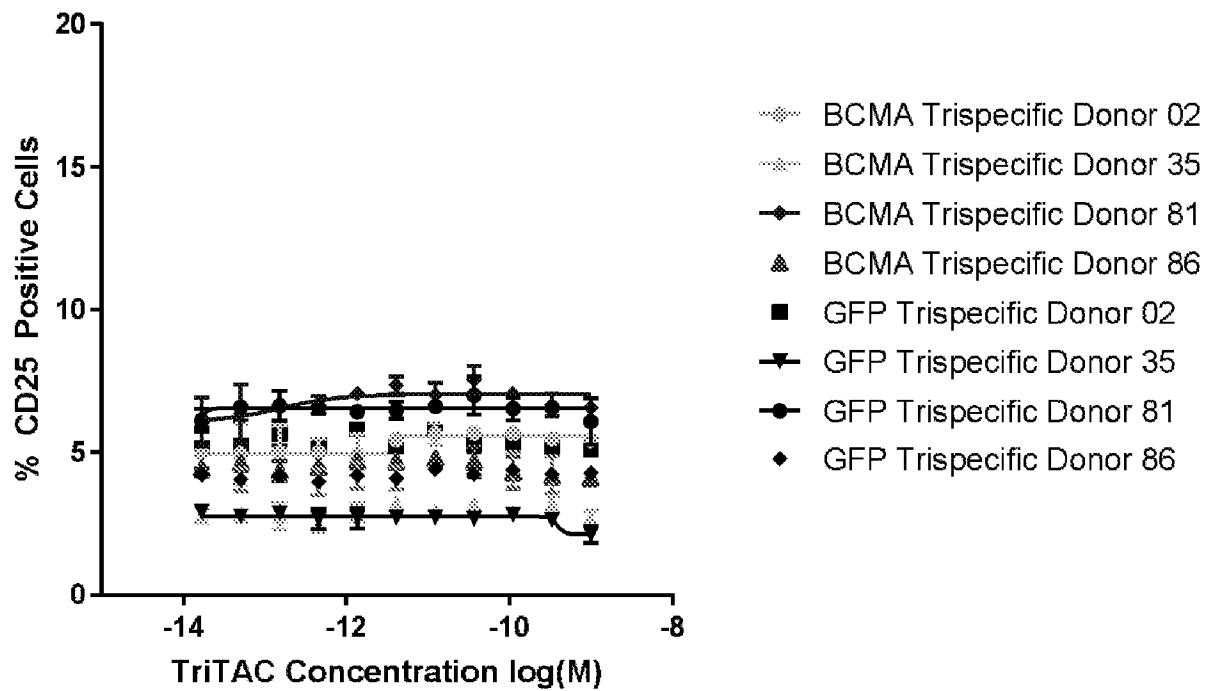


FIG. 26

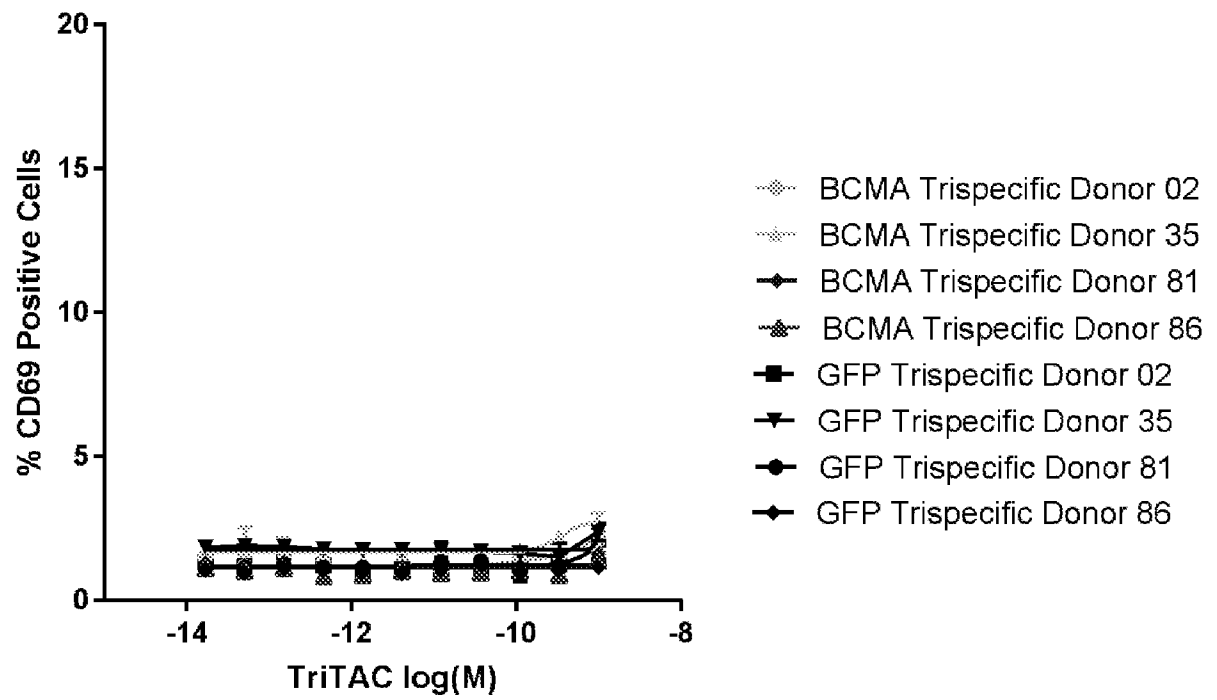


FIG. 27

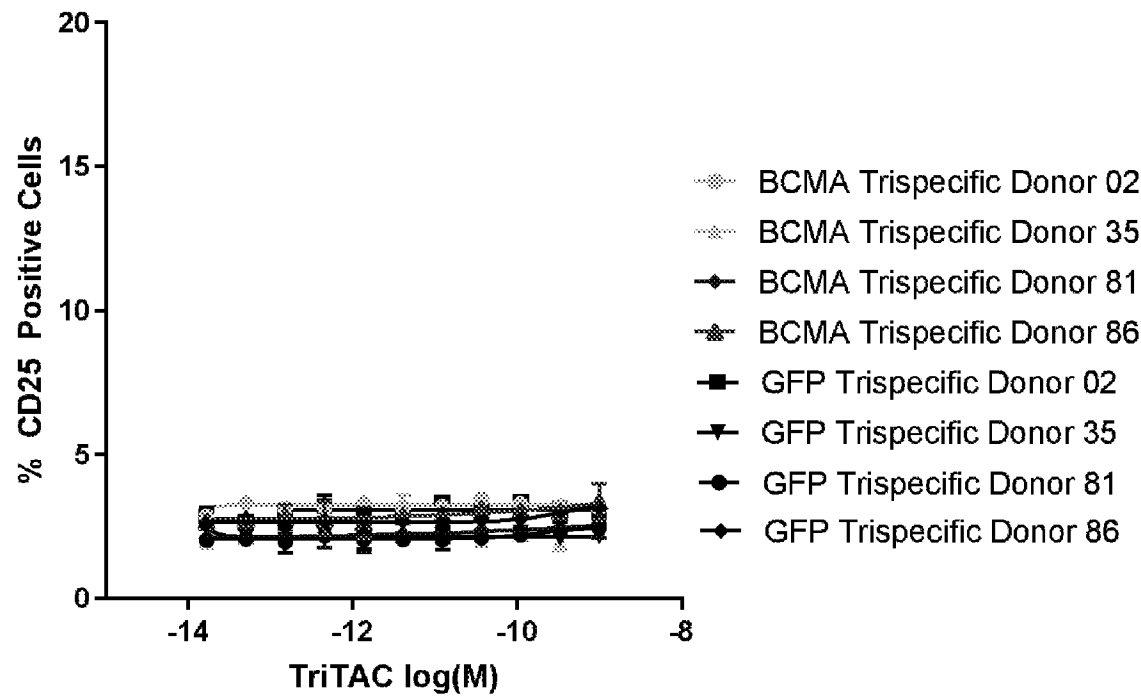


FIG. 28

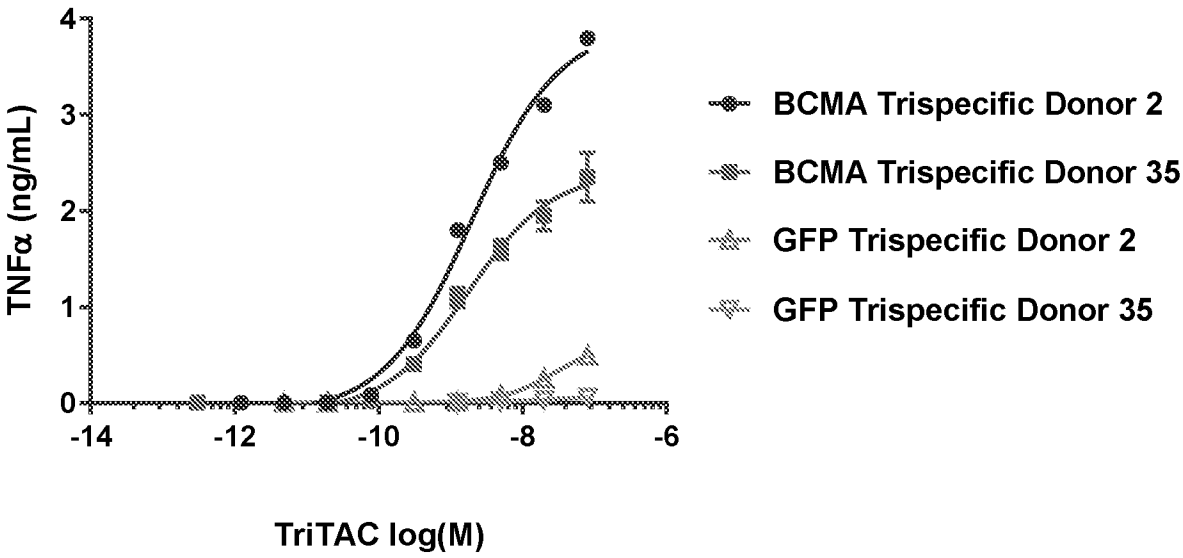


FIG. 29

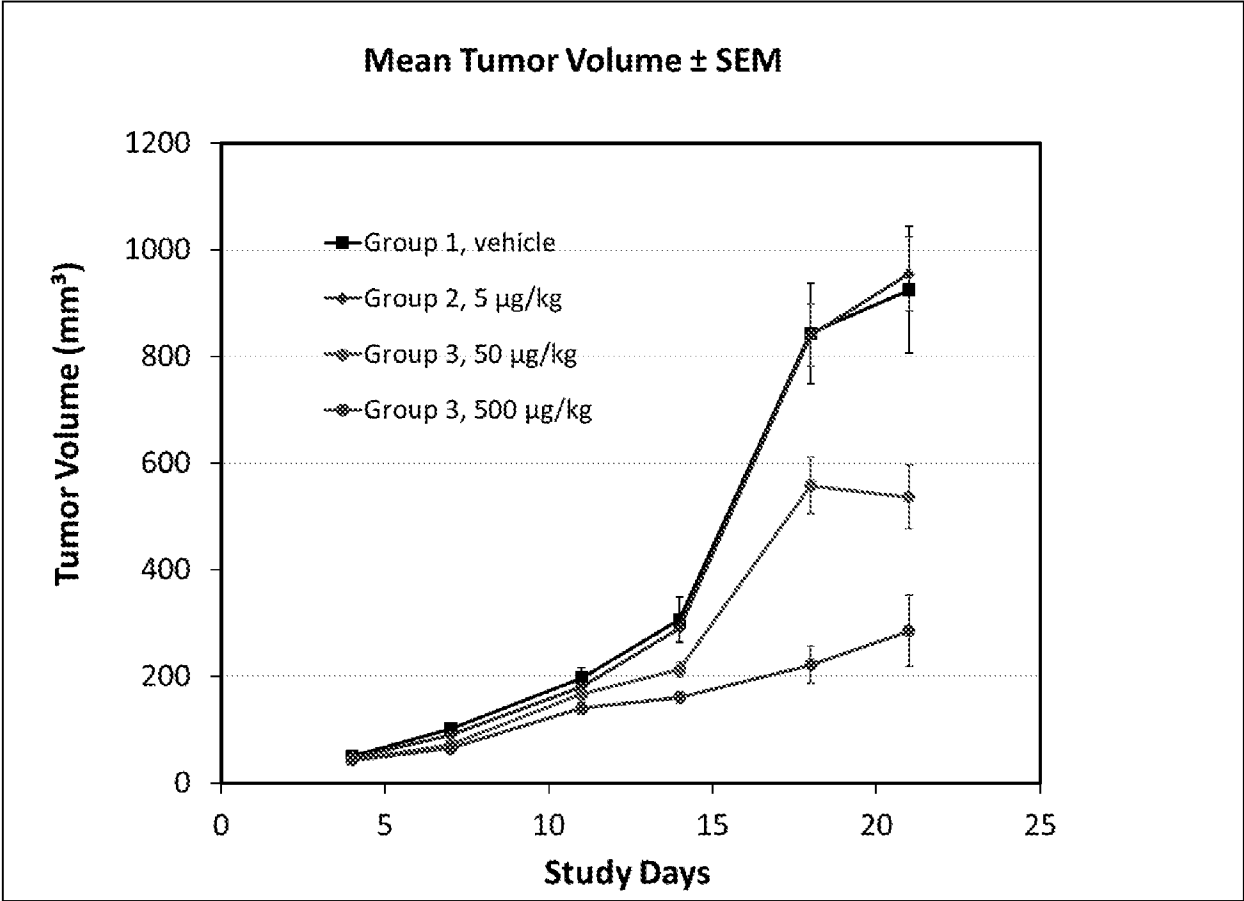
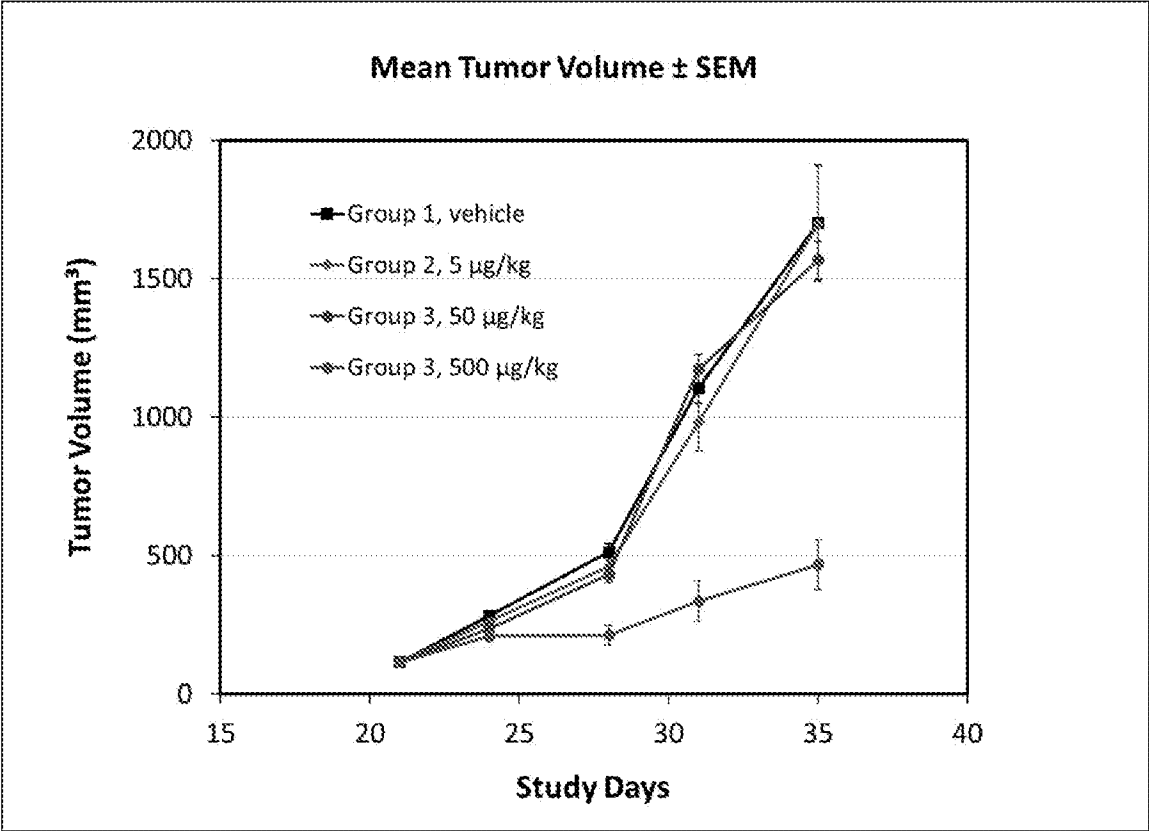
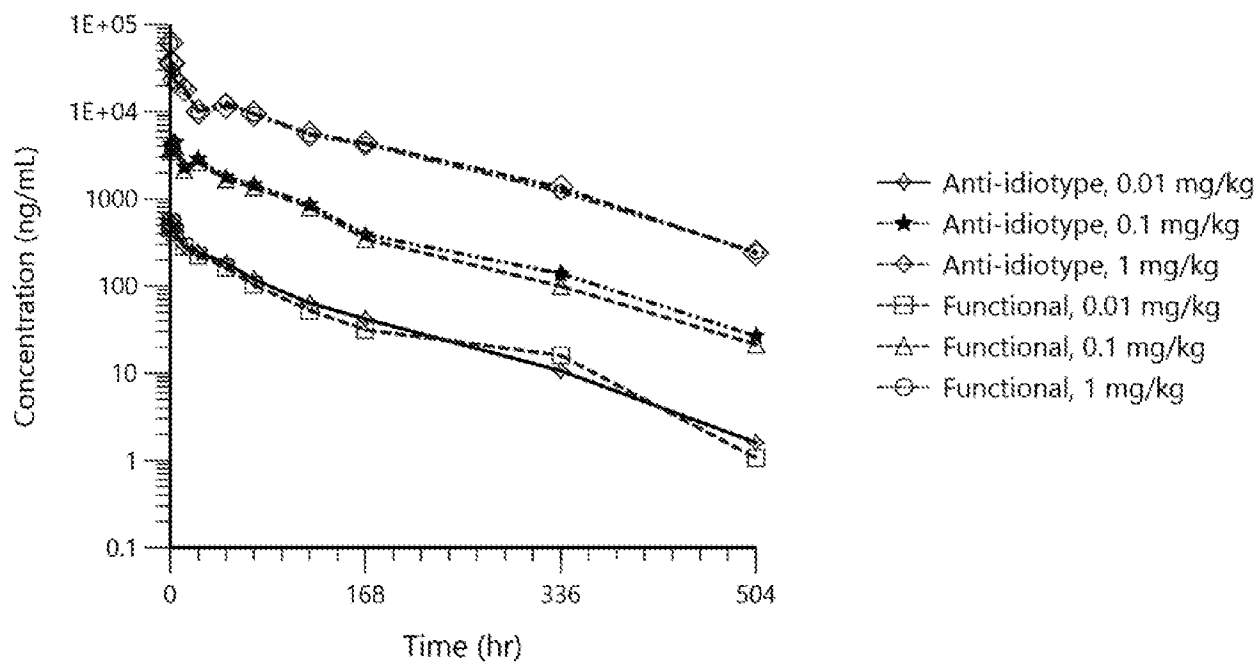


FIG. 30



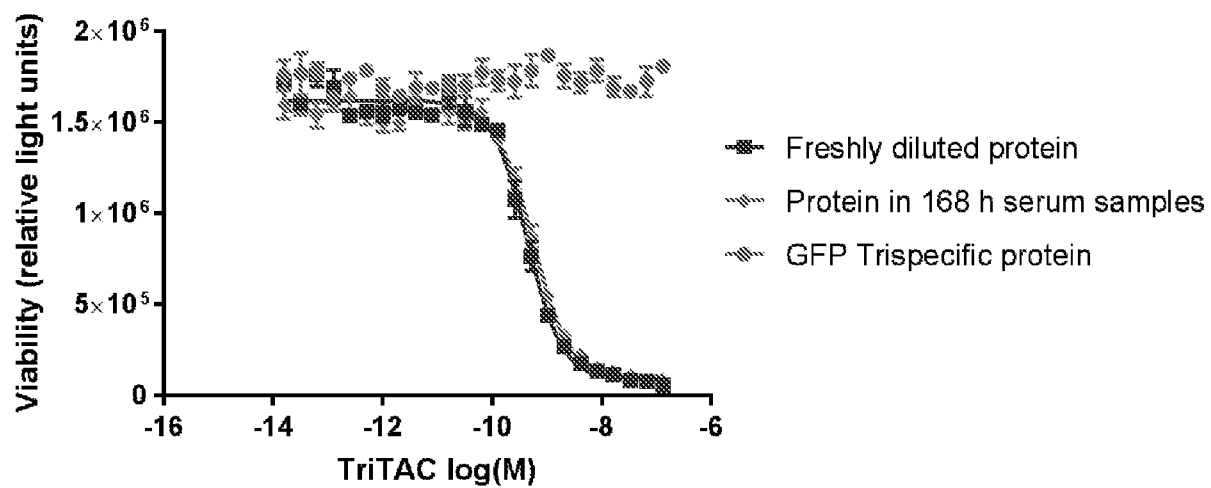
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FIG. 31



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FIG. 32



Sample	EC50 (M)
Freshly diluted protein	4.4E-10
Protein from 168 h samples	5.8E-10

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peptide

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 46

Thr	Asn	Ile	Phe	Ser	Glu	Ser	Pro	Met	Gly
1				5					10

<210> 47

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 47

Thr	Asn	Ile	Asp	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 48

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 48

Thr	Asn	Ile	Phe	Ser	Ser	Ser	Pro	Met	Gly
1				5					10

<210> 49

<211> 10

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 49

Thr	Asn	Ile	Phe	Ser	Thr	Ser	Pro	Met	Gly
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<210> 50

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 50

Thr	Asn	Ile	Thr	Ser	Val	Ser	Pro	Met	Gly
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<210> 51

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 51

Thr	Asn	Ile	Ser	Ser	Ile	Ser	Pro	Met	Gly

1

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<210> 52

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 52

Ser Asn Ile Phe Ser Ile Ser Pro Met Gly

1

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<210> 53

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 53

Thr Asn Ile Phe Arg Ile Ser Pro Met Gly

1

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<210> 54

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 54

Thr Asn Ile Val Ser Ile Ser Pro Met Gly

1

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<210> 55

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 55

Thr	Asn	Ile	Asp	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 56

<211> 10

<212> PRT

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<400> 56

Thr	Asn	Ile	Phe	Ser	Arg	Ser	Pro	Met	Gly
1				5					10

<210> 57

<211> 10

<212> PRT

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<400> 57

Thr	Asn	Ile	Gln	Ser	Ile	Ser	Pro	Met	Gly
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<210> 58

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 58

Thr Asn Ile Phe Asn Ile Ser Pro Met Gly
1 5 10

<210> 59

<211> 10

<212> PRT

<213> Artificial Sequence

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<400> 59

Thr Asn Glu Phe Ser Ile Ser Pro Met Gly
1 5 10

<210> 60

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 60

Thr Asn Ile Pro Ser Ile Ser Pro Met Gly
1 5 10

<210> 61

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 61

Thr Asn Ile Gly Ser Ile Ser Pro Met Gly
1 5 10

<210> 62

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

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Thr	Asn	Ile	Phe	Ser	Lys	Ser	Pro	Met	Gly
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<210> 63

<211> 10

<212> PRT

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<400> 63

Thr	Asn	Ile	Phe	Ser	Ile	Thr	Pro	Met	Gly
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<210> 64

<211> 10

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<400> 64

Thr	Ser	Asp	Phe	Ser	Ile	Ser	Pro	Met	Gly
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<210> 65

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic

peptide

<400> 65

Thr	Asn	Ile	Met	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 66

<211> 10

<212> PRT

<213> Artificial Sequence

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<400> 66

Thr	Asn	Ile	Met	Ser	Ile	Ser	Pro	Met	Gly
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<210> 67

<211> 10

<212> PRT

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<400> 67

Thr	Asn	Ile	Pro	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 68

<211> 10

<212> PRT

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<400> 68

Thr	Asn	Ile	Phe	Ser	Thr	Ser	Pro	Met	Gly
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<400> 69
 Thr Asn Ile Phe Ser Gln Ser Pro Met Gly
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 Thr Asn Ile Ala Ser Ile Ser Pro Met Gly
 1 5 10

<210> 71
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 Thr Asn Ile Phe Ser Lys Ser Pro Met Gly
 1 5 10

<210> 72
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<400> 72

Thr	Asn	Ile	Phe	Ser	Arg	Ser	Pro	Met	Gly
1				5					10

<210> 73

<211> 10

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<400> 73

Thr	Asn	His	Phe	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 74

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 74

Thr	Asn	Ile	Phe	Ser	Asn	Ser	Pro	Met	Gly
1				5					10

<210> 75

<211> 10

<212> PRT

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<400> 75

Thr	Asn	Ile	Phe	Ser	Thr	Ser	Pro	Met	Gly

1 5

10

<210> 76

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
peptide

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Thr Asn Ile Phe Ser Ile Ser Pro Tyr Gly

1

5

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<210> 77

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 77

Thr Asn Ile Phe Ser Asn Ser Pro Met Gly

1

5

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<210> 78

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

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peptide

<400> 78

Thr Asn Ile Phe Ser Ser Ser Pro Met Gly

1

5

10

<210> 79

<211> 10

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

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1				5					10

<210> 80

<211> 10

<212> PRT

<213> Artificial Sequence

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1				5					10

<210> 81

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 81

Thr	Asn	Ile	Ile	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 82

<211> 10

<212> PRT

<213> Artificial Sequence

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<400> 82

Thr Asn Ile Ala Ser Ile Ser Pro Met Gly
1 5 10

<210> 83

<211> 10

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 83

Thr Asn Ile Phe Ser Glu Ser Pro Met Gly
1 5 10

<210> 84

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 84

Thr Asn Ile Phe Ser Thr Ser Pro Met Gly
1 5 10

<210> 85

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 85

Thr Asn Ile Ser Ser Ile Ser Pro Met Gly
1 5 10

<210> 86

<211> 10
 <212> PRT
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<220>
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<400> 86
 Thr Asn Val Val Ser Ile Ser Pro Met Gly
 1 5 10

<210> 87
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
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<400> 87
 Thr Asn Glu Phe Ser Ile Ser Pro Met Gly
 1 5 10

<210> 88
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
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<400> 88
 Thr Asn Ile Phe Ser Asn Ser Pro Met Gly
 1 5 10

<210> 89
 <211> 10
 <212> PRT
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<220>
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peptide

<400> 89

Thr	Asn	Ile	Phe	Ser	Arg	Ser	Pro	Met	Gly
1				5					10

<210> 90

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 90

Thr	Asn	Ile	Phe	Ser	Asp	Ser	Pro	Met	Gly
1				5					10

<210> 91

<211> 10

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 91

Thr	Asn	Asp	Phe	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 92

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 92

Thr	Asn	Ile	Phe	Ser	Lys	Ser	Pro	Met	Gly
1				5					10

<210> 93
 <211> 10
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<400> 93
 Thr Asn Ile Phe Ser Ile Tyr Pro Met Gly
 1 5 10

<210> 94
 <211> 10
 <212> PRT
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<220>
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<400> 94
 Thr Asn Ile Phe Ser Ser Ser Pro Met Gly
 1 5 10

<210> 95
 <211> 10
 <212> PRT
 <213> Artificial Sequence

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<400> 95
 Thr Asn Ile Phe Ser Val Ser Pro Met Gly
 1 5 10

<210> 96
 <211> 10
 <212> PRT
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<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 96

Thr	Asn	Ile	Phe	Ser	Ile	Thr	Pro	Met	Gly
1				5					10

<210> 97

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 97

Thr	Asn	Ile	Glu	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 98

<211> 10

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 98

Thr	Asn	Ile	Phe	Ser	Thr	Ser	Pro	Met	Gly
1				5					10

<210> 99

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 99

Thr	Asn	Ile	Glu	Ser	Ile	Ser	Pro	Met	Gly

1

5

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<210> 100

<211> 10

<212> PRT

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<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 100

Thr Asn Ile Phe Ser Ile Asn Pro Met Gly

1

5

10

<210> 101

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 101

Thr Asn Ile Phe Ser Ile Thr Pro Met Gly

1

5

10

<210> 102

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 102

Thr Asn Ile Thr Ser Ile Ser Pro Met Gly

1

5

10

<210> 103

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 103

Thr	Asn	Ile	Phe	Ser	Gly	Ser	Pro	Met	Gly
1				5					10

<210> 104

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 104

Thr	Asn	Ile	Phe	Ser	Ile	Thr	Pro	Met	Gly
1				5					10

<210> 105

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 105

Thr	Asn	Ile	Asp	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 106

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 106

Thr Asn Ile Phe Ser Asp Ser Pro Met Gly
1 5 10

<210> 107

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 107

Thr Asn Ile Asp Ser Ile Ser Pro Met Gly
1 5 10

<210> 108

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 108

Thr Asn Ile Phe Ser Lys Ser Pro Met Gly
1 5 10

<210> 109

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 109

Thr Asn Ile Phe Ser Val Ser Pro Met Gly
1 5 10

<210> 110

<211> 10
 <212> PRT
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<220>
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<400> 110
 Thr Asn Gln Phe Ser Ile Ser Pro Met Gly
 1 5 10

<210> 111
 <211> 10
 <212> PRT
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<220>
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<400> 111
 Thr Asn Ile Arg Ser Ile Ser Pro Met Gly
 1 5 10

<210> 112
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
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<400> 112
 Thr Asn Ile Phe Ser Arg Ser Pro Met Gly
 1 5 10

<210> 113
 <211> 10
 <212> PRT
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peptide

<400> 113

Thr	Asn	Ile	Thr	Ser	Ile	Ser	Pro	Met	Gly
1				5					10

<210> 114

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 114

Thr	Asn	Ile	Phe	Ser	Thr	Ser	Pro	Tyr	Gly
1				5					10

<210> 115

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 115

Thr	Asn	Ile	Phe	Ser	Thr	Ser	Pro	Gly	Gly
1				5					10

<210> 116

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 116

Thr	Asn	Ile	Phe	Ser	Ile	Thr	Pro	Tyr	Gly
1				5					10

<210> 117

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 117

Thr Asn Ile Phe Ser Ile Thr Pro Gly Gly
1 5 10

<210> 118

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 118

Ala Ile His Gly Gly Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 119

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 119

Ala Ile Asn Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 120

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 120

Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 121

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 121

Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 122

<211> 14

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 122

Ala	Ile	His	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 123

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 123

Ala	Ile	His	Gly	Phe	Ser	Thr	Val	Tyr	Ala	Asp	Ser	Val	Lys

1

5

10

<210> 124

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 124

Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys

1

5

10

<210> 125

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 125

Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys

1

5

10

<210> 126

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 126

Ala Ile His Gly Arg Ser Thr Leu Tyr Ala Asp Ser Val Lys

1

5

10

<210> 127

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 127

Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 128

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 128

Ala	Ile	Ser	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 129

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 129

Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 130

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 130

Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 131

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 131

Ala Ile His Gly Phe Glu Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 132

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 132

Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 133

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 133

Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 134

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 134

Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 135

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 135

Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 136

<211> 14

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 136

Ala	Ile	His	Gly	Phe	Gln	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 137

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic

peptide

<400> 137

Ala	Ile	His	Gly	His	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 138

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 138

Ala	Ile	His	Gly	Asn	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 139

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 139

Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 140

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 140

Ala	Ile	His	Gly	Phe	Lys	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 141

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 141

Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 142

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 142

Ala Ile His Gly Phe Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10

<210> 143

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 143

Ala Ile His Gly Gly Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 144

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 144

Ala	Ile	His	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 145

<211> 14

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Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 146

<211> 14

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<210> 147

<211> 14

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<210> 148

<211> 14

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peptide

<400> 148

Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 149

<211> 14

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Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 150

<211> 14

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<213> Artificial Sequence

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Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 151

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<210> 154

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Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 155

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peptide

<400> 155

Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 156

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<400> 156

Ala Ile His Gly Gln Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 157

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peptide

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Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 158

<211> 14

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<400> 158

Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 159

<211> 14

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Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 160

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<400> 160

Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 161

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peptide

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<210> 164

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<210> 165

<211> 14

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<400> 165

Ala Ile His Gly His Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 166

<211> 14

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<400> 166

Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 167

<211> 14

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<400> 167

Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys
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Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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Ala	Ile	His	Gly	Phe	Glu	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys

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<210> 172

<211> 14

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<223> Description of Artificial Sequence: Synthetic
peptide

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Ala Ile His Gly Phe Ser Thr Tyr Tyr Ala Asp Ser Val Lys

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<210> 173

<211> 14

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<223> Description of Artificial Sequence: Synthetic
peptide

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Ala Ile His Gly Leu Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 174

<211> 14

<212> PRT

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<223> Description of Artificial Sequence: Synthetic
peptide

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Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 175

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Ala	Ile	His	Gly	Gln	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 176

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Ala	Ile	His	Gly	Gln	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 177

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Ala	Ile	His	Gly	Thr	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 178

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<400> 178

Ala Ile His Gly Phe Glu Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 179

<211> 14

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 179

Ala Ile His Gly Phe Ser Thr Val Tyr Ala Asp Ser Val Lys
1 5 10

<210> 180

<211> 14

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peptide

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Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 181

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peptide

<400> 181

Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 182

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Ala	Ile	His	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 184

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Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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peptide

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Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 187

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Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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Ala	Ile	His	Gly	Arg	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 189

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<400> 189

Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys
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<210> 190

<211> 14

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<400> 190

Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 191

<211> 14

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<400> 191

Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 192

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<400> 192

Ala	Ile	His	Gly	His	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 193

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<400> 193

Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 194

<211> 14

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Ala	Ile	His	Gly	Phe	Asp	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 195

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1

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<210> 196

<211> 14

<212> PRT

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 196

Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 197

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 197

Ala Ile His Gly Phe Thr Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 198

<211> 14

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peptide

<400> 198

Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 199

<211> 14

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<400> 199

Ala	Ile	His	Gly	Phe	Ser	Thr	Val	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 200

<211> 14

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Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 201

<211> 14

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<400> 201

Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 202

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 202

Ala Ile His Gly Pro Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 203

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 203

Ala Ile His Gly Ile Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 204

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 204

Ala Ile His Gly Phe Ser Thr Phe Tyr Ala Asp Ser Val Lys
1 5 10

<210> 205

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 205

Ala Ile His Gly Gly Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 206

<211> 14

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<400> 206

Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 207

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Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 208

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<400> 208

Ala	Ile	His	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 209

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peptide

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Ala	Ile	His	Gly	Asn	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 210

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Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 211

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Ala	Ile	His	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 212

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Ala	Ile	His	Gly	Thr	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 213
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<400> 213
 Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys
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<210> 214
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<400> 214
 Ala Ile His Gly Phe Asp Thr Leu Tyr Ala Asp Ser Val Lys
 1 5 10

<210> 215
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<220>
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<400> 215
 Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys
 1 5 10

<210> 216
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<400> 216

Ala	Ile	His	Gly	Asn	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 217

<211> 14

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<400> 217

Ala	Ile	His	Gly	Asn	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 218

<211> 14

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<400> 218

Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 219

<211> 14

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Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys

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<210> 220

<211> 14

<212> PRT

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peptide

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Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 221

<211> 14

<212> PRT

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peptide

<400> 221

Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 222

<211> 14

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peptide

<400> 222

Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys

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<210> 223

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<400> 223

Ala	Ile	His	Gly	Asn	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 224

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<400> 224

Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 225

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<400> 225

Ala	Ile	His	Gly	Ser	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 226

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 226

Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 227

<211> 14

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 227

Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 228

<211> 14

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 228

Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys
1 5 10

<210> 229

<211> 14

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 229

Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys
1 5 10

<210> 230

<211> 14

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<400> 230

Ala	Ile	His	Gly	Ala	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10				

<210> 231

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<400> 231

Ala	Ile	His	Gly	Ala	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys
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<210> 232

<211> 12

<212> PRT

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<400> 232

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Ala
1				5					10		

<210> 233

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic

peptide

<400> 233

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	His
1				5					10		

<210> 234

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 234

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr
1				5					10		

<210> 235

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 235

Val	Pro	Trp	Gly	Arg	Tyr	His	Pro	Arg	Asn	Val	Tyr
1				5					10		

<210> 236

<211> 12

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 236

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr
1				5					10		

<210> 237

<211> 12

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
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<210> 239

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<210> 243

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Val

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<210> 244

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Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Lys

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<210> 245

<211> 12

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

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<210> 246

<211> 12

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Val Pro Trp Gly Glu Tyr His Pro Arg Asn Val Tyr

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<210> 247

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Val Pro Trp Gly Ile Tyr His Pro Arg Asn Val Tyr
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<210> 248

<211> 12

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Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr
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<210> 249

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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<210> 250

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<210> 251

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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<210> 252

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<210> 253

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peptide

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Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr
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<210> 254

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<210> 256

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<211> 12

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peptide

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<210> 260

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Asn
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<210> 268

<211> 12

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peptide

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Val Pro Trp Gly Lys Tyr His Pro Arg Asn Val Tyr

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<210> 269

<211> 12

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peptide

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<210> 270

<211> 12

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peptide

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<210> 271

<211> 12

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<400> 271

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Cys
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<210> 272

<211> 12

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<400> 272

Val Pro Trp Gly Asp Tyr His Pro Arg Arg Val Tyr
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<211> 12

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<400> 273

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr
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Val Pro Trp Gly Thr Tyr His Pro Arg Asn Val Tyr
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<210> 275

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<213> Artificial Sequence

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr
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<210> 277

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<400> 277

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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 Val Pro Trp Gly Asp Tyr His Pro Thr Asn Val Tyr
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<400> 279
 Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr
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<210> 280
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peptide

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Arg	Val	Tyr
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<400> 283

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<210> 284

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<213> Artificial Sequence

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<210> 285

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
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<210> 286

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Val	Pro	Trp	Gly	Arg	Tyr	His	Pro	Arg	Asn	Val	Tyr
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<210> 287

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<400> 287

Val	Pro	Trp	Gly	Ala	Tyr	His	Pro	Arg	Asn	Val	Tyr
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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Ala
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<210> 289

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<400> 289

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gln	Asn	Val	Tyr
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<210> 290

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<400> 290

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Thr
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<210> 291

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<400> 291

Val	Pro	Trp	Gly	Arg	Tyr	His	Pro	Arg	Asn	Val	Tyr

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<210> 292

<211> 12

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peptide

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

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<210> 293

<211> 12

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 293

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

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<210> 294

<211> 12

<212> PRT

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peptide

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

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<210> 295

<211> 12

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr
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<210> 296

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<400> 296

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
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<210> 297

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<400> 297

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Ser	Asn	Val	Tyr
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<210> 298

<211> 12

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<400> 298

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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<210> 299

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<213> Artificial Sequence

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<400> 299

Val Pro Trp Gly Asp Tyr His Pro Arg Glu Val Tyr
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<210> 300

<211> 12

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 300

Val Pro Trp Gly Arg Tyr His Pro Gly Asn Val Tyr
1 5 10

<210> 301

<211> 12

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<213> Artificial Sequence

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<400> 301

Val Pro Trp Gly Asp Tyr His Pro Arg Val Val Tyr
1 5 10

<210> 302

<211> 12
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<400> 302
 Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Met
 1 5 10

<210> 303
 <211> 12
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<400> 303
 Val Pro Trp Gly Asp Tyr His Pro Leu Asn Val Tyr
 1 5 10

<210> 304
 <211> 12
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<400> 304
 Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
 1 5 10

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peptide

<400> 305

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<210> 306

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Thr
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<210> 307

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Ser
1				5					10		

<210> 308

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<400> 308

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr
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<210> 309

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
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<210> 310

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Thr
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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
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<210> 313

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Val	Pro	Trp	Gly	Arg	Tyr	His	Pro	Arg	Asn	Val	Tyr
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<210> 314

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Asn	Asn	Val	Tyr
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<210> 315

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr

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<210> 316

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peptide

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Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr

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<210> 317

<211> 12

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peptide

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

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<210> 318

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peptide

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

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5

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<210> 319

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<400> 319

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala
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<400> 320

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
1 5 10

<210> 321

<211> 12

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 321

Val Pro Trp Gly Asp Tyr His Pro Lys Asn Val Tyr
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<210> 322

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 322

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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<210> 323

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 323

Val Pro Trp Gly Lys Tyr His Pro Arg Asn Val Tyr
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<210> 324

<211> 12

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peptide

<400> 324

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr
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<210> 325

<211> 12

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peptide

<400> 325

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr
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<211> 12
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peptide

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<210> 330

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
1				5					10		

<210> 331

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Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
1				5					10		

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<400> 332

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asp	Val	Tyr
1				5					10		

<210> 333
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<400> 333
 Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr
 1 5 10

<210> 334
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<400> 334
 Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala
 1 5 10

<210> 335
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<400> 335
 Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr
 1 5 10

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<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 336

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr
1				5					10		

<210> 337

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 337

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr
1				5					10		

<210> 338

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 338

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Val
1				5					10		

<210> 339

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 339

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Val

1 5

10

<210> 340

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 340

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

1

5

10

<210> 341

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 341

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr

1

5

10

<210> 342

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 342

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr

1

5

10

<210> 343

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 343

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
1				5					10		

<210> 344

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 344

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
1				5					10		

<210> 345

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 345

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr
1				5					10		

<210> 346

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 346

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 347

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 347

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asp Ile Phe Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Gly Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 348

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 348

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Asp Phe Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Gly Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 349

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 349

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Lys Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln


```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Val Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 350
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 350
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Asp Phe Ser Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

```

47517-722_601_SL.txt

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Lys Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 351

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 351

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Gln Phe Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Val Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 352

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 352

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Phe	Ser	Ser	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	Asn	Gly	Phe	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75					80

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	His	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 353

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 353

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ser Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 354

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 354

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Gln Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Val Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 355

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 355

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Glu Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Leu Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 356

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 356

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Glu Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Phe Thr Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 357

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 357

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asp Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 358
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 358
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asn Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Gly Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

```


47517-722_601_SL.txt

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val His Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 359

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 359

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asn Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Arg Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Met Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 360

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 360

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asn Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Pro Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 361

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 361

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asn Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Arg Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 362

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 362

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 363

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 363

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Lys Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Gln Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 364

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 364

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ser Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

47517-722_601_SL.txt

Ala Ala Ile His Gly His Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 365

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 365

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ser Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Arg Lys Val Tyr Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 366
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 366
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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47517-722_601_SL.txt

Val Pro Trp Gly Ile Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 367

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 367

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Glu Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Thr Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 368

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 368

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Phe	Ser	Val	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Asn	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75				80	

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Lys	Tyr	His	Pro	Arg	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 369

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 369

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Val Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 370

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 370

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Lys Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Glu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 371

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 371

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asp Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 372

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 372

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Lys Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 373

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 373

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser His Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
      100             105             110

Thr Gln Val Thr Val Ser Ser
      115

<210> 374
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 374
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10             15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75             80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 375

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 375

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Gln Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 376

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 376

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Phe	Ser	Leu	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75					80

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 377

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 377

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Ser
20 25 30

Pro Gly Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 378

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 378

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn His Phe Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Val Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 379

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 379

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ala Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Asn Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 380

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 380

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ala Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 381

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 381

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ser Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
      100             105             110

Thr Gln Val Thr Val Ser Ser
      115

<210> 382
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 382
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10             15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Glu Ser Ile Ser
      20             25             30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35             40             45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50             55             60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 383

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 383

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Ser
20 25 30

Pro Tyr Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 384

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 384

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Ala	Ser	Ile	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Thr	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75				80	

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 385

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 385

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ala Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 386

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

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<400> 386

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ala Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 387

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 387

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Thr Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 388

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 388

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Met Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 389

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 389

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Thr Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
      100            105            110

Thr Gln Val Thr Val Ser Ser
      115

<210> 390
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 390
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Val Ser Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly His Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 391
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 391
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Val Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 392

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 392

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Val	Val	Ser	Ile	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Lys	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75					80

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Asn	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 393

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 393

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ile Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 394

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 394

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 395

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 395

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Thr Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Glu Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 396

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 396

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Gln Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

47517-722_601_SL.txt

Ala Ala Ile His Gly Phe Glu Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 397

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 397

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Ser Asp Phe Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Glu Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
      100             105             110

Thr Gln Val Thr Val Ser Ser
      115

<210> 398
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 398
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10             15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Asp Ser Ile Ser
      20             25             30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35             40             45

Ala Ala Ile His Gly Phe Gln Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50             55             60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 399

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 399

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Met Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Ser Thr Val Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 400

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 400

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Glu Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 401

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 401

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ser Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Lys Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Arg Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 402

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 402

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ser Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 403

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 403

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asn Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 404

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 404

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 405

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 405

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

47517-722_601_SL.txt

65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys

85 90 95

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Leu	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr Gln Val Thr Val Ser Ser
115

<210> 406
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 406
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Val Ala Ser Thr Asn Ile Phe Ser Thr Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

47517-722_601_SL.txt

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 407

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 407

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Asp Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Ser Thr Phe Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 408

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 408

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Phe	Ser	Gln	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75				80	

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Gly	Asn	Val	Cys	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 409

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 409

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Gln Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Ser Asn Val Tyr Trp Gly Lys Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 410

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 410

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Arg Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 411

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 411

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Ile Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 412

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 412

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Arg Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 413

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 413

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Gly Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln


```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
      100            105            110

Thr Gln Val Thr Val Ser Ser
      115

<210> 414
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 414
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Ser Asn Ile Phe Ser Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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47517-722_601_SL.txt

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 415

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 415

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Tyr
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Lys Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 416

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 416

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Lys Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 417

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 417

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Lys Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 418

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 418

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Glu Phe Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Leu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Ala Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 419

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 419

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Glu Phe Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 420

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 420

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Pro Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

47517-722_601_SL.txt

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 421

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 421

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Pro Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ala Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 422
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 422
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Pro Ser Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

```


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Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 423

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 423

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Pro Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 424

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 424

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Thr Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Val Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Gln Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 425

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 425

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Pro Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Gln Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Gln Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 426

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 426

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Val Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ser Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 427

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 427

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Ser Asn Ile Phe Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 428

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 428

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Asp Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

47517-722_601_SL.txt

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 429

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 429

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Asp Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Thr Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 430
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 430
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Arg Ser Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Val Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 431

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 431

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Thr Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile Ser Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Glu
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 432

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 432

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5				10						15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Thr	Ser	Ile	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Glu	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75					80

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Asp	Tyr	His	Pro	Arg	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 433

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 433

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Thr Ser Val Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Pro Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Thr Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 434

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 434

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Gly Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Gln Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gln Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 435

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 435

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Glu Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Lys Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Arg Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 436

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 436

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Val Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Arg Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 437

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 437

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Asp Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Asp Tyr His Pro Arg Met Val Tyr Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 438
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 438
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Met Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 439

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 439

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Arg Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 440

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 440

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Phe	Ser	Ile	Ser
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Asp	Ser	Thr	Leu	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75				80	

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Glu	Tyr	His	Pro	Arg	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 441

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 441

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Asp Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Lys Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 442

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

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<400> 442

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Glu Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Ser Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 443

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 443

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Glu Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Asn Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 444

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 444

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ser Ser Ile Ser
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Tyr Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 445

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 445

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ser Ser Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly His Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
      100              105              110

Thr Gln Val Thr Val Ser Ser
      115

<210> 446
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 446
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10              15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ser Ser Ile Ser
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Phe Ser Thr Val Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 447

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 447

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Arg
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Ser Thr Val Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 448

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 448

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5					10					15	

Ser	Leu	Thr	Leu	Ser	Cys	Ala	Ala	Ser	Thr	Asn	Ile	Phe	Ser	Ile	Tyr
			20					25					30		

Pro	Met	Gly	Trp	Tyr	Arg	Gln	Ala	Pro	Gly	Lys	Gln	Arg	Glu	Leu	Val
		35					40					45			

Ala	Ala	Ile	His	Gly	Phe	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Gly
		50				55					60				

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu	Gln
65					70					75					80

Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn	Lys
				85					90					95	

Val	Pro	Trp	Gly	Ser	Tyr	His	Pro	Arg	Asn	Val	Tyr	Trp	Gly	Gln	Gly
			100					105					110		

Thr	Gln	Val	Thr	Val	Ser	Ser
						115

<210> 449

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 449

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Asn Ile Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 450

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 450

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ser Ser
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Trp Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 451

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 451

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Ser Ser Ile Ser

20

25

30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Phe Asp Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 452

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 452

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Asn
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

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Ala Ala Ile His Gly Phe Asp Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Ser Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 453

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 453

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr
20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Arg Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln

```

65              70              75              80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

Val Pro Trp Gly Ser Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
      100             105             110

Thr Gln Val Thr Val Ser Ser
      115

<210> 454
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 454
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1              5              10             15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr
      20              25              30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
      35              40              45

Ala Ala Ile His Gly Thr Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
      50              55              60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65              70              75             80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
      85              90              95

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47517-722_601_SL.txt

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 455

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 455

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Arg Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser

115

<210> 456

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 456

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr
 20 25 30

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Glu Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asp Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 457

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 457

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
20 25 30

Pro Tyr Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 458

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

47517-722_601_SL.txt

<400> 458

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Thr Ser
20 25 30

Pro Gly Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Ile Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 459

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 459

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr

20

25

30

Pro Tyr Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

Ala Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
 65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
 85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

<210> 460

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 460

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Thr
 20 25 30

Pro Gly Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
 35 40 45

47517-722_601_SL.txt

Ala Ala Ile His Gly Ala Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Gly Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 461

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 461

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Ala Ala Ser
20 25

<210> 462

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

47517-722_601_SL.txt

<400> 462

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Thr Leu Ser Cys Val Ala Ser
20 25

<210> 463

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 463

Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val Ala
1 5 10

<210> 464

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 464

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Ile Tyr Leu
1 5 10 15

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys Asn
20 25 30

Lys

<210> 465

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 465

Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Ile	Tyr	Leu
1				5				10					15		

Gln	Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	Asn
		20					25					30			

Glu

<210> 466

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 466

Trp	Gly	Gln	Gly	Thr	Gln	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 467

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 467

Trp	Gly	Lys	Gly	Thr	Gln	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 468

47517-722_601_SL.txt

<211> 184

<212> PRT

<213> Homo sapiens

<400> 468

Met Leu Gln Met Ala Gly Gln Cys Ser Gln Asn Glu Tyr Phe Asp Ser
1 5 10 15

Leu Leu His Ala Cys Ile Pro Cys Gln Leu Arg Cys Ser Ser Asn Thr
20 25 30

Pro Pro Leu Thr Cys Gln Arg Tyr Cys Asn Ala Ser Val Thr Asn Ser
35 40 45

Val Lys Gly Thr Asn Ala Ile Leu Trp Thr Cys Leu Gly Leu Ser Leu
50 55 60

Ile Ile Ser Leu Ala Val Phe Val Leu Met Phe Leu Leu Arg Lys Ile
65 70 75 80

Asn Ser Glu Pro Leu Lys Asp Glu Phe Lys Asn Thr Gly Ser Gly Leu
85 90 95

Leu Gly Met Ala Asn Ile Asp Leu Glu Lys Ser Arg Thr Gly Asp Glu
100 105 110

Ile Ile Leu Pro Arg Gly Leu Glu Tyr Thr Val Glu Glu Cys Thr Cys
115 120 125

Glu Asp Cys Ile Lys Ser Lys Pro Lys Val Asp Ser Asp His Cys Phe
130 135 140

Pro Leu Pro Ala Met Glu Glu Gly Ala Thr Ile Leu Val Thr Thr Lys
145 150 155 160

Thr Asn Asp Tyr Cys Lys Ser Leu Pro Ala Ala Leu Ser Ala Thr Glu
165 170 175

Ile Glu Lys Ser Ile Ser Ala Arg
180

<210> 469
<211> 185
<212> PRT
<213> Mus sp.

<400> 469
Met Ala Gln Gln Cys Phe His Ser Glu Tyr Phe Asp Ser Leu Leu His
1 5 10 15

Ala Cys Lys Pro Cys His Leu Arg Cys Ser Asn Pro Pro Ala Thr Cys
20 25 30

Gln Pro Tyr Cys Asp Pro Ser Val Thr Ser Ser Val Lys Gly Thr Tyr
35 40 45

Thr Val Leu Trp Ile Phe Leu Gly Leu Thr Leu Val Leu Ser Leu Ala
50 55 60

Leu Phe Thr Ile Ser Phe Leu Leu Arg Lys Met Asn Pro Glu Ala Leu
65 70 75 80

Lys Asp Glu Pro Gln Ser Pro Gly Gln Leu Asp Gly Ser Ala Gln Leu
85 90 95

Asp Lys Ala Asp Thr Glu Leu Thr Arg Ile Arg Ala Gly Asp Asp Arg
100 105 110

Ile Phe Pro Arg Ser Leu Glu Tyr Thr Val Glu Glu Cys Thr Cys Glu
115 120 125

Asp Cys Val Lys Ser Lys Pro Lys Gly Asp Ser Asp His Phe Phe Pro
130 135 140

Leu Pro Ala Met Glu Glu Gly Ala Thr Ile Leu Val Thr Thr Lys Thr

47517-722_601_SL.txt

145 150 155 160

Gly Asp Tyr Gly Lys Ser Ser Val Pro Thr Ala Leu Gln Ser Val Met
165 170 175

Gly Met Glu Lys Pro Thr His Thr Arg
180 185

<210> 470

<211> 183

<212> PRT

<213> Macaca fascicularis

<400> 470

Met Leu Gln Met Ala Arg Gln Cys Ser Gln Asn Glu Tyr Phe Asp Ser
1 5 10 15

Leu Leu His Asp Cys Lys Pro Cys Gln Leu Arg Cys Ser Ser Thr Pro
20 25 30

Pro Leu Thr Cys Gln Arg Tyr Cys Asn Ala Ser Met Thr Asn Ser Val
35 40 45

Lys Gly Met Asn Ala Ile Leu Trp Thr Cys Leu Gly Leu Ser Leu Ile
50 55 60

Ile Ser Leu Ala Val Phe Val Leu Thr Phe Leu Leu Arg Lys Met Ser
65 70 75 80

Ser Glu Pro Leu Lys Asp Glu Phe Lys Asn Thr Gly Ser Gly Leu Leu
85 90 95

Gly Met Ala Asn Ile Asp Leu Glu Lys Gly Arg Thr Gly Asp Glu Ile
100 105 110

Val Leu Pro Arg Gly Leu Glu Tyr Thr Val Glu Glu Cys Thr Cys Glu
115 120 125

47517-722_601_SL.txt

Asp Cys Ile Lys Asn Lys Pro Lys Val Asp Ser Asp His Cys Phe Pro
 130 135 140

Leu Pro Ala Met Glu Glu Gly Ala Thr Ile Leu Val Thr Thr Lys Thr
 145 150 155 160

Asn Asp Tyr Cys Asn Ser Leu Ser Ala Ala Leu Ser Val Thr Glu Ile
 165 170 175

Glu Lys Ser Ile Ser Ala Arg
 180

<210> 471

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 6xHis tag

<400> 471

His His His His His His
 1 5

<210> 472

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 472

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Glu
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Thr Asn Ile Phe Ser Ile Ser
 20 25 30

47517-722_601_SL.txt

Pro Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val
35 40 45

Ala Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Ile Tyr Leu Gln
65 70 75 80

Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Asn Lys
85 90 95

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr Trp Gly Gln Gly
100 105 110

Thr Gln Val Thr Val Ser Ser
115

<210> 473

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 473

Thr Asn Ile Phe Ser Ile Ser Pro Met Gly
1 5 10

<210> 474

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

47517-722_601_SL.txt

<400> 474

Ala Ile His Gly Phe Ser Thr Leu Tyr Ala Asp Ser Val Lys
1 5 10

<210> 475

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 475

Val Pro Trp Gly Asp Tyr His Pro Arg Asn Val Tyr
1 5 10