



US 20130251703A1

(19) **United States**(12) **Patent Application Publication**
ELIS et al.(10) **Pub. No.: US 2013/0251703 A1**(43) **Pub. Date: Sep. 26, 2013**(54) **ANTIBODIES FOR EPIDERMAL GROWTH
FACTOR RECEPTOR 3 (HER3) DIRECTED
TO DOMAIN III AND DOMAIN IV OF HER3****Publication Classification**(71) Applicant: **NOVARTIS AG**, Basel (CH)(72) Inventors: **Winfried ELIS**, Munchen-Pasing (DE);
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SHENG, Sharon, MA (US)(73) Assignee: **NOVARTIS AG**, Basel (CH)(21) Appl. No.: **13/693,347**(22) Filed: **Dec. 4, 2012****Related U.S. Application Data**(60) Provisional application No. 61/566,890, filed on Dec.
5, 2011.(51) **Int. Cl.****C07K 16/28** (2006.01)**A61K 45/06** (2006.01)**A61K 39/395** (2006.01)(52) **U.S. Cl.**CPC **C07K 16/28** (2013.01); **A61K 39/3955**
(2013.01); **A61K 45/06** (2013.01)USPC **424/133.1**; 530/387.9; 530/387.3; 424/139.1

(57)

ABSTRACT

The present invention relates to antibodies or fragments thereof that bind to a non-linear epitope within domain 3 of the HER3 receptor and inhibit both ligand-dependent and ligand-independent signal transduction. The invention also relates antibodies or fragments thereof that bind to amino acid residues within domains 3-4 of HER3 and inhibit both ligand-dependent and ligand-independent signal transduction; and compositions and methods of use of such antibodies or fragments thereof.

Figure 1

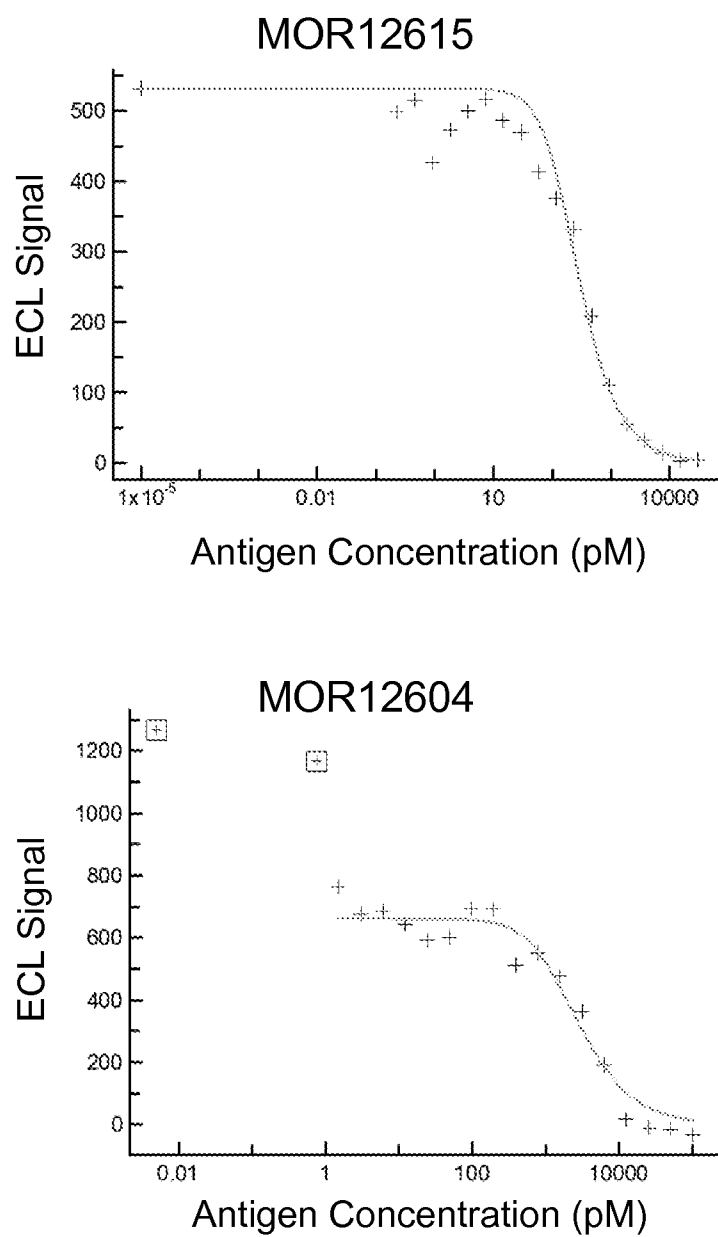


Figure 2

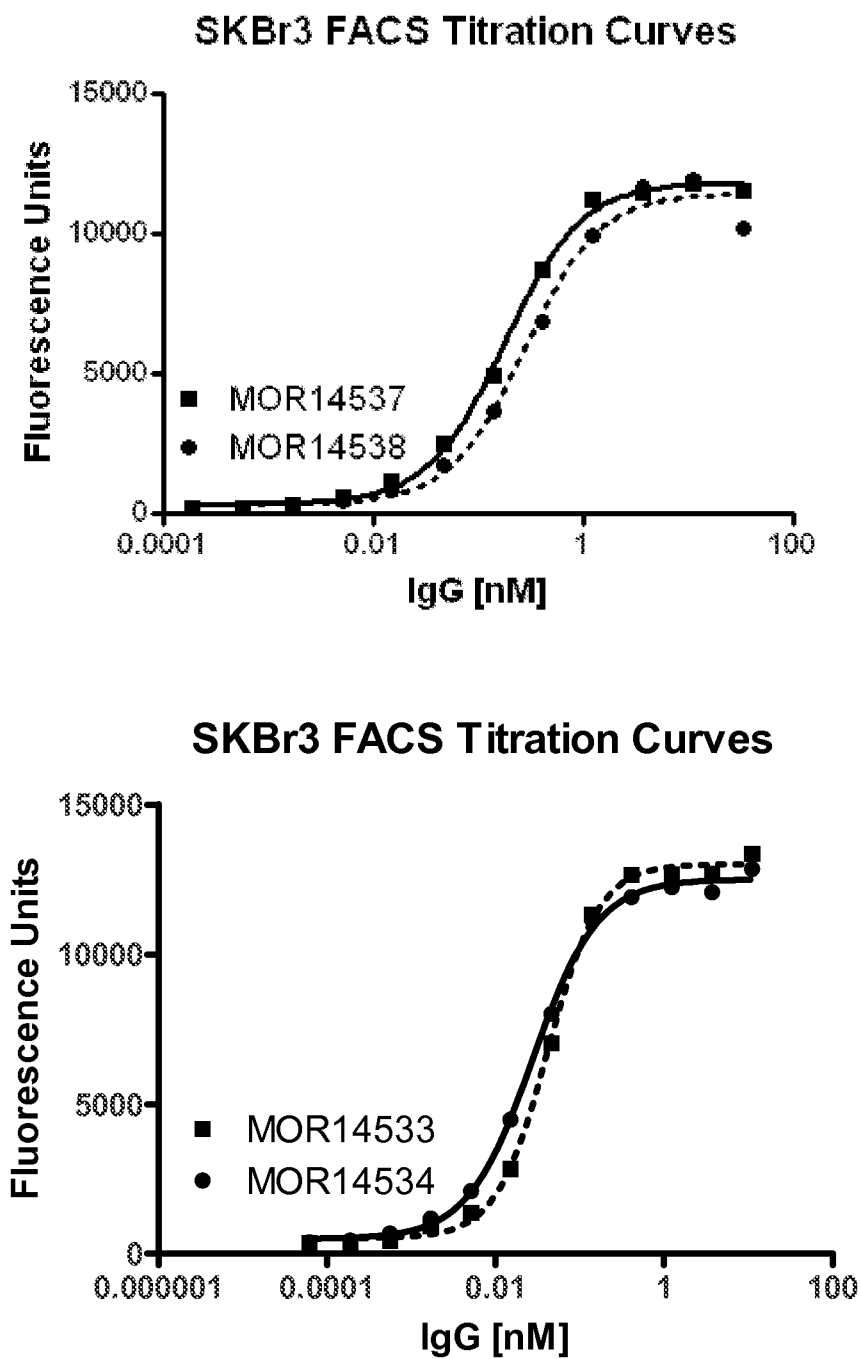
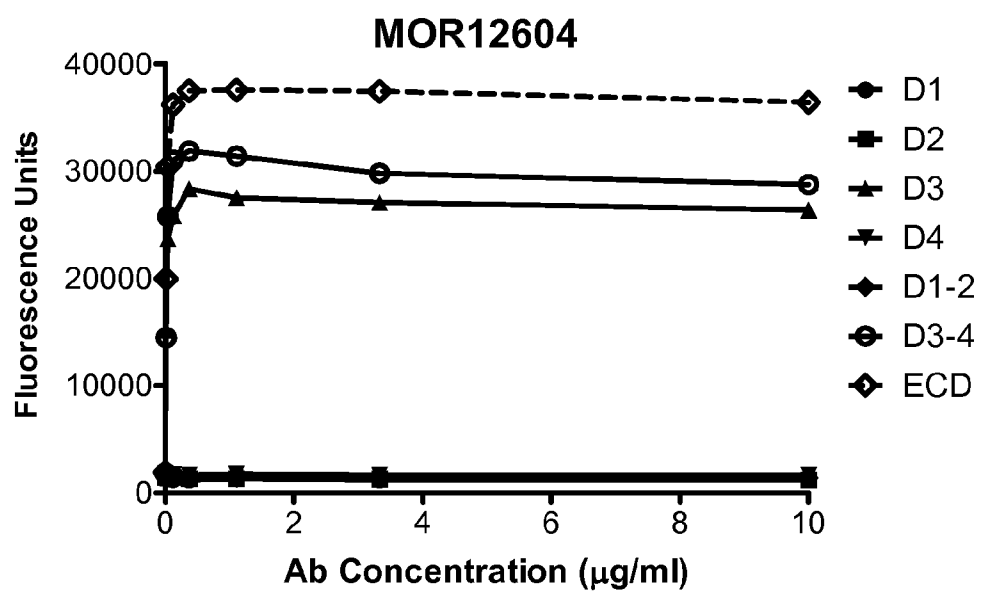
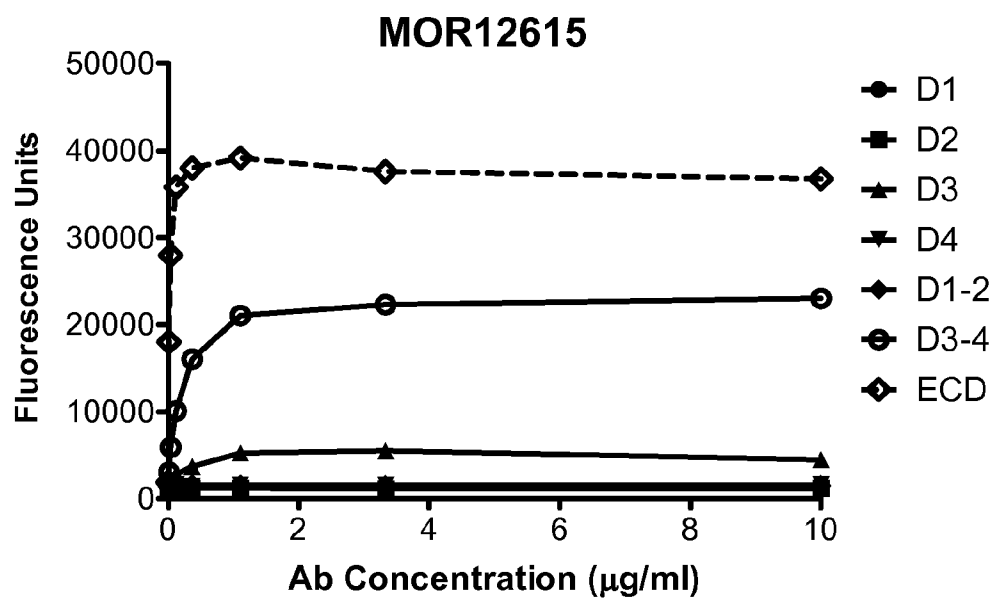


Figure 3



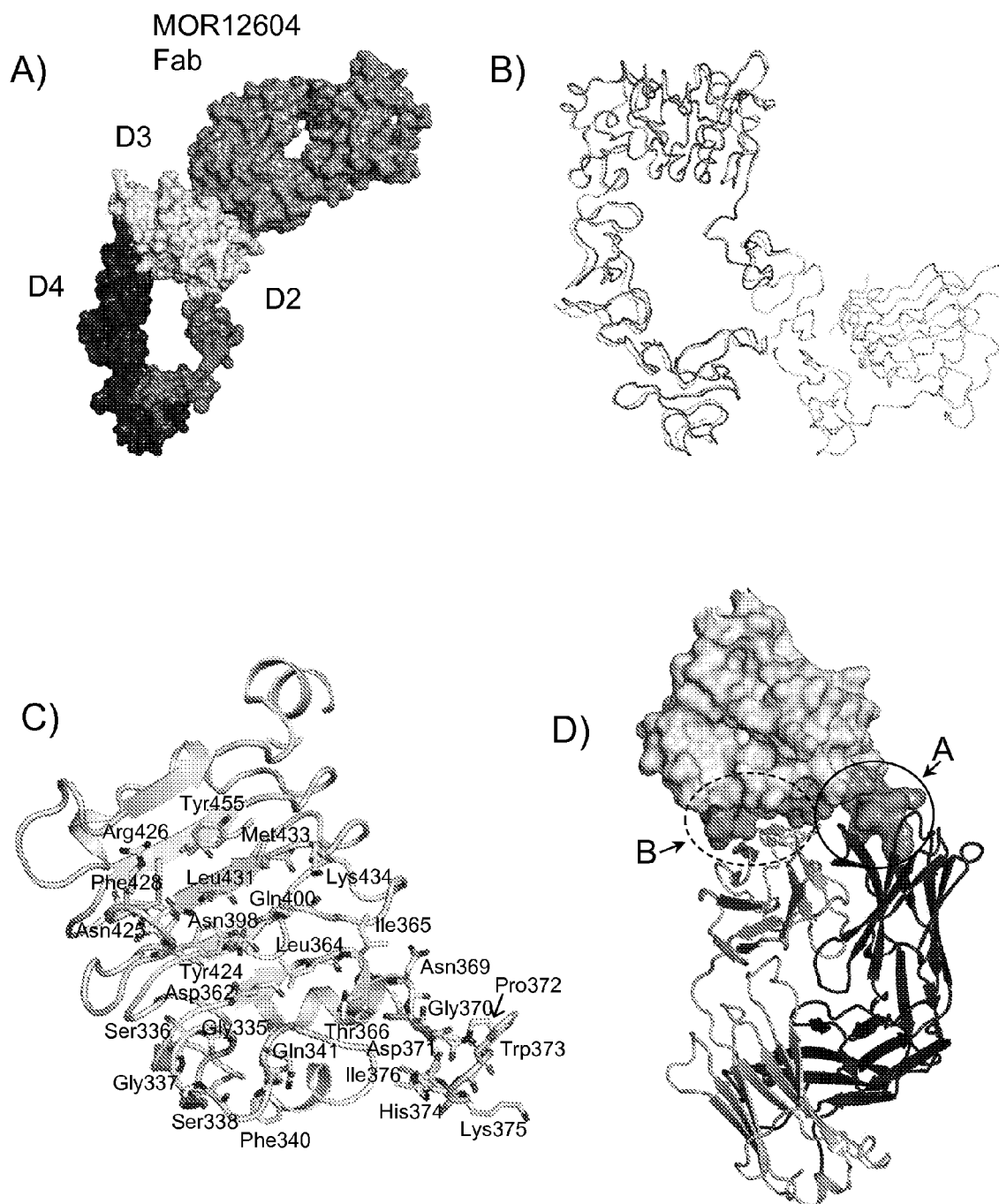


Figure 4

Figure 5

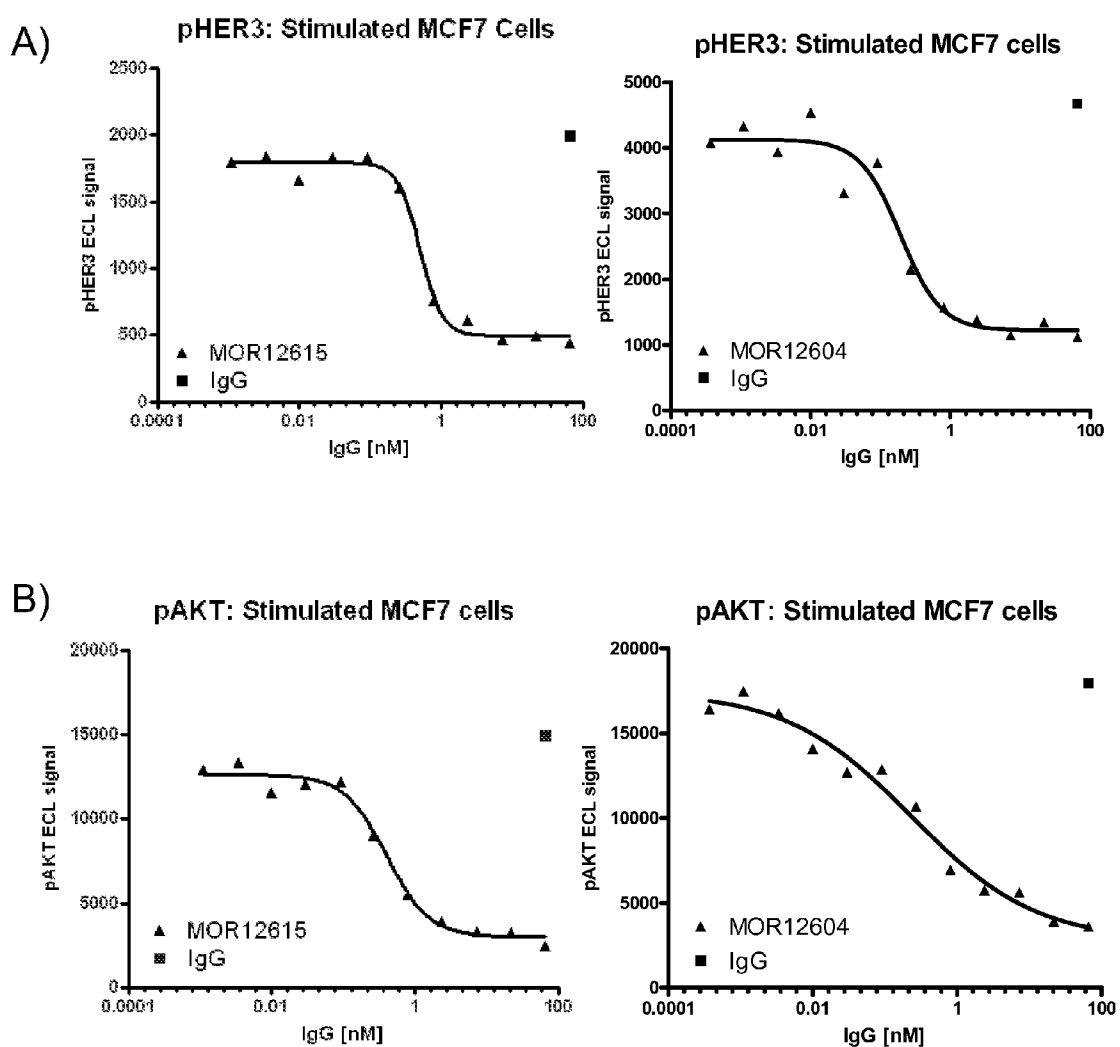


Figure 6

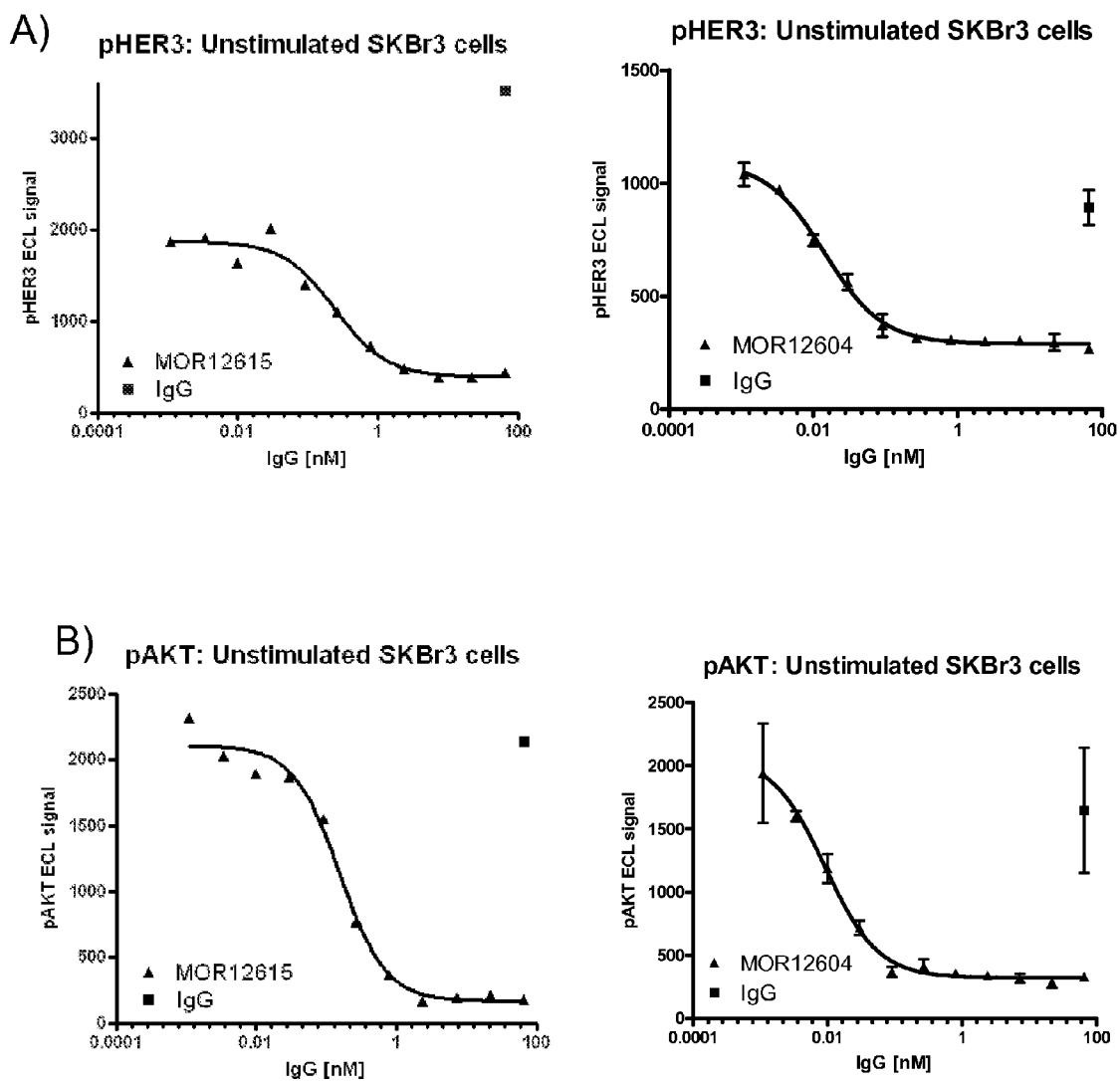
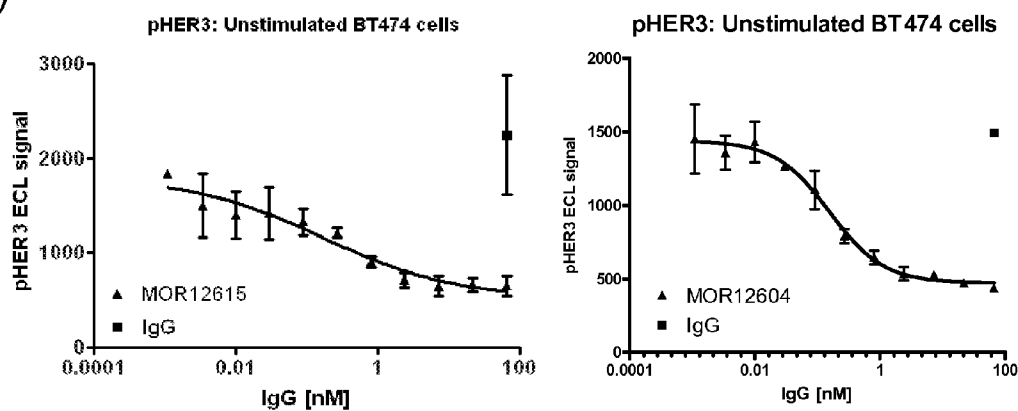


Figure 7

A)



B)

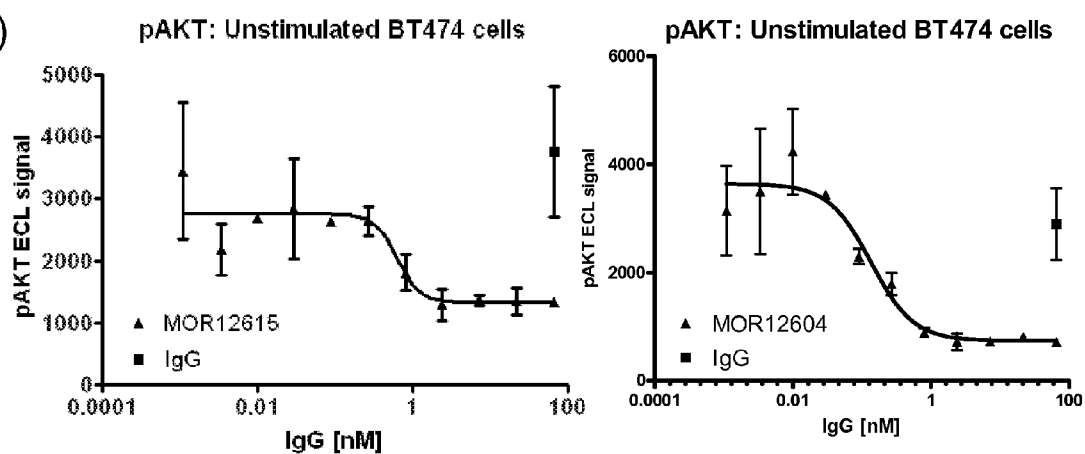


Figure 8

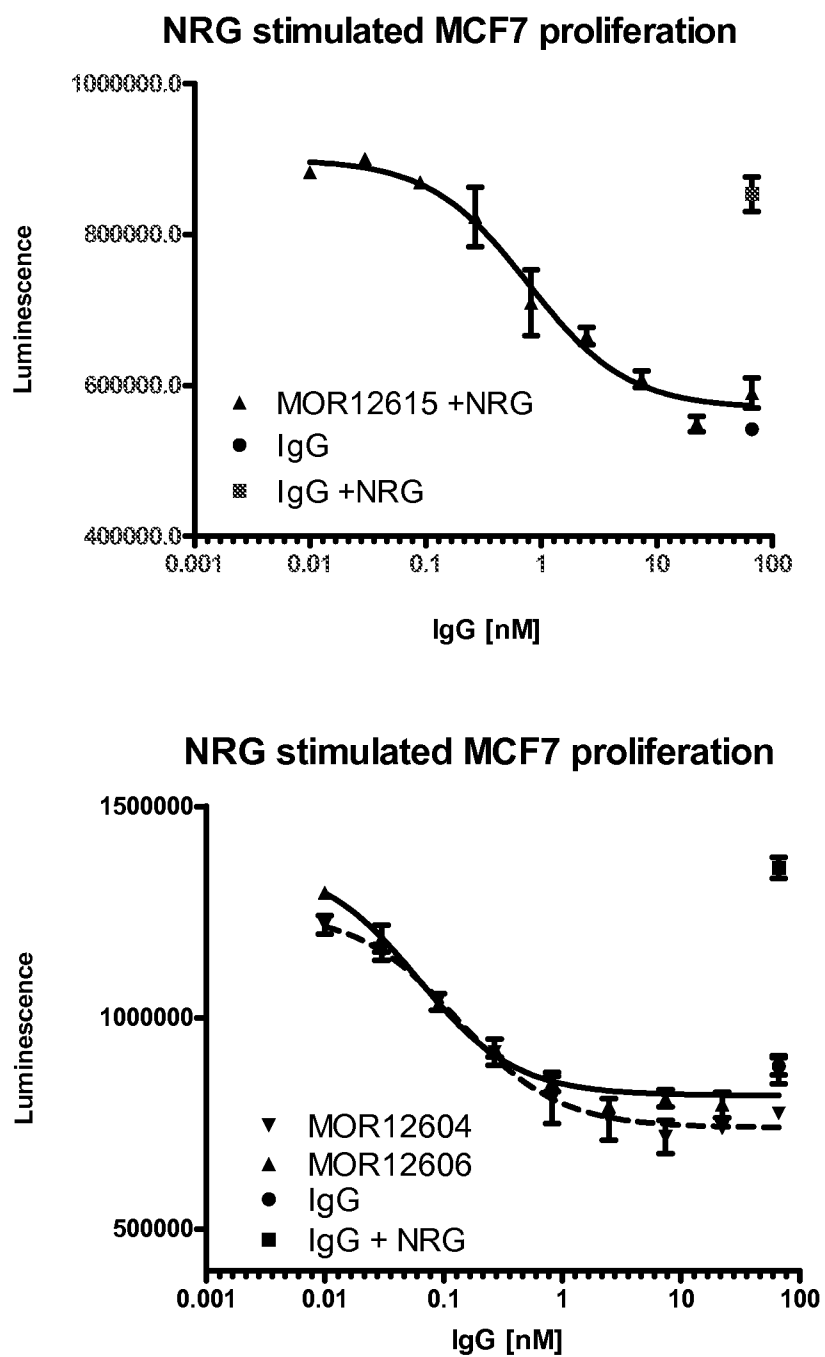


Figure 9

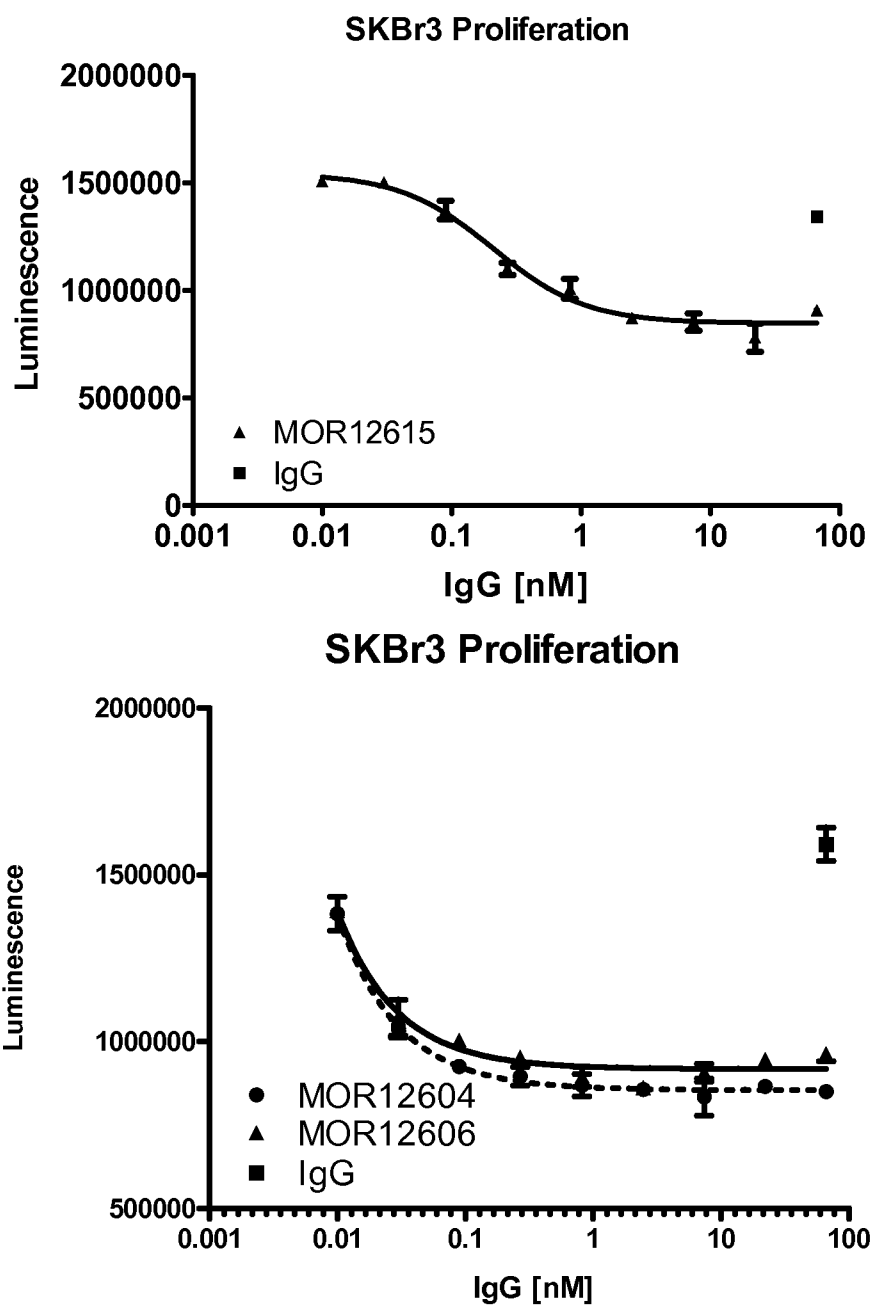
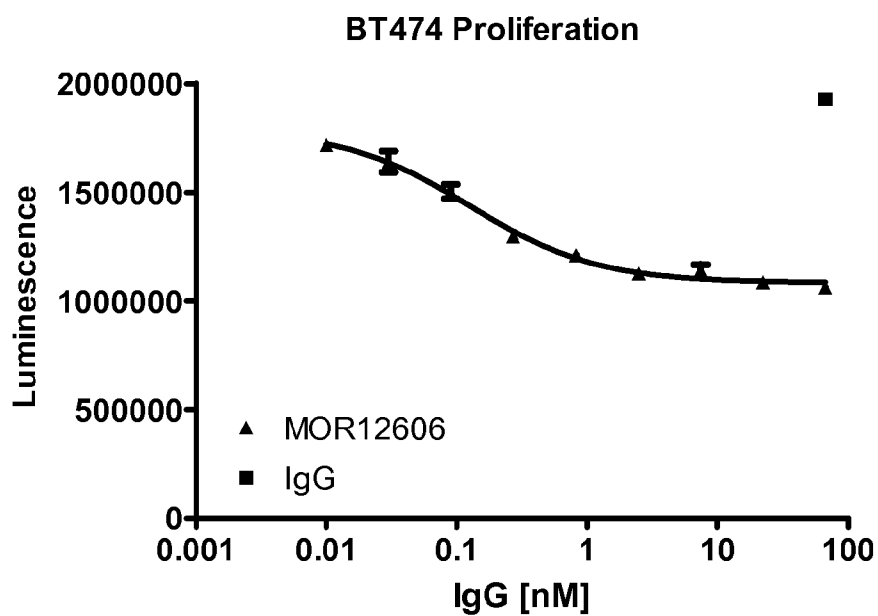
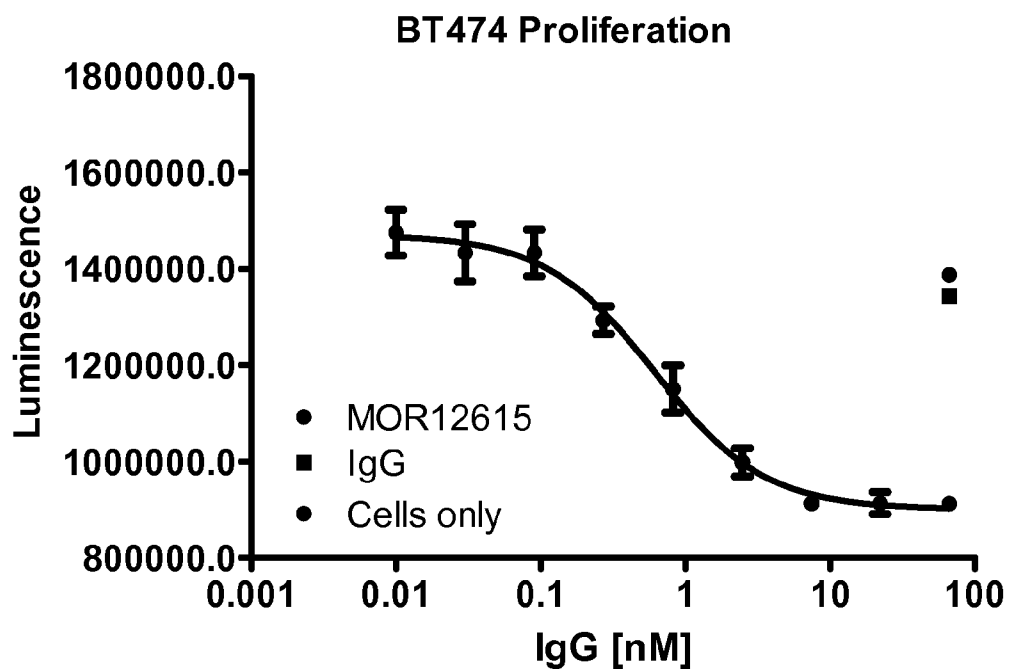


Figure 10



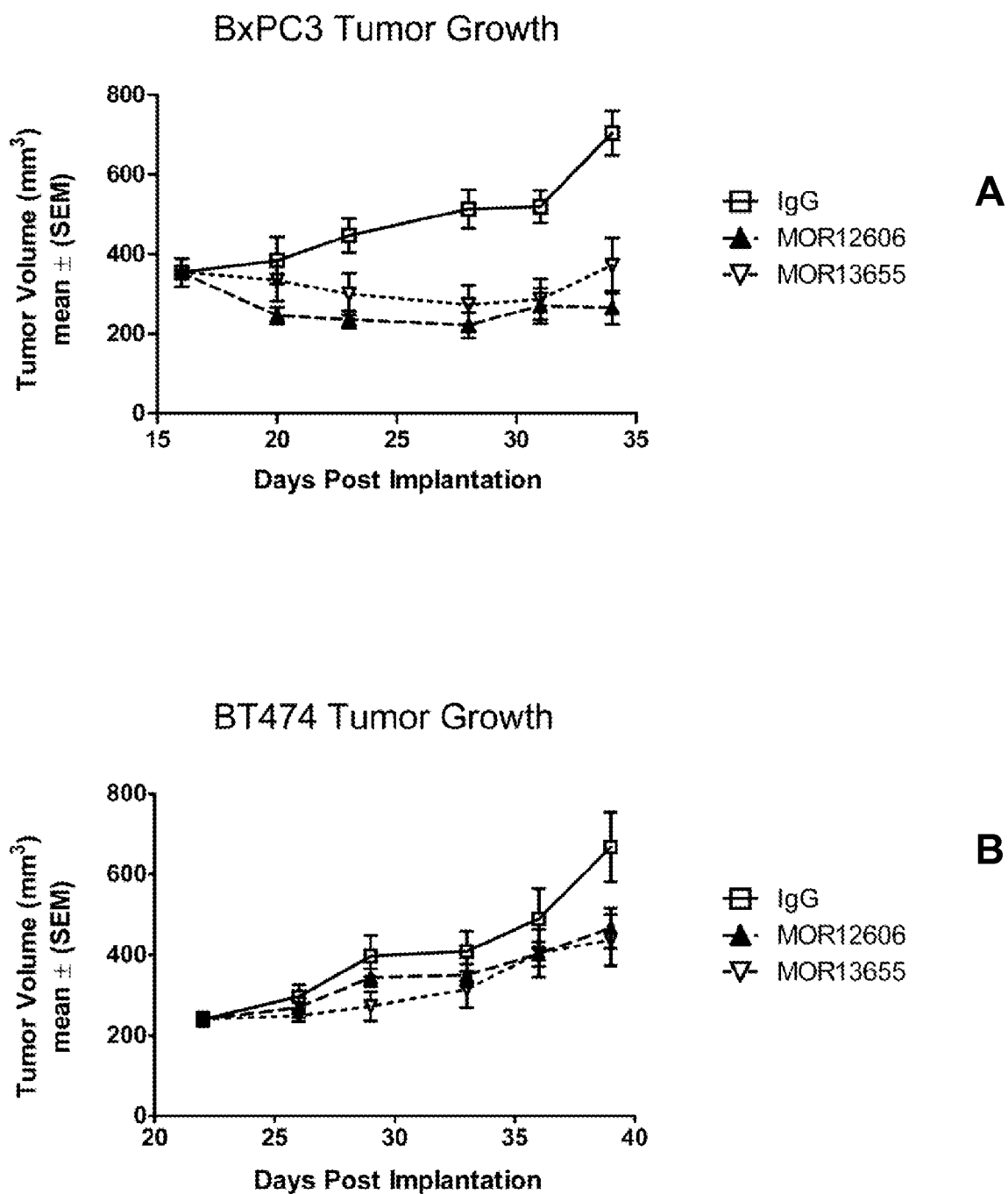


Figure 11

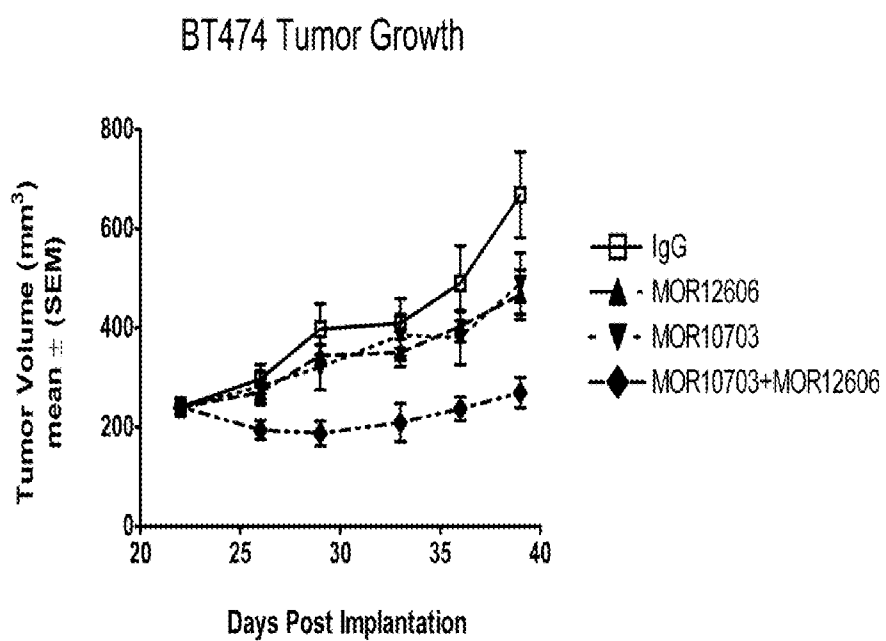


Figure 12

ANTIBODIES FOR EPIDERMAL GROWTH FACTOR RECEPTOR 3 (HER3) DIRECTED TO DOMAIN III AND DOMAIN IV OF HER3

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 61/566,912 filed on Dec. 5, 2011, the contents of which are incorporated herein by reference in their entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted in ASCII format via EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Apr. 2, 2013, is named PAT054914-US-NP_SL.txt and is 561,528 bytes in size.

FIELD OF THE INVENTION

[0003] The present invention relates to antibodies or fragments thereof that bind to a non-linear epitope within domain 3 of the HER3 receptor and inhibit both ligand-dependent and ligand-independent signal transduction. The invention also relates antibodies or fragments thereof that bind to amino acid residues within domains 3-4 of HER3 and inhibit both ligand-dependent and ligand-independent signal transduction; and compositions and methods of use of such antibodies or fragments thereof.

BACKGROUND OF THE INVENTION

[0004] The human epidermal growth factor receptor 3 (ErbB3, also known as HER3) is a receptor protein tyrosine kinase and belongs to the epidermal growth factor receptor (EGFR) subfamily of receptor protein tyrosine kinases, which also includes EGFR (HER1, ErbB1), HER2 (ErbB2, Neu), and HER4 (ErbB4) (Plowman et al., (1990) Proc. Natl. Acad. Sci. U.S.A. 87:4905-4909; Kraus et al., (1989) Proc. Natl. Acad. Sci. U.S.A. 86:9193-9197; and Kraus et al., (1993) Proc. Natl. Acad. Sci. U.S.A. 90:2900-2904). Like the prototypical epidermal growth factor receptor, the transmembrane receptor HER3 consists of an extracellular ligand-binding domain (ECD), a dimerization domain within the ECD, a transmembrane domain, an intracellular protein tyrosine kinase-like domain (TKD) and a C-terminal phosphorylation domain. Unlike the other HER family members, the kinase domain of HER3 displays very low intrinsic kinase activity.

[0005] The ligands neuregulin 1 (NRG) or neuregulin 2 bind to the extracellular domain of HER3 and activate receptor-mediated signaling pathway by promoting dimerization with other dimerization partners such as HER2. Heterodimerization results in activation and transphosphorylation of HER3's intracellular domain and is a means not only for signal diversification but also signal amplification. In addition, HER3 heterodimerization can also occur in the absence of activating ligands and this is commonly termed ligand-independent HER3 activation. For example, when HER2 is expressed at high levels as a result of gene amplification (e.g. in breast, lung, ovarian or gastric cancer) spontaneous HER2/HER3 dimers can be formed. In this situation the HER2/HER3 is considered the most active ErbB signaling dimer and is therefore highly transforming.

[0006] Increased HER3 has been found in several types of cancer such as breast, lung, gastrointestinal and pancreatic cancers. Interestingly, a correlation between the expression of

HER2/HER3 and the progression from a non-invasive to an invasive stage has been shown (Alimandi et al., (1995) Oncogene 10:1813-1821; DeFazio et al., (2000) Cancer 87:487-498; Naidu et al., (1988) Br. J. Cancer 78:1385-1390). Accordingly, agents that interfere with HER3 mediated signaling are needed.

SUMMARY OF THE INVENTION

[0007] The invention is based on the surprising discovery of antibodies or fragments thereof that bind to a non-linear epitope of HER3 receptor comprising amino acid residues within domain 3 of HER3 and block both ligand-dependent (e.g. neuregulin) and ligand-independent HER3 signaling pathways. The invention is also based on the discovery of antibodies or fragments thereof that bind to amino acid residues within domains 3-4 of HER3 and block both ligand-dependent (e.g. neuregulin) and ligand-independent HER3 signaling pathways.

[0008] Accordingly, in one aspect, the invention pertains to an isolated antibody or fragment thereof that recognizes a non-linear epitope of a HER3 receptor, wherein the non-linear epitope comprises amino acid residues within domain 3 of the HER3 receptor, wherein the antibody or fragment thereof binds to binding surface B, and wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

[0009] In one embodiment, binding surface B comprises at least one amino acid residue selected from a group consisting of amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455. In another embodiment, the antibody or fragment thereof further binds to binding surface A. In one embodiment, binding surface A comprises at least one amino acid residue selected from a group consisting of amino acid residues 362-376.

[0010] In another aspect, the invention pertains to an isolated antibody or fragment thereof that recognizes a non-linear epitope of a HER3 receptor, wherein the non-linear epitope comprises amino acid residues within domain 3 of the HER3 receptor, wherein the antibody or fragment thereof binds to a binding surface comprising at least one amino acid residue selected from binding surface A and at least one amino acid residue selected from binding surface B, and wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

[0011] In one embodiment, the antibody or fragment thereof blocks HER3 ligand binding on the HER3 receptor. In one embodiment, the HER3 ligand is selected from the group consisting of neuregulin 1 (NRG), neuregulin 2, betacellulin, heparin-binding epidermal growth factor, and epiregulin. In one embodiment, the antibody or fragment thereof has any one of the characteristics selected from the group consisting of binding to the inactive state of the HER3 receptor, preventing HER3 adopting an active conformation due to steric hindrance between the antibody or fragment thereof and domains of HER3, preventing HER3 adopting an active conformation by reducing the degree of flexibility in domain 3, inducing a conformational change in domain 3 residues 371-377 that prevents HER3 from adopting an active conformation, destabilizing HER3 such that it is susceptible to degradation, accelerating down regulation of cell surface HER3, and generating an un-natural HER3 dimer that is susceptible to proteolytic degradation or unable to dimerize with other receptor tyrosine kinases. In one embodiment, binding surface A comprises amino acid residues 362-376. In one

embodiment, binding surface B comprises amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455.

[0012] In one embodiment, the non-linear epitope comprises amino acid residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), or a subset thereof. In one embodiment, the VH of the antibody or fragment thereof binds to at least one of the following HER3 residues: Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, and Lys434. In one embodiment, the VL of the antibody or fragment thereof binds to at least one of the following HER3 residues: Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364, Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455. In one embodiment, binding of the antibody or fragment thereof to the HER3 receptor in the absence of a HER3 ligand reduces ligand-independent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3. In one embodiment, the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by a HER3 ligand-independent phosphorylation assay. In one embodiment, the HER3 ligand-independent phosphorylation assay uses HER2 amplified cells, wherein the HER2 amplified cells are SK-Br-3 cells and BT-474. In one embodiment, binding of the antibody or fragment thereof to the HER3 receptor in the presence of a HER3 ligand reduces ligand-dependent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3. In one embodiment, the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by HER3 ligand-dependent phosphorylation assay. In one embodiment, the HER3 ligand-dependent phosphorylation assay uses stimulated MCF7 cells in the presence of neuregulin (NRG). In one embodiment, the antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a chimeric antibody, a humanized antibody, and a synthetic antibody.

[0013] In another aspect, the invention pertains to isolated antibody or fragment thereof that recognizes an epitope of a HER3 receptor, wherein the epitope comprises amino acid residues within domains 3-4 of the HER3 receptor, and wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

[0014] In one embodiment, the epitope comprises at least one amino acid residue selected from the group consisting of amino acid residues: 329-498 (domain 3) of SEQ ID NO: 1, and at least one amino acid residue selected from the group consisting of amino acid residues 499-642 (domain 4) of SEQ ID NO: 1. In one embodiment, the epitope comprising amino acid residues within domains 3-4 is selected from the group consisting of a linear epitope, a non-linear epitope, and a conformational epitope. In one embodiment, binding of the antibody or fragment thereof to the HER3 receptor in the absence of a HER3 ligand reduces ligand-independent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3. In one embodiment, the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by a HER3 ligand-independent phosphorylation assay. In one embodiment, the HER3 ligand-independent phosphorylation assay uses HER2 amplified cells, wherein the HER2 amplified cells are SK-Br-3 cells and BT-474. In one embodiment, binding of the antibody or fragment thereof to the HER3 receptor in the presence of a HER3 ligand reduces ligand-dependent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3. In

one embodiment, the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by HER3 ligand-dependent phosphorylation assay. In one embodiment, the HER3 ligand-dependent phosphorylation assay uses stimulated MCF7 cells in the presence of neuregulin (NRG).

[0015] In another aspect, the invention pertains to an isolated antibody or fragment thereof to a HER3 receptor, having a dissociation (K_D) of at least $1 \times 10^7 \text{ M}^{-1}$, 10^8 M^{-1} , 10^9 M^{-1} , 10^{10} M^{-1} , 10^{11} M^{-1} , 10^{12} M^{-1} , 10^{13} M^{-1} , wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction. In one embodiment, the antibody or fragment thereof inhibits phosphorylation of HER3 as measured by an in vitro phosphorylation assay selected from the group consisting of phospho-HER3 and phospho-Akt.

[0016] In another aspect, the invention pertains to an isolated antibody or fragment thereof binds to the same non-linear epitope within domain 3 of HER3 as an antibody described in Table 1.

[0017] In another aspect, the invention pertains to an isolated antibody or fragment thereof, binds to the same amino acid residues within domains 3-4 of HER3 as an antibody described in Table 2.

[0018] In another aspect, the invention pertains to a fragment of an antibody that binds to HER3 selected from the group consisting of; Fab, $F(ab_2)'$, $F(ab_2)_2$, scFv, VHH, VH, VL, dAbs, wherein the fragment of the antibody blocks both ligand-dependent and ligand-independent signal transduction.

[0019] In another aspect, the invention pertains to a pharmaceutical composition comprising an antibody or fragment thereof and a pharmaceutically acceptable carrier. In one embodiment, the pharmaceutical composition further comprises an additional therapeutic agent. In one embodiment, the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor. In one embodiment, the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix®/Panitumumab, mAb 806, Nimotuzumab, Iressa®/Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb®/Lapatinib Ditosylate, Tarceva®/Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate/Tykerb®; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203 (Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor. In one embodiment, the additional therapeutic agent is a HER3 inhibitor, wherein the HER3 inhibitor is MOR10703. In one embodiment, the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus/Deforolimus, AP23573, MK8669, everolimus/Afinitor®. In one embodiment, the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BKM120 and BYL719.

[0020] In one aspect, the invention pertains to a method of treating a cancer comprising selecting a subject having an HER3 expressing cancer, administering to the subject an effective amount of a composition comprising an antibody or fragment thereof disclosed in Table 1 or Table 2. In one

embodiment, the subject is a human and the cancer is selected from the group consisting of breast cancer, colorectal cancer, lung cancer, multiple myeloma, ovarian cancer, liver cancer, gastric cancer, acute myeloid leukemia, chronic myeloid leukemia, osteosarcoma, squamous cell carcinoma, peripheral nerve sheath tumors, schwannoma, head and neck cancer, bladder cancer, esophageal cancer, Barretts esophageal cancer, glioblastoma, clear cell sarcoma of soft tissue, malignant mesothelioma, neurofibromatosis, renal cancer, and melanoma, prostate cancer, benign prostatic hyperplasia (BPH), gynecomastica, and endometriosis. In one embodiment, the cancer is breast cancer.

[0021] In one aspect, the invention pertains to use of the antibody or fragment thereof for use as a medicament. In one aspect, the invention pertains to use of the antibody or fragment thereof for use in treating a cancer mediated by a HER3 ligand-dependent signal transduction or ligand-independent signal transduction pathway. In one aspect, the invention pertains to use of the antibody or fragment thereof for the manufacture of a medicament for the treatment of a cancer mediated by a HER3 ligand-dependent signal transduction or ligand-independent signal transduction pathway selected from the group consisting of breast cancer, colorectal cancer, lung cancer, multiple myeloma, ovarian cancer, liver cancer, gastric cancer, pancreatic cancer, acute myeloid leukemia, chronic myeloid leukemia, osteosarcoma, squamous cell carcinoma, peripheral nerve sheath tumors, schwannoma, head and neck cancer, bladder cancer, esophageal cancer, Barretts esophageal cancer, glioblastoma, clear cell sarcoma of soft tissue, malignant mesothelioma, neurofibromatosis, renal cancer, melanoma, prostate cancer, benign prostatic hyperplasia (BPH), gynecomastica, and endometriosis.

BRIEF DESCRIPTION OF FIGURES

[0022] FIG. 1 Representative MOR12615 SET curves obtained with human HER3;

[0023] FIG. 2 SK-Br-3 cell binding determination by FACS titration;

[0024] FIG. 3 HER3 domain binding ELISA;

[0025] FIG. 4 (A) Surface representation of the HER3/MOR12604 x-ray crystal structure. HER3 (labeled by domains: D2, D3 & D4) is in the closed conformation, and MOR12604 binds to domain 3. (B) C α -superposition of HER3 from the HER3/MOR12604 structure (dark gray) with an unbound HER3 structure (light gray; Cho et al., (2003) Nature 421:756-760) aligned by domain 3. (C) View of the domain 3 epitope recognized by 12604. Highlighted HER3 residues are within 5Å of MOR12604 in the x-ray crystal structure (all positions disclosed in FIG. 4C are residues of SEQ ID NO: 1). (D) View of domain 3/MOR12604 interaction. The MOR12604 binding surface is highlighted in dark gray with surface A (solid line) and surface B (dashed line) indicated;

[0026] FIG. 5 Inhibition of ligand induced (A) HER3 and (B) Akt phosphorylation in MCF7 cells;

[0027] FIG. 6 Inhibition of ligand independent (A) HER3 and (B) Akt phosphorylation in HER2 amplified SKBr3 cells;

[0028] FIG. 7 Inhibition of ligand independent (A) HER3 and (B) Akt phosphorylation in HER2 amplified BT474 cells;

[0029] FIG. 8 Inhibition of ligand stimulated proliferation of MCF7 cells;

[0030] FIG. 9 Inhibition of ligand-independent proliferation of SKBr3 cells;

[0031] FIG. 10 Inhibition of ligand-independent proliferation of BT474 cells;

[0032] FIG. 11 Data showing inhibition of tumor growth in vivo in BxPC3 (A) and BT474 (B) using MOR12606 and MOR13655; and

[0033] FIG. 12 Data showing improved inhibition of tumor growth in vivo in BxPC3 using a combination of MOR12606 (DIII binder) and MOR10703 (DII+IV binder).

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0034] In order that the present invention may be more readily understood, certain terms are first defined. Additional definitions are set forth throughout the detailed description.

[0035] The phrase “signal transduction” or “signaling activity” as used herein refers to a biochemical causal relationship generally initiated by a protein-protein interaction such as binding of a growth factor to a receptor, resulting in transmission of a signal from one portion of a cell to another portion of a cell. For HER3, the transmission involves specific phosphorylation of one or more tyrosine, serine, or threonine residues on one or more proteins in the series of reactions causing signal transduction. Penultimate processes typically include nuclear events, resulting in a change in gene expression.

[0036] The term “HER3” or “HER3 receptor” also known as “ErbB3” as used herein refers to mammalian HER3 protein and “her3” or “erbB3” refers to mammalian her3 gene. The preferred HER3 protein is human HER3 protein present in the cell membrane of a cell. The human her3 gene is described in U.S. Pat. No. 5,480,968 and Plowman et al., (1990) Proc. Natl. Acad. Sci. USA, 87:4905-4909.

[0037] Human HER3 as defined in Accession No. NP_001973 (human), and represented below as SEQ ID NO: 1. All nomenclature is for full length, immature HER3 (amino acids 1-1342). The immature HER3 is cleaved between positions 19 and 20, resulting in the mature HER3 protein (20-1342 amino acids).

(SEQ ID NO: 1)
 mrandalqvl gllfslargs evgnsqavcp gtlnglsvtg
 daenqyqtly klyercevnm gnleivltgh nadlsflqwi
 revtgyvlva mnefstlplp nlrvvrgtqv ydgkfaifvm
 lnyntnssha lrqlrltqlt eilsggvvie kndklchmdt
 idwrdivrdr daeivvkdng rscppchevc kgrcwpggse
 dcqtltktic apqcnghcfcg pnpnqccnde caggsgpqp
 tdcfacrhfn dsgacvprcp qplvynkltf qlepnphtky
 qyggvcvasc phnfvvdqts cvracppdkm evdknglkmc
 epcgglcпка cegtsggsrf qtvdsnidg fvnctkilgn
 ldflitglnq dpwhkipald peklnvfrtv reitgylniq
 swpphmnfs vfsnlttigg rslynrgfsl limknlvts
 lgfrslkeis agriyisanr qlcyhhslnw tkvlrgptee
 rldikhnrpr rdcvaegkvc dplcssggcw gpgpgqclsc

-continued

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rnysrggv cv thcnflngep refaheaecf schpecqpm
gtatcngsgs dtcaqcahfr dgphcvsscp hgvlgakgpi
ykypdvq nec rpchenctqg ckgpelqdc1 gqtlvligkt
hltmaltvia glvvifmmlg gtflwrgrr ignkramrry
lorgesiepl dpsekankvl arifketelr klkvlsgsvf
gtvhkgvwip egesikipvc ikviedksgr qsfqavtdhm
laigsldhah ivrllglcpg sslqlvtqyl plgslldhvr
qhrgalgpql llngwvqiak gmyyleehgm vhrnlaarnv
llkspsqvqv adfgvadllp pddkqllyse aktpikwmal
esihfgkyth qsdvwsygvv vwelmtfgae pyaglr laev
pdllekgerl aqpqictidv ymvvmkcwmi denirptfke
laneftmar dpprylvikr esgpgiapgp ephgltnkkl
eevelepeld ldldeleaed nlatttlgsa lslpvgtlnr
prgsqsllep ssgympmnqg nlgescquesa vsgssercpr
pvslhpmprg classessegh vtgseaelqe kvsmcrsrer
srsprprgds ayhsqrhsl1 tpvtplspgg leeedvngyv
mpdthlkgtp ssregt1ssv glssvlgtee ededeeyeym
nrrrrhspph pprpssleel gyeymdvgsd lsaslgstqs
cplhvpimp tagttdedy eymnqrqdg gpggdyaaamg
acpaseqgye emrafqgpg qaphvhyarl ktlrsleatd
safndpdywh srlfpkanaq rt

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[0038] The term “HER3 ligand” as used herein refers to polypeptides which bind and activate HER3. Examples of HER3 ligands include, but are not limited to neuregulin 1 (NRG) and neuregulin 2, betacellulin, heparin-binding epidermal growth factor, and epi-regulin. The term includes biologically active fragments and/or variants of a naturally occurring polypeptide.

[0039] The “HER2-HER3 protein complex” is a non-covalently associated oligomer containing HER2 receptor and the HER3 receptor. This complex can form when a cell expressing both of these receptors is exposed to a HER3 ligand e.g., NRG or when HER2 is active/overexpressed

[0040] The phrase “HER3 activity” or “HER3 activation” as used herein refers to an increase in oligomerization (e.g. an increase in HER3 containing complexes), HER3 phosphorylation, conformational rearrangements (for example those induced by ligands), and HER3 mediated downstream signaling.

[0041] The term “stabilization” or “stabilized” used in the context of HER3 refers to an antibody or fragment thereof that directly maintains (locks, tethers, holds, preferentially binds, favors) the inactive state or conformation of HER3 without blocking ligand binding to HER3, such that ligand binding is no longer able to activate HER3.

[0042] The term “ligand-dependent signaling” as used herein refers to the activation of HER3 via ligand. HER3 activation is evidenced by increased heterodimerization and/or HER3 phosphorylation such that downstream signaling pathways (e.g. PI3K) are activated. The antibody or fragment thereof can statistically significantly reduce the amount of

phosphorylated HER3 in a stimulated cell exposed to an antibody or fragment thereof relative to an untreated (control) cell, as measured using the assays described in the Examples. The cell which expresses HER3 can be a naturally occurring cell line (e.g. MCF7) or can be recombinantly produced by introducing nucleic acids encoding HER3 protein into a host cell. Cell stimulation can occur either via the exogenous addition of an activating HER3 ligand or by the endogenous expression of an activating ligand.

[0043] The antibody or fragment thereof which “reduces neuregulin-induced HER3 activation in a cell” is one which statistically significantly reduces HER3 tyrosine phosphorylation relative to an untreated (control) cell, as measured using the assays described in the Examples. This can be determined based on HER3 phosphotyrosine levels following exposure of HER3 to NRG and the antibody of interest. The cell which expresses HER3 protein can be a naturally occurring cell or cell line (e.g. MCF7) or can be recombinantly produced.

[0044] The term “ligand-independent signaling” as used herein refers to cellular HER3 activity (e.g phosphorylation) in the absence of a requirement for ligand binding. For example, ligand-independent HER3 activation can be a result of HER2 overexpression or activating mutations in HER3 heterodimer partners such as EGFR and HER2. The antibody or fragment thereof can statistically significantly reduce the amount of phosphorylated HER3 in a cell exposed to an antibody or fragment thereof relative to an untreated (control) cell. The cell which expresses HER3 can be a naturally occurring cell line (e.g. SK-Br-3) or can be recombinantly produced by introducing nucleic acids encoding HER3 protein into a host cell.

[0045] The term “blocks” as used herein refers to stopping or preventing an interaction or a process, e.g., stopping ligand-dependent or ligand-independent signaling.

[0046] The term “recognize” as used herein refers to an antibody or fragment thereof that finds and interacts (e.g., binds) with its epitope in domain 3 of HER3; domain 4 of HER3; or both domain 3 and domain 4 of HER3. The epitope can be a linear, non-linear, or conformational epitope. For example, an antibody or fragment thereof interacts with amino acid residues: 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), or a subset thereof of HER3. In another example, the antibody or fragment thereof interacts with at least one amino acid residue selected from amino acid residues: 329-498 (domain 3), or a subset thereof. In another example, the antibody or fragment thereof interacts with at least one amino acid residue selected from amino acid residues: 499-642 (domain 4), or a subset thereof. In another example, the antibody or fragment thereof interacts with at least one amino acid residue selected from domain 3 of HER3 (amino acid residues 329-498 of SEQ ID NO: 1), and at least one amino acid residue selected from domain 4 (amino acid residues 499-642 of SEQ ID NO: 1), or a subset thereof.

[0047] The phrase “concurrently binds” as used herein refers to a HER3 ligand that can bind to a ligand binding site on the HER3 receptor along with the HER3 antibody or fragment thereof. This means that both the antibody and ligand can bind to the HER3 receptor together. For the sake of illustration only, the HER3 ligand NRG, can bind to the HER3 receptor along with the HER3 antibody. Assay to measure concurrent binding of the ligand and antibody are described in the Examples section.

[0048] The term “fails” as used herein refers to an antibody or fragment thereof that does not do a particular event. For example, an antibody or fragment thereof that “fails to activate signal transduction” is one that does not trigger signal transduction.

[0049] The term “antibody” as used herein refers to whole antibodies that interact with (e.g., by binding, steric hindrance, stabilizing/destabilizing, spatial distribution) an HER3 epitope and inhibit signal transduction. A naturally occurring “antibody” is a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1q) of the classical complement system. The term “antibody” includes for example, monoclonal antibodies, human antibodies, humanized antibodies, camelised antibodies, chimeric antibodies, single-chain Fvs (scFv), disulfide-linked Fvs (sdFv), Fab fragments, F (ab') fragments, and anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. The antibodies can be of any isotype (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass.

[0050] Both the light and heavy chains are divided into regions of structural and functional homology. The terms “constant” and “variable” are used functionally. In this regard, it will be appreciated that the variable domains of both the light (VL) and heavy (VH) chain portions determine antigen recognition and specificity. Conversely, the constant domains of the light chain (CL) and the heavy chain (CH1, CH2 or CH3) confer important biological properties such as secretion, transplacental mobility, Fc receptor binding, complement binding, and the like. By convention the numbering of the constant region domains increases as they become more distal from the antigen binding site or amino-terminus of the antibody. The N-terminus is a variable region and at the C-terminus is a constant region; the CH3 and CL domains actually comprise the carboxy-terminus of the heavy and light chain, respectively.

[0051] The phrase “antibody fragment”, as used herein, refers to one or more portions of an antibody that retain the ability to specifically interact with (e.g., by binding, steric hindrance, stabilizing/destabilizing, spatial distribution) an HER3 epitope and inhibit signal transduction. Examples of binding fragments include, but are not limited to, a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; a F(ab)₂ fragment, a bivalent fragment

comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consisting of the VH and CH1 domains; a Fv fragment consisting of the VL and VH domains of a single arm of an antibody; a dAb fragment (Ward et al., (1989) *Nature* 341:544-546), which consists of a VH domain; and an isolated complementarity determining region (CDR).

[0052] Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Bird et al., (1988) *Science* 242:423-426; and Huston et al., (1988) *Proc. Natl. Acad. Sci.* 85:5879-5883). Such single chain antibodies are also intended to be encompassed within the term “antibody fragment”. These antibody fragments are obtained using conventional techniques known to those of skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

[0053] Antibody fragments can also be incorporated into single domain antibodies, maxibodies, minibodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, (2005) *Nature Biotechnology* 23:1126-1136). Antibody fragments can be grafted into scaffolds based on polypeptides such as Fibronectin type 111 (Fn3) (see U.S. Pat. No. 6,703,199, which describes fibronectin polypeptide monobodies).

[0054] Antibody fragments can be incorporated into single chain molecules comprising a pair of tandem Fv segments (VH-CH1-VH-CH1) which, together with complementary light chain polypeptides, form a pair of antigen binding regions (Zapata et al., (1995) *Protein Eng.* 8:1057-1062; and U.S. Pat. No. 5,641,870).

[0055] The term “epitope” includes any protein determinant capable of specific binding to an immunoglobulin or otherwise interacting with a molecule. Epitopic determinants generally consist of chemically active surface groupings of molecules such as amino acids or carbohydrate or sugar side chains and can have specific three-dimensional structural characteristics, as well as specific charge characteristics. An epitope may be “linear,” “non-linear” or “conformational.”

[0056] The term “linear epitope” refers to an epitope with all of the points of interaction between the protein and the interacting molecule (such as an antibody) occur linearly along the primary amino acid sequence of the protein (continuous). Once a desired epitope on an antigen is determined, it is possible to generate antibodies to that epitope, e.g., using the techniques described in the present invention. Alternatively, during the discovery process, the generation and characterization of antibodies may elucidate information about desirable epitopes. From this information, it is then possible to competitively screen antibodies for binding to the same epitope. An approach to achieve this is to conduct cross-competition studies to find antibodies that competitively bind with one another, e.g., the antibodies compete for binding to the antigen. A high throughput process for “binning” antibodies based upon their cross-competition is described in International Patent Application No. WO 2003/48731. As will be appreciated by one of skill in the art, practically anything to which an antibody can specifically bind could be an epitope. An epitope can comprises those residues to which the antibody binds.

[0057] The term “non-linear epitope” refers to epitope with non-contiguous amino acids that form a three-dimensional

structure within a particular domain (e.g., within domain 1, within domain 2, within domain 3, or within domain 4). In one embodiment, the non-linear epitope is within domain 2. The non-linear epitope may also occur between two or more domains (e.g., the interface between domains 3-4). Non-linear epitope also refers to non-contiguous amino acids that are a result of a three-dimensional structure within a particular domain.

[0058] The term “conformational epitope” refers to an epitope in which discontinuous amino acids come together in a three dimensional configuration. In a conformational epitope, the points of interaction occur across amino acid residues on the protein that are separated from one another in the sequence. As will be appreciated by one of skill in the art, the space that is occupied by a residue or side chain that creates the shape of a molecule helps to determine what an epitope is.

[0059] In one embodiment, the epitope is within domain 3 of HER3. In one embodiment, the epitope is a non-linear epitope comprising amino acids residues within domain 3 of HER3. In one embodiment, the non-linear epitope comprises amino acid residues: 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), or a subset thereof of SEQ ID NO:1.

[0060] In another embodiment, the epitope is within domain 4 of HER3. In one embodiment, the epitope comprises at least one amino acid residue selected from domain 4 (amino acid residues 499-642 of SEQ ID NO: 1), or a subset thereof. In one embodiment, the epitope is a linear epitope within domain 4 of HER3. In one embodiment, the epitope is a non-linear epitope within domain 4 of HER3. In another embodiment, the epitope is a conformational epitope within domain 4 of HER3.

[0061] In another embodiment, the epitope is within domains 3-4 of HER3. In one embodiment, the epitope comprises at least one amino acid residue selected from domain 3 (amino acid residues 329-498 of SEQ ID NO: 1), or a subset thereof. In one embodiment, the epitope comprises at least one amino acid residue selected from domain 4 (amino acid residues 499-642 of SEQ ID NO: 1), or a subset thereof. In one embodiment, the epitope comprises at least one amino acid residue selected from domain 3 (amino acid residues 329-498 of SEQ ID NO: 1) and least one amino acid residue selected from domain 4 (amino acid residues 499-642 of SEQ ID NO: 1) or a subset thereof. In one embodiment, the epitope is a linear epitope. In one embodiment, the epitope is a non-linear epitope. In another embodiment, the epitope is a conformational epitope.

[0062] Generally, antibodies specific for a particular target antigen will preferentially recognize an epitope on the target antigen in a complex mixture of proteins and/or macromolecules. Regions of a given polypeptide that include an epitope can be identified using any number of epitope mapping techniques, well known in the art. See, e.g., *Epitope Mapping Protocols in Methods in Molecular Biology*, Vol. 66 (Glenn E. Morris, Ed., 1996) Humana Press, Totowa, N.J. For example, linear epitopes may be determined by e.g., concurrently synthesizing large numbers of peptides on solid supports, the peptides corresponding to portions of the protein molecule, and reacting the peptides with antibodies while the peptides are still attached to the supports. Such techniques are known in the art and described in, e.g., U.S. Pat. No. 4,708,871; Geysen et al., (1984) *Proc. Natl. Acad. Sci. USA* 8:3998-4002; Geysen et al., (1985) *Proc. Natl. Acad. Sci. USA* 82:78-

182; Geysen et al., (1986) *Mol. Immunol.* 23:709-715. Similarly, non-linear and conformational epitopes are readily identified by determining spatial conformation of amino acids such as by, e.g., hydrogen/deuterium exchange, x-ray crystallography and two-dimensional nuclear magnetic resonance. See, e.g., *Epitope Mapping Protocols*, supra. Antigenic regions of proteins can also be identified using standard antigenicity and hydropathy plots, such as those calculated using, e.g., the Omega version 1.0 software program available from the Oxford Molecular Group. This computer program employs the Hopp/Woods method, Hopp et al., (1981) *Proc. Natl. Acad. Sci. USA* 78:3824-3828; for determining antigenicity profiles, and the Kyte-Doolittle technique, Kyte et al., (1982) *J. Mol. Biol.* 157:105-132; for hydropathy plots.

[0063] The term “binding surface” as used herein refers to multiple contiguous or non-contiguous surfaces in a 3D configuration on HER3, e.g., domain 3 of HER3. These surfaces form part of the epitope and interact with an antibody or fragment thereof. For example, a binding surface can comprise at least two surfaces (e.g., surface A and surface B, see FIG. 4D), at least three surfaces (e.g., surface A, surface B, and surface C), at least four surfaces (e.g., surface A, surface B, surface C, and surface D), at least five surfaces (e.g., surface A, surface B, surface C, surface D, and surface E), at least six surfaces (e.g., surface A, surface B, surface C, surface D, surface E, and surface F), at least seven surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, and surface G), at least eight surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, surface G, and surface H), at least nine surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, surface G, surface H, and surface I), or at least ten surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, surface G, surface H, surface I, and surface J).

[0064] The term “binding surface A” as used herein refers to a surface on domain 3 of HER3 comprising at least one amino acid residue selected from a group consisting of amino acid residues 362-376.

[0065] The term “binding surface B” as used herein refers to a surface on domain 3 of HER3 comprising at least one amino acid residue selected from a group consisting of amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455.

[0066] The phrases “monoclonal antibody” or “monoclonal antibody composition” as used herein refers to polypeptides, including antibodies, antibody fragments, bispecific antibodies, etc. that have substantially identical to amino acid sequence or are derived from the same genetic source. This term also includes preparations of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope.

[0067] The phrase “human antibody”, as used herein, includes antibodies having variable regions in which both the framework and CDR regions are derived from sequences of human origin. Furthermore, if the antibody contains a constant region, the constant region also is derived from such human sequences, e.g., human germline sequences, or mutated versions of human germline sequences or antibody containing consensus framework sequences derived from human framework sequences analysis, for example, as described in Knappik et al., (2000) *J Mol Biol* 296:57-86). The structures and locations of immunoglobulin variable domains, e.g., CDRs, may be defined using well known num-

bering schemes, e.g., the Kabat numbering scheme, the Chothia numbering scheme, or a combination of Kabat and Chothia (see, e.g., Sequences of Proteins of Immunological Interest, U.S. Department of Health and Human Services (1991), eds. Kabat et al.; Lazikani et al., (1997) J. Mol. Biol. 273:927-948); Kabat et al., (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services; Chothia et al., (1987) J. Mol. Biol. 196:901-917; Chothia et al., (1989) Nature 342:877-883; and Al-Lazikani et al., (1997) J. Mol. Biol. 273:927-948.

[0068] The human antibodies of the invention may include amino acid residues not encoded by human sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo, or a conservative substitution to promote stability or manufacturing).

[0069] The phrase "human monoclonal antibody" as used herein refers to antibodies displaying a single binding specificity which have variable regions in which both the framework and CDR regions are derived from human sequences. In one embodiment, the human monoclonal antibodies are produced by a hybridoma which includes a B cell obtained from a transgenic nonhuman animal, e.g., a transgenic mouse, having a genome comprising a human heavy chain transgene and a light chain transgene fused to an immortalized cell.

[0070] The phrase "recombinant human antibody", as used herein, includes all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom, antibodies isolated from a host cell transformed to express the human antibody, e.g., from a transfectoma, antibodies isolated from a recombinant, combinatorial human antibody library, and antibodies prepared, expressed, created or isolated by any other means that involve splicing of all or a portion of a human immunoglobulin gene, sequences to other DNA sequences. Such recombinant human antibodies have variable regions in which the framework and CDR regions are derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies can be subjected to in vitro mutagenesis (or, when an animal transgenic for human Ig sequences is used, in vivo somatic mutagenesis) and thus the amino acid sequences of the V_H and V_L regions of the recombinant antibodies are sequences that, while derived from and related to human germline V_H and V_L sequences, may not naturally exist within the human antibody germline repertoire in vivo.

[0071] Specific binding between two entities means a binding with an equilibrium constant (K_d) (k_{on}/k_{off}) of at least $10^2 M^{-1}$, at least $5 \times 10^2 M^{-1}$, at least $10^3 M^{-1}$, at least $5 \times 10^3 M^{-1}$, at least $10^4 M^{-1}$, at least $5 \times 10^4 M^{-1}$, at least $10^5 M^{-1}$, at least $5 \times 10^5 M^{-1}$, at least $10^6 M^{-1}$, at least $5 \times 10^6 M^{-1}$, at least $10^7 M^{-1}$, at least $5 \times 10^7 M^{-1}$, at least $10^8 M^{-1}$, at least $5 \times 10^8 M^{-1}$, at least $10^9 M^{-1}$, at least $5 \times 10^9 M^{-1}$, at least $10^{10} M^{-1}$, at least $5 \times 10^{10} M^{-1}$, at least $10^{11} M^{-1}$, at least $5 \times 10^{11} M^{-1}$, at least $10^{12} M^{-1}$, at least $5 \times 10^{12} M^{-1}$, at least $10^{13} M^{-1}$, at least $5 \times 10^{13} M^{-1}$, at least $10^{14} M^{-1}$, at least $5 \times 10^{14} M^{-1}$, at least $10^{15} M^{-1}$, or at least $5 \times 10^{15} M^{-1}$.

[0072] The phrase "specifically (or selectively) binds" refers to a binding reaction of a HER3 binding antibody and HER3 receptor in a heterogeneous population of proteins and other biologics. In addition to the equilibrium constant (K_d) noted above, an HER3 binding antibody of the invention

typically also has a dissociation rate constant (K_D) (k_{off}/k_{on}) of less than $5 \times 10^{-2} M$, less than $10^{-2} M$, less than $5 \times 10^{-3} M$, less than $10^{-3} M$, less than $5 \times 10^{-4} M$, less than $10^{-4} M$, less than $5 \times 10^{-5} M$, less than $10^{-5} M$, less than $5 \times 10^{-6} M$, less than $10^{-6} M$, less than $5 \times 10^{-7} M$, less than $10^{-7} M$, less than $5 \times 10^{-8} M$, less than $10^{-8} M$, less than $5 \times 10^{-9} M$, less than $10^{-9} M$, less than $5 \times 10^{-10} M$, less than $10^{-10} M$, less than $5 \times 10^{-11} M$, less than $10^{-11} M$, less than $5 \times 10^{-12} M$, less than $10^{-12} M$, less than $5 \times 10^{-13} M$, less than $10^{-13} M$, less than $5 \times 10^{-14} M$, less than $10^{-14} M$, less than $5 \times 10^{-15} M$, or less than $10^{-15} M$ or lower, and binds to HER3 with an affinity that is at least two-fold greater than its affinity for binding to a non-specific antigen (e.g., HSA).

[0073] In one embodiment, the antibody or fragment thereof has dissociation constant (K_d) of less than 3000 pM, less than 2500 pM, less than 2000 pM, less than 1500 pM, less than 1000 pM, less than 750 pM, less than 500 pM, less than 250 pM, less than 200 pM, less than 150 pM, less than 100 pM, less than 75 pM, less than 10 pM, less than 1 pM as assessed using a method described herein or known to one of skill in the art (e.g., a BIAcore assay, ELISA, FACS, SET) (Biacore International AB, Uppsala, Sweden).

[0074] The term " K_{assoc} " or " K_a ", as used herein, refers to the association rate of a particular antibody-antigen interaction, whereas the term " K_{dis} " or " K_d ", as used herein, refers to the dissociation rate of a particular antibody-antigen interaction. The term " K_D ", as used herein, refers to the dissociation constant, which is obtained from the ratio of K_d to K_a (i.e. K_d/K_a) and is expressed as a molar concentration (M). K_D values for antibodies can be determined using methods well established in the art. A method for determining the K_D of an antibody is by using surface plasmon resonance, or using a biosensor system such as a Biacore® system.

[0075] The term "affinity" as used herein refers to the strength of interaction between antibody and antigen at single antigenic sites. Within each antigenic site, the variable region of the antibody "arm" interacts through weak non-covalent forces with antigen at numerous sites; the more interactions, the stronger the affinity.

[0076] The term "avidity" as used herein refers to an informative measure of the overall stability or strength of the antibody-antigen complex. It is controlled by three major factors: antibody epitope affinity; the valence of both the antigen and antibody; and the structural arrangement of the interacting parts. Ultimately these factors define the specificity of the antibody, that is, the likelihood that the particular antibody is binding to a precise antigen epitope.

[0077] The term "valency" as used herein refers to the number of potential target binding sites in a polypeptide. Each target binding site specifically binds one target molecule or specific site (i.e., epitope) on a target molecule. When a polypeptide comprises more than one target binding site, each target binding site may specifically bind the same or different molecules (e.g., may bind to different molecules, e.g., different antigens, or different epitopes on the same molecule).

[0078] The phrase "inhibiting antibody" as used herein refers to an antibody that binds with HER3 and inhibits the biological activity of HER3 signaling, e.g., reduces, decreases and/or inhibits HER3 induced signaling activity, e.g., in a phospho-HER3 or phospho-Akt assay. Examples of assays are described in more details in the examples below. Accordingly, an antibody that "inhibits" one or more of these HER3 functional properties (e.g., biochemical, immunochemical, cellular, physiological or other biological activi-

ties, or the like) as determined according to methodologies known to the art and described herein, will be understood to relate to a statistically significant decrease in the particular activity relative to that seen in the absence of the antibody (e.g., or when a control antibody of irrelevant specificity is present). An antibody that inhibits HER3 activity effects such a statistically significant decrease by at least 10% of the measured parameter, by at least 50%, 80% or 90%, and in certain embodiments an antibody of the invention may inhibit greater than 95%, 98% or 99% of HER3 functional activity as evidenced by a reduction in the level of cellular HER3 phosphorylation.

[0079] The phrase “isolated antibody” refers to an antibody that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds HER3 is substantially free of antibodies that specifically bind antigens other than HER3). An isolated antibody that specifically binds HER3 may, however, have cross-reactivity to other antigens. Moreover, an isolated antibody may be substantially free of other cellular material and/or chemicals.

[0080] The phrase “conservatively modified variant” applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given protein. For instance, the codons GCA, GCC, GCG and GCU all encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to any of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are “silent variations,” which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes every possible silent variation of the nucleic acid. One of skill will recognize that each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, each silent variation of a nucleic acid that encodes a polypeptide is implicit in each described sequence.

[0081] For polypeptide sequences, “conservatively modified variants” include individual substitutions, deletions or additions to a polypeptide sequence which result in the substitution of an amino acid with a chemically similar amino acid. Conservative substitution tables providing functionally similar amino acids are well known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention. The following eight groups contain amino acids that are conservative substitutions for one another: 1) Alanine (A), Glycine (G); 2) Aspartic acid (D), Glutamic acid (E); 3) Asparagine (N), Glutamine (Q); 4) Arginine (R), Lysine (K); 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W); 7) Serine (S), Threonine (T); and 8) Cysteine (C), Methionine (M) (see, e.g., Creighton, *Proteins* (1984)). In some embodiments, the term “conservative sequence modifications” are used to refer to amino acid modi-

fications that do not significantly affect or alter the binding characteristics of the antibody containing the amino acid sequence.

[0082] The terms “cross-compete” and “cross-competing” are used interchangeably herein to mean the ability of an antibody or fragment thereof to interfere with the binding of other antibodies or fragments thereof to HER3 in a standard competitive binding assay.

[0083] The ability or extent to which an antibody or fragment thereof is able to interfere with the binding of another antibody or fragment thereof to HER3, and therefore whether it can be said to cross-compete according to the invention, can be determined using standard competition binding assays. One suitable assay involves the use of the Biacore technology (e.g. by using the BIAcore 3000 instrument (Biacore, Uppsala, Sweden)), which can measure the extent of interactions using surface plasmon resonance technology. Another assay for measuring cross-competing uses an ELISA-based approach.

[0084] The term “optimized” as used herein refers to a nucleotide sequence has been altered to encode an amino acid sequence using codons that are preferred in the production cell or organism, generally a eukaryotic cell, for example, a cell of *Pichia*, a cell of *Trichoderma*, a Chinese Hamster Ovary cell (CHO) or a human cell. The optimized nucleotide sequence is engineered to retain completely or as much as possible the amino acid sequence originally encoded by the starting nucleotide sequence, which is also known as the “parental” sequence.

[0085] Standard assays to evaluate the binding ability of the antibodies toward HER3 of various species are known in the art, including for example, ELISAs, western blots and RIAs. Suitable assays are described in detail in the Examples. The binding kinetics (e.g., binding affinity) of the antibodies also can be assessed by standard assays known in the art, such as by Biacore analysis, or FACS relative affinity (Scatchard). Assays to evaluate the effects of the antibodies on functional properties of HER3 (e.g., receptor binding assays, modulating the HER3 signal pathway) are described in further detail in the Examples.

[0086] The phrases “percent identical” or “percent identity,” in the context of two or more nucleic acids or polypeptide sequences, refers to two or more sequences or subsequences that are the same. Two sequences are “substantially identical” if two sequences have a specified percentage of amino acid residues or nucleotides that are the same (i.e., 60% identity, optionally 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identity over a specified region, or, when not specified, over the entire sequence), when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by manual alignment and visual inspection. Optionally, the identity exists over a region that is at least about 50 nucleotides (or 10 amino acids) in length, or more preferably over a region that is 100 to 500 or 1000 or more nucleotides (or 20, 50, 200 or more amino acids) in length.

[0087] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Default program parameters can be used, or alternative

parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

[0088] A “comparison window”, as used herein, includes reference to a segment of any one of the number of contiguous positions selected from the group consisting of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith and Waterman, (1970) *Adv. Appl. Math.* 2:482c, by the homology alignment algorithm of Needleman and Wunsch, (1970) *J. Mol. Biol.* 48:443, by the search for similarity method of Pearson and Lipman, (1988) *Proc. Nat'l. Acad. Sci. USA* 85:2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by manual alignment and visual inspection (see, e.g., Brent et al., (2003) *Current Protocols in Molecular Biology*).

[0089] Two examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al., (1977) *Nuc. Acids Res.* 25:3389-3402; and Altschul et al., (1990) *J. Mol. Biol.* 215:403-410, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul et al., *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) or 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff, (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

[0090] The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, e.g.,

Karlin and Altschul, (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5787). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001.

[0091] The percent identity between two amino acid sequences can also be determined using the algorithm of E. Meyers and W. Miller, (1988) *Comput. Appl. Biosci.* 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. In addition, the percent identity between two amino acid sequences can be determined using the Needleman and Wunsch (1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6.

[0092] Other than percentage of sequence identity noted above, another indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second polypeptide, for example, where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequence.

[0093] The phrase “nucleic acid” is used herein interchangeably with the term “polynucleotide” and refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. The term encompasses nucleic acids containing known nucleotide analogs or modified backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides, peptide-nucleic acids (PNAs).

[0094] Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions) and complementary sequences, as well as the sequence explicitly indicated. Specifically, as detailed below, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., (1991) *Nucleic Acid Res.* 19:5081; Ohtsuka et al., (1985) *J. Biol. Chem.* 260:2605-2608; and Rossolini et al., (1994) *Mol. Cell. Probes* 8:91-98).

[0095] The phrase “operably linked” refers to a functional relationship between two or more polynucleotide (e.g., DNA) segments. Typically, it refers to the functional relationship of a transcriptional regulatory sequence to a transcribed sequence. For example, a promoter or enhancer sequence is operably linked to a coding sequence if it stimulates or modulates the transcription of the coding sequence in an appropriate host cell or other expression system. Generally, promoter transcriptional regulatory sequences that are operably linked to a transcribed sequence are physically contiguous to the transcribed sequence, i.e., they are cis-acting. However, some transcriptional regulatory sequences, such as enhancers, need not be physically contiguous or located in close proximity to the coding sequences whose transcription they enhance.

[0096] The terms “polypeptide” and “protein” are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer. Unless otherwise indicated, a particular polypeptide sequence also implicitly encompasses conservatively modified variants thereof.

[0097] The term “subject” as used herein includes human and non-human animals. Non-human animals include all vertebrates, e.g., mammals and non-mammals, such as non-human primates, sheep, dog, cow, chickens, amphibians, and reptiles. Except when noted, the terms “patient” or “subject” are used herein interchangeably.

[0098] The term “anti-cancer agent” as used herein refers to any agent that can be used to treat a cell proliferative disorder such as cancer, including cytotoxic agents, chemotherapeutic agents, radiotherapy and radiotherapeutic agents, targeted anti-cancer agents, and immunotherapeutic agents.

[0099] The term “tumor” as used herein refers to neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues.

[0100] The term “anti-tumor activity” as used herein refers to a reduction in the rate of tumor cell proliferation, viability, or metastatic activity. A possible way of showing anti-tumor activity is show a decline in growth rate of abnormal cells that arises during therapy or tumor size stability or reduction. Such activity can be assessed using accepted in vitro or in vivo tumor models, including but not limited to xenograft models, allograft models, MMTV models, and other known models known in the art to investigate anti-tumor activity.

[0101] The term “malignancy” as used herein refers to a non-benign tumor or a cancer.

[0102] The term “cancer” as used herein refers to a malignancy characterized by deregulated or uncontrolled cell growth. Exemplary cancers include: carcinomas, sarcomas, leukemias, and lymphomas. The term “cancer” includes primary malignant tumors (e.g., those whose cells have not migrated to sites in the subject’s body other than the site of the original tumor) and secondary malignant tumors (e.g., those arising from metastasis, the migration of tumor cells to secondary sites that are different from the site of the original tumor).

[0103] Various aspects of the invention are described in further detail in the following sections and subsections.

Structure and Mechanism of Activation of the HER Receptors

[0104] All four HER receptors have an extracellular ligand-binding domain, a single trans-membrane domain and a cyto-

plasmic tyrosine kinase-containing domain. The intracellular tyrosine kinase domain of HER receptors is highly conserved, although the kinase domain of HER3 contains substitutions of critical amino acids and therefore lacks kinase activity (Guy et al., (1994): PNAS 91, 8132-8136). Ligand-induced dimerisation of the HER receptors induces activation of the kinase, receptor transphosphorylation on tyrosine residues in the C-terminal tail, followed by recruitment and activation of intracellular signalling effectors (Yarden and Slivkowski, (2001) Nature Rev 2, 127-137; Jorissen et al., (2003) Exp Cell Res 284, 31-53).

[0105] The crystal structures of the extracellular domains of HERs have provided some insight into the process of ligand-induced receptor activation (Schlessinger, (2002) Cell 110, 669-672). The extracellular domain of each HER receptor consists of four subdomains: Subdomain I and III cooperate in forming the ligand-binding site, whereas subdomain II (and perhaps also subdomain IV) participates in receptor dimerisation via direct receptor-receptor interactions. In the structures of ligand-bound HER1, a β hairpin (termed the dimerisation loop) in subdomain II interacts with the dimerisation loop of the partner receptor, mediating receptor dimerisation (Garrett et al, (2002) Cell 110, 763-773; Ogiso et al., (2002) Cell 110, 775-787). In contrast, in the structures of the inactive HER1, HER3 and HER4, the dimerisation loop is engaged in intramolecular interactions with subdomain IV, which prevents receptor dimerisation in the absence of ligand (Cho and Leahy, (2002) Science 297, 1330-1333; Ferguson et al., (2003) Mol Cell 12, 541-552; Bouyan et al., (2005) PNAS 102, 15024-15029). The structure of HER2 is unique among the HERs. In the absence of a ligand, HER2 has a conformation that resembles the ligand-activated state of HER1 with a protruding dimerisation loop, available to interact with other HER receptors (Cho et al., (2003) Nature 421, 756-760; Garrett et al., (2003) Mol Cell 11, 495-505). This may explain the enhanced heterodimerisation capacity of HER2.

[0106] Although the HER receptor crystal structures provide a model for HER receptor homo- and heterodimerisation, the background for the prevalence of some HER homo- and heterodimers over others (Franklin et al., (2004) Cancer Cell 5, 317-328) as well as the role of each of the domain in receptor dimerisation and autoinhibition (Burgess et al., (2003) Mol Cell 12, 541-552; Mattoon et al., (2004) PNAS 101, 923-928) remains somewhat unclear.

HER3 Structure and Epitopes

[0107] A conformational epitope to which anti-HER3 antibodies bind, has previously been described in PCT/EP2011/064407, and U.S. Ser. No. 61/375,408, both filed Aug. 22, 2011, and which are incorporated herein by reference in their entirety. The three dimensional structure of a truncated form of HER3 complexed with a HER3 antibody fragment, showed conformational epitope comprising domain 2 and domain 4 of HER3.

[0108] The present invention provides an additional class of antibodies or fragments thereof that bind a non-linear epitope within domain 3 of HER3. These antibodies or fragments thereof bind with HER3 to inhibit both ligand dependent and ligand independent signal transduction.

[0109] The present invention further provides a class of antibodies or fragments thereof that bind within domains 3-4 of HER3 to inhibit both ligand dependent and ligand independent signal transduction. In one embodiment, the class of antibodies or fragments thereof binds to domain 3 or domain

4 of HER3 to inhibit both ligand dependent and ligand independent signal transduction. In another embodiment, the class of antibodies or fragments thereof binds to domain 3 and domain 4 of HER3 to inhibit both ligand dependent and ligand independent signal transduction.

[0110] The present Examples present the crystal structure of HER3 bound to the Fab fragment of MOR12604 determined at 3.38 Å resolution.

[0111] The three dimensional structure of a truncated form (residues 20-640) of the extracellular domain of HER3 complexed with an antibody have been shown. The HER3-MOR12604 Fab complex was determined at 3.38 Å resolution, and shown in FIG. 4.

[0112] Although not bound to provide a theory, one possible model for the mechanism of action is that HER3 typically exists in an inactive (closed, tethered) or active (open) state. Ligand binding induces a conformational change such that HER3 exists in the active (open) state which is capable of binding heterodimer partners resulting in activation in downstream signaling. Antibodies such as MOR12604 bind the inactive (tethered) state of HER3 and apparently block the ligand binding site.

[0113] Binding within domain 3 by MOR12604 suggests that MOR12604 could function by a mechanisms selected from the group consisting of blocking HER3 residues required for ligand binding, preventing HER3 adopting the active conformation due to steric hindrance between the antibody and domains of HER3, preventing HER3 adopting the active conformation by reducing the degree of flexibility in HER3 hinge regions (e.g. domain 3), inducing a conformational change in domain 3 loop 371-377 that prevents HER3 from transitioning to the open conformation, destabilizing HER3 such that it is prone to degradation, acting as a partial agonist to accelerate the down regulation of HER3, and by each arm of MOR12604 binding a molecule of HER3 such that the antibody generates an un-natural HER3 dimer that is either prone to proteolytic degradation or cannot dimerize with other receptor tyrosine kinases

[0114] To examine the crystal structure of domain 3 antibodies or fragments thereof bound to HER3, crystals of HER3 were prepared by expressing a nucleotide sequence encoding HER3 or a variant thereof in a suitable host cell, and then crystallising the purified protein(s) in the presence of the relevant HER3 targeted Fab. Preferably the HER3 polypeptide contains the extracellular domain (amino acids 20 to 640 of the human polypeptide (SEQ ID NO: 1) or a truncated version thereof, preferably comprising amino acids 20-640) but lacks the transmembrane and intracellular domains.

[0115] HER3 polypeptides may also be produced as fusion proteins, for example to aid in extraction and purification. Examples of fusion protein partners include glutathione-S-transferase (GST), histidine (HIS), hexahistidine (6HIS) (SEQ ID NO: 702), GAL4 (DNA binding and/or transcriptional activation domains) and beta-galactosidase. It may also be convenient to include a proteolytic cleavage site between the fusion protein partner and the protein sequence of interest to allow removal of fusion protein sequences.

[0116] After expression, the proteins may be purified and/or concentrated, for example by immobilised metal affinity chromatography, ion-exchange chromatography, and/or gel filtration.

[0117] The protein(s) may be crystallised using techniques described herein. Commonly, in a crystallisation process, a drop containing the protein solution is mixed with the crys-

tallisation buffer and allowed to equilibrate in a sealed container. Equilibration may be achieved by known techniques such as the "hanging drop" or the "sitting drop" method. In these methods, the drop is hung above or sitting beside a much larger reservoir of crystallization buffer and equilibration is reached through vapor diffusion. Alternatively, equilibration may occur by other methods, for example under oil, through a semi-permeable membrane, or by free-interface diffusion (See e.g., Chayen et al., (2008) *Nature Methods* 5, 147-153).

[0118] Once the crystals have been obtained, the structure may be solved by known X-ray diffraction techniques. Many techniques use chemically modified crystals, such as those modified by heavy atom derivatization to approximate phases. In practice, a crystal is soaked in a solution containing heavy metal atom salts, or organometallic compounds, e.g., lead chloride, gold thiomalate, thimerosal or uranyl acetate, which can diffuse through the crystal and bind to the surface of the protein. The location(s) of the bound heavy metal atom(s) can then be determined by X-ray diffraction analysis of the soaked crystal. The patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centres) of the crystal can be solved by mathematical equations to give mathematical coordinates. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. Another method of obtaining phase information is using a technique known as molecular replacement.

[0119] In this method, rotational and translational algorithms are applied to a search model derived from a related structure, resulting in an approximate orientation for the protein of interest (See Rossmann, (1990) *Acta Crystals A* 46, 73-82). The electron density maps are used to establish the positions of the individual atoms within the unit cell of the crystal (Blundel et al., (1976) *Protein Crystallography*, Academic Press).

[0120] The present disclosure describes the three-dimensional structure of HER3 and a Fab of an anti-HER3 antibody. The approximate domain boundaries of extracellular domain of HER3 are as follows; domain 1: amino acids 20-207; domain 2: amino acids 208-328; domain 3: amino acids 329-498; and domain 4: amino acids 499-642. The three-dimensional structure of HER3 and the antibody allows the identification of target binding sites for potential HER3 modulators. Preferred target binding sites are those involved in the activation of HER3. In one embodiment, the target binding site is located within domain 3 of HER3. Thus an antibody or fragment thereof which binds to domain 3 can, for example, modulate HER3 activation by modifying the relative position of the domain relative to itself or other HER3 domains. Thus binding an antibody or fragment thereof to amino acid residues within domain 3 may cause the protein to adopt a configuration that prevents activation.

[0121] In some embodiments, the antibody or fragment thereof binds to a binding surface of HER3. This binding surface comprises multiple contiguous or non-contiguous surfaces in a 3D configuration that form part of the epitope which interacts with the antibody or fragment thereof. For example, a binding surface can comprise at least two surfaces (e.g., surface A and surface B, see FIG. 4D), at least three surfaces (e.g., surface A, surface B, and surface C), at least four surfaces (e.g., surface A, surface B, surface C, and surface D), at least five surfaces (e.g., surface A, surface B, surface C, surface D, and surface E), at least six surfaces (e.g., surface A, surface B, surface C, surface D, surface E, and surface F), at least seven surfaces (e.g., surface A, surface B,

surface C, surface D, surface E, surface F, and surface G), at least eight surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, surface G, and surface H), at least nine surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, surface G, surface H, and surface I), or at least ten surfaces (e.g., surface A, surface B, surface C, surface D, surface E, surface F, surface G, surface H, surface I, and surface J).

[0122] In one embodiment, the antibody or fragment thereof binds to binding surface A. In one embodiment, the antibody or fragment thereof binds to binding surface B. In another embodiment, the antibody or fragment thereof binds to both binding surface A and binding surface B. In one embodiment, binding surface A comprises at least one amino acid residue selected from amino acid residues 362-376. In one embodiment, binding surface B comprises at least one amino acid residue selected from amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455. In another embodiment, the antibody or fragment thereof binds to binding surface A, wherein at least one amino acid residue is selected from amino acid residues 362-376; and binding surface B, wherein at least one amino acid residue is selected from amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455.

[0123] In some embodiments, the antibody or fragment thereof binds to human HER3 protein having a non-linear epitope comprising HER3 amino acid residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), of SEQ ID NO: 1, or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within or overlapping amino acid residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), of SEQ ID NO: 1, or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within (and/or amino acid sequences consisting of) amino acids 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), of SEQ ID NO: 1, or a subset thereof.

[0124] In some embodiments, the antibody or fragment thereof binds to human HER3 protein having an epitope (linear, non-linear, conformational) comprising HER3 amino acid residues 499-642 (of domain 4) of SEQ ID NO: 1, or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within or overlapping amino acid residues 499-642 (of domain 4) of SEQ ID NO: 1, or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within (and/or amino acid sequences consisting of) amino acids residues 499-642 (of domain 4) of SEQ ID NO: 1, or a subset thereof, or a subset thereof.

[0125] In some embodiments, the antibody or fragment thereof binds to human HER3 protein having a non-linear epitope comprising HER3 amino acid residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3) and an epitope (linear, non-linear, conformational) comprising HER3 amino acid residues 499-642 (of domain 4) of SEQ ID NO: 1, or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within or overlapping amino acid residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), of SEQ ID NO: 1 and an epitope (linear, non-linear, conformational) comprising HER3 amino acid residues 499-642 (of domain 4) of SEQ ID NO: 1 or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within

(and/or amino acid sequences consisting of) amino acids 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), and an epitope (linear, non-linear, conformational) comprising HER3 amino acid residues 499-642 (of domain 4) of SEQ ID NO: 1 of SEQ ID NO: 1, or a subset thereof.

[0126] In some embodiments, the antibody or fragment thereof binds to human HER3 protein having a epitope (linear, non-linear, conformational) comprising HER3 amino acid residues within domain 3 and an epitope (linear, non-linear, conformational) comprising HER3 amino acid residues within of domain 4 of SEQ ID NO: 1, or a subset thereof. In some embodiments, the antibody or fragment thereof binds to amino acids within or overlapping amino acid residues of domain 3 and amino acids of domain 4 of SEQ ID NO: 1, or a subset thereof.

[0127] In some embodiments, the antibody or fragment thereof binds to the inactive state of the HER3 receptor, thereby preventing HER3 adopting an active conformation. In some embodiments, the antibody or fragment thereof prevents HER3 adopting an active conformation due to steric hindrance between the antibody or fragment thereof and domains of HER3 (e.g., with MOR12604, steric interference with domain 1 of HER3). In some embodiments, the antibody or fragment thereof prevents HER3 adopting an active conformation by reducing the degree of flexibility in domain 3. In some embodiments, the antibody or fragment thereof induces a conformational change in domain 3 loop 371-377 of SEQ ID NO: 1 that prevents HER3 from adopting an active conformation. In some embodiments, the antibody or fragment thereof destabilizes HER3 such that it is susceptible to degradation. In some embodiments, the antibody or fragment thereof accelerates down regulation of cell surface HER3. In some embodiments, the antibody or fragment thereof generates an un-natural HER3 dimer that is susceptible to proteolytic degradation or unable to dimerize with other receptor tyrosine kinases.

[0128] In some embodiments, the antibody or fragment thereof can bind to either the active or inactive state of HER3. In some embodiments, the antibody or fragment thereof stabilizes the HER3 receptor in an inactive state such that the HER3 receptor fails to dimerize with a co-receptor to form a receptor-receptor complex. The failure to form a receptor-receptor complex prevents activation of both ligand-dependent and ligand-independent signal transduction.

[0129] In some embodiments, the antibody or fragment thereof induces dimerization of HER3 with HER3 to form an inactive receptor-receptor complex. The formation of the inactive receptor-receptor complex prevents activation of HER3 mediated signal transduction since HER3 is sequestered in inactive receptor-receptor complexes.

[0130] The depicted structure also allows one to identify specific HER3 amino acid residues for the interaction interface of an antibody or fragment thereof (e.g., MOR12604) with HER3. This was defined as residues that are within 5 Å of the MOR12604 protein VH chain. The residues are as follows: Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, and Lys434. The depicted structure also allows one to identify specific HER3 amino acid residues for the interaction interface of an antibody or fragment thereof (e.g., MOR12604) with HER3. This was defined as residues that are within 5 Å of the MOR12604 protein VL chain. The residues are as follows: Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364,

Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455. As can be seen in Tables 5 and 6 (MOR12604), respectively, both the light and heavy chains are involved in the antigen binding protein's binding to amino acid residues within domain 3 of the epitope.

[0131] As such, one of skill in the art, given the present teachings, can predict which residues and areas of the antigen binding proteins can be varied without unduly interfering with the antigen binding protein's ability to bind to domains 3 and 4 of HER3.

[0132] Core interaction interface amino acids were determined as being all amino acid residues with at least one atom less than or equal to 5 Å from the HER3 partner protein. 5 Å was chosen as the core region cutoff distance to allow for atoms within a van der Waals radius plus a possible water-mediated hydrogen bond.

[0133] In some embodiments, any antigen binding protein that binds to, covers, or prevents MOR12604 from interacting with any of the above residues can be employed to bind to or neutralize HER3. In some embodiments, the antibodies or fragments thereof binds to or interacts with at least one of the following HER3 residues (SEQ ID NO: 1): Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, and Lys434. In some embodiments, the antibodies and fragments thereof binds to or interacts with at least one of the following HER3 residues (SEQ ID NO: 1): Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364, Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455. In some embodiments, the antibodies or fragments thereof binds to or interacts with at least one of the following HER3 residues (SEQ ID NO: 1): Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, Lys434, Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364, Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455. In some embodiments, the antibodies or fragments thereof binds to or interacts with a combination of the following HER3 residues (SEQ ID NO: 1): Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, Lys434, Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364, Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455. In some embodiments, the antibodies or fragments thereof binds to or interacts with all of the following HER3 residues (SEQ ID NO: 1): Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, Lys434, Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364, Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455. In some embodiments, the antibody or fragment thereof is within 5 angstroms of one or more of the above residues. In some embodiments, the antibody or fragment thereof is 5 to 8 angstroms from one or more of the above residues. In some embodiments, the antibody or fragment thereof interacts, blocks, or is within 8 angstroms of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 28, 30, 35, 40, 45, or 50 of the above residues.

[0134] The availability of 3D structures for the HER3 and the complex of HER3: MOR12604, for example, provides the framework to explore other HER3 antibodies in more detail. The 3D structure of HER3 allows the epitopes for monoclonal antibodies to be mapped and their mode of action inferred,

since some inhibit, some stimulate and others have no effect on cell growth. The non-linear epitope for MOR12604 has been located to the domain 3 of HER3. The availability of the 3D structures of this receptor will facilitate the determination of the precise mechanism of action of these inhibitory agents and the design of new approaches to interfering with HER3 receptor function. In one embodiment, the antibodies of the invention bind to the same non-linear epitope as MOR12604.

[0135] In some embodiments, the non-linear epitope bound by any of the antibodies listed in Table 1 is especially useful. In certain embodiments, a HER3 non-linear epitope can be utilized to isolate antibodies of fragments thereof that bind to HER3. In certain embodiments, a HER3 non-linear epitope can be utilized to generate antibodies or fragments thereof which bind to HER3. In certain embodiments, a HER3 non-linear epitope can be utilized as an immunogen to generate antibodies of fragments thereof that bind to the HER3 non-linear epitope. In certain embodiments, a HER3 non-linear epitope can be administered to an animal, and antibodies that bind to HER3 can subsequently be obtained from the animal.

[0136] The present invention also provides a class of antibodies that bind to an epitope (linear, non-linear, or conformational) within domains 3-4 of HER3. Examples of such antibodies or fragments thereof that bind within domains 3-4 are shown in Table 2. The above methodology and the methods described in the Example section below, can be also used to generate domain 3-4 antibodies or fragments thereof complexed to HER3.

[0137] In some embodiments, the domain(s)/region(s) containing residues that are in contact with or are buried by an antibody can be identified by mutating specific residues in HER3 (e.g., a wild-type antigen) and determining whether antibody or fragment thereof can bind the mutated or variant HER3 protein or measure changes of affinity from wild-type. By making a number of individual mutations, residues that play a direct role in binding or that are in sufficiently close proximity to the antibody such that a mutation can affect binding between the antibody and antigen can be identified. From a knowledge of these amino acids, the domain(s) or region(s) of the antigen (HER3) that contain residues in contact with the antibody or covered by the antibody can be elucidated. Mutagenesis using known techniques such as alanine-scanning can help define functionally relevant epitopes. Mutagenesis utilizing an arginine/glutamic acid scanning protocol can also be employed (see, e.g., Nanevich et al., (1995), J. Biol. Chem. 270(37):21619-21625 and Zupnick et al., (2006), J. Biol. Chem. 281(29):20464-20473). In general, arginine and glutamic acids are substituted (typically individually) for an amino acid in the wild-type polypeptide because these amino acids are charged and bulky and thus have the potential to disrupt binding between an antigen binding protein and an antigen in the region of the antigen where the mutation is introduced. Arginines that exist in the wild-type antigen are replaced with glutamic acid. A variety of such individual mutants can be obtained and the collected binding results analyzed to determine what residues affect binding. A series of mutant HER3 antigens can be created, with each mutant antigen having a single mutation. Binding of each mutant HER3 antigen with various HER3 antibodies or fragments thereof can be measured and compared to the ability of the selected an antibody or fragments thereof to bind wild-type HER3 (SEQ ID NO: 1).

[0138] An alteration (for example a reduction or increase) in binding between an antibody or fragment thereof and a

mutant or variant HER3 as used herein means that there is a change in binding affinity (e.g., as measured by known methods such as Biacore testing or the bead based assay described below in the examples), EC_{50} , and/or a change (for example a reduction) in the total binding capacity of the antigen binding protein (for example, as evidenced by a decrease in B_{max} in a plot of antigen binding protein concentration versus antigen concentration). A significant alteration in binding indicates that the mutated residue is involved in binding to the antibody or fragment thereof.

[0139] In some embodiments, a significant reduction in binding means that the binding affinity, EC_{50} , and/or capacity between an antibody or fragments thereof and a mutant HER3 antigen is reduced by greater than 10%, greater than 20%, greater than 40%, greater than 50%, greater than 55%, greater than 60%, greater than 65%, greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90% or greater than 95% relative to binding between the an antibody or fragment thereof and a wild type HER3 (e.g., SEQ ID NO: 1).

[0140] In some embodiments, binding of an antibody or fragments thereof is significantly reduced or increased for a mutant HER3 protein having one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) mutations as compared to a wild-type HER3 protein (e.g., SEQ ID NO: 1).

[0141] Although the variant forms are referenced with respect to the wild-type sequence shown in SEQ ID NO: 1, it will be appreciated that in an allelic or splice variants of HER3 the amino acids could differ. Antibodies or fragments thereof showing significantly altered binding (e.g., lower or higher binding) for such allelic forms of HER3 are also contemplated.

[0142] In addition to the general structural aspects of antibodies, the more specific interaction between the paratope and the epitope may be examined through structural approaches. In one embodiment, the structure of the CDRs contribute to a paratope, through which an antibody is able to bind to an epitope. The shape of such a paratope may be determined in a number of ways. Traditional structural examination approaches can be used, such as NMR or x-ray crystallography. These approaches can examine the shape of the paratope alone, or while it is bound to the epitope. Alternatively, molecular models may be generated in silico. A structure can be generated through homology modeling, aided with a commercial package, such as InsightII modeling package from Accelrys (San Diego, Calif.). Briefly, one can use the sequence of the antibody to be examined to search against a database of proteins of known structures, such as the Protein Data Bank. After one identifies homologous proteins with known structures, these homologous proteins are used as modeling templates. Each of the possible templates can be aligned, thus producing structure based sequence alignments among the templates. The sequence of the antibody with the unknown structure can then be aligned with these templates to generate a molecular model for the antibody with the unknown structure. As will be appreciated by one of skill in the art, there are many alternative methods for generating such structures in silico, any of which may be used. For instance, a process similar to the one described in Hardman et al., issued U.S. Pat. No. 5,958,708 employing QUANTA (Polygen Corp., Waltham, Mass.) and CHARM (Brooks et al., (1983), J. Comp. Chem. 4:187) may be used (hereby incorporated in its entirety by reference).

[0143] Not only is the shape of the paratope important in determining whether and how well a possible paratope will bind to an epitope, but the interaction itself, between the epitope and the paratope is a source of great information in the design of variant antibodies. As appreciated by one of skill in the art, there are a variety of ways in which this interaction can be studied. One way is to use the structural model generated, perhaps as described above, and then to use a program such as InsightII (Accelrys, San Diego, Calif.), which has a docking module, which, among other things, is capable of performing a Monte Carlo search on the conformational and orientational spaces between the paratope and its epitope. The result is that one is able to estimate where and how the epitope interacts with the paratope. In one embodiment, only a fragment, or variant, of the epitope is used to assist in determining the relevant interactions. In one embodiment, the entire epitope is used in the modeling of the interaction between the paratope and the epitope.

[0144] Through the use of these modelled structures, one is able to predict which residues are the most important in the interaction between the epitope and the paratope. Thus, in one embodiment, one is able to readily select which residues to change in order to alter the binding characteristics of the antibody. For instance, it may be apparent from the docking models that the side chains of certain residues in the paratope may sterically hinder the binding of the epitope, thus altering these residues to residues with smaller side chains may be beneficial. One can determine this in many ways. For example, one may simply look at the two models and estimate interactions based on functional groups and proximity. Alternatively, one may perform repeated pairings of epitope and paratope, as described above, in order to obtain more favorable energy interactions. One can also determine these interactions for a variety of variants of the antibody to determine alternative ways in which the antibody may bind to the epitope. One can also combine the various models to determine how one should alter the structure of the antibodies in order to obtain an antibody with the particular characteristics that are desired.

[0145] The models determined above can be tested through various techniques. For example, the interaction energy can be determined with the programs discussed above in order to determine which of the variants to further examine. Also, coulombic and van der Waals interactions are used to determine the interaction energies of the epitope and the variant paratopes. Also site directed mutagenesis is used to see if predicted changes in antibody structure actually result in the desired changes in binding characteristics. Alternatively, changes may be made to the epitope to verify that the models are correct or to determine general binding themes that may be occurring between the paratope and the epitope.

[0146] As will be appreciated by one of skill in the art, while these models will provide the guidance necessary to make the antibodies and variants thereof of the present embodiments, it may still be desirable to perform routine testing of the in silico models, perhaps through in vitro studies. In addition, as will be apparent to one of skill in the art, any modification may also have additional side effects on the activity of the antibody. For instance, while any alteration predicted to result in greater binding, may induce greater binding, it may also cause other structural changes which might reduce or alter the activity of the antibody. The determination of whether or not this is the case is routine in the art and can be achieved in many ways. For example, the activity

can be tested through an ELISA test. Alternatively, the samples can be tested through the use of a surface plasmon resonance device.

HER3 Antibodies

[0147] The present invention provides a class of antibodies that recognize a non-linear epitope within domain 3 of HER3

and inhibit both ligand-dependent and ligand-independent HER3 signal transduction pathways as shown in Table 1. The present invention also provides a class of antibodies that recognize an epitope (linear, non-linear, conformational) within domains 3-4 of HER3 that inhibit both ligand-dependent and ligand-independent HER3 signal transduction pathways, as shown in Table 2

TABLE 1

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
MOR09627		
SEQ ID NO: 2 (Kabat)	HCDR1	SYAIS
SEQ ID NO: 3 (Kabat)	HCDR2	LIIPRYGKARYAQKFQG
SEQ ID NO: 4 (Kabat)	HCDR3	NWPYYMDF
SEQ ID NO: 5 (Chothia)	HCDR1	GGTFSSY
SEQ ID NO: 6 (Chothia)	HCDR2	IPRYGK
SEQ ID NO: 7 (Chothia)	HCDR3	NWPYYMDF
SEQ ID NO: 8 (Kabat)	LCDR1	RASQNIVFNLA
SEQ ID NO: 9 (Kabat)	LCDR2	DASNRAT
SEQ ID NO: 10 (Kabat)	LCDR3	QQHSGPPT
SEQ ID NO: 11 (Chothia)	LCDR1	SQNIVFN
SEQ ID NO: 12 (Chothia)	LCDR2	DAS
SEQ ID NO: 13 (Chothia)	LCDR3	HGSGPT
SEQ ID NO: 14	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAIWVRQAPGQGLEWMGLIIPRYGKARYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSS
SEQ ID NO: 15	VL	DIVLTQSPATLSLSPGERATLSCRASQNIVFNLAWYQQKPGQAPRLLIYDASNRATGVPARFSGSGSGTDFTLTISLSEPEDFAVYYCQHGSGPTTFGQGTKVEIK
SEQ ID NO: 16	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAGCTGCAAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGGCAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTTTCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACCAGCGTATATGGAACGTAGCAGCCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATTTTTGGGCCAAGGCACCTGGTGACGGTTAGCTCA
SEQ ID NO: 17	DNA VL	GATATCGTGCTGACCCAGAGCCCGCGACCCCTGAGCCTGTCTCCGGCGCAACGTGCGACCCCTGAGCTGCAGAGCGAGCCAGAAATATTGTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAGCACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCGGCGCGTTTTAGCGGCTCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTTTATTATGCCAGCAGCATGGTCTCTGGTCTACTACCTTTGGCCAGGTACGAAAGTTGAAATTAAA
SEQ ID NO: 18	Heavy Chain	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAIWVRQAPGQGLEWMGLIIPRYGKARYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKSCDKHTCTPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNATKPREBQYNSTYRVVSVLTVLHGDWLNQKEYKC KVSNAKALPAIEKTIKSAKQPREPVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFLYSLKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 19	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNIVFNLAWYQQKPGQAPRLLIYDASNRATGVPARFSGSGSGTDFTLTISLSEPEDFAVYYCQHGSGPTTFGQGTKVEIKRTVAAPSVFIFPPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSLSPVTKSFNRGEC
SEQ ID NO: 20	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAGCTGCAAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGGCAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTTTCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACCAGCGTATATGGAACGTAGCAGCCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATTTTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCAGCCTCCACCAAGGTCCTATCGGTCTTCCCCTGCGACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.			
			CTACTTCCCCGAACCGGTGACGGTGTCTGGAACCTCAGGCGCCCTGACCAGCGCGTGCACACC TTCCCCGGTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCAGCAACACCAAGGTGGAC AAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCATGATCTCCCGG ACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA CAGCACGTACCGGGTGGTCAGCGTCCCTCACCCTCTGCACCAGGACTGGCTGAATGGCAAGGA GTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCCAAGGCC AAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAGGAGATGACCAAG AACCAAGTACGCCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCCTCCCGTGTGGACTCCGACGGCT CCTTCTTCTCTACAGCAAGCTCACCCTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTTCTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAAGAGCCTCTCCCTGTCTCCG GGTAAA
SEQ ID NO: 21	DNA Light Chain	GATATCGTGTGACCCAGAGCCCGGCGACCCCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCTTGGTACCAGCAGAAACCAAGGTCAAG CACCCTGCTCTATTAATTTATGATGCTTCTAATCTGTGCAACTGGGGTCCCGGCGCGTTTTAGCGGC TCTGGATCCGGCAGCGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTTTA TTATTGCCAGCAGCATGGTTCTGGTCTTACTACCTTTGGCCAGGGTACGAAAGTTGAAATTAAC GTACGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGCAC CGCCAGCGTGGTGTGCTGCTGAACAACCTTACCCCCGGGAGGCCAAGGTGCAAGTGAAGGT GGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAGCGTCACCGAGCAGGACAGCAAGGACT CCACCTACAGCCTGAGCAGCACCTGACCCCTGAGCAAGGCCGACTACGAGAAGCACAAGGTGT ACGCCGCGAGGTGACCCACAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGGGCG AGTGT	
MOR12603			
SEQ ID NO: 22 (Kabat)	HCDR1	SYAIS	
SEQ ID NO: 23 (Kabat)	HCDR2	LIIPRYGKARYAQKFGQ	
SEQ ID NO: 24 (Kabat)	HCDR3	NWPYYMDF	
SEQ ID NO: 25 (Chothia)	HCDR1	GGTFSSY	
SEQ ID NO: 26 (Chothia)	HCDR2	IPRYGK	
SEQ ID NO: 27 (Chothia)	HCDR3	NWPYYMDF	
SEQ ID NO: 28 (Kabat)	LCDR1	RASQNVFNLA	
SEQ ID NO: 29 (Kabat)	LCDR2	DASNRA	
SEQ ID NO: 30 (Kabat)	LCDR3	QQTKNRPPT	
SEQ ID NO: 31 (Chothia)	LCDR1	SQNVFN	
SEQ ID NO: 32 (Chothia)	LCDR2	DAS	
SEQ ID NO: 33 (Chothia)	LCDR3	TKNRPP	
SEQ ID NO: 34	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMGLIIPRYGKARYAQKFG GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSS	
SEQ ID NO: 35	VL	DIVLTQSPATLSLSPGERATLSCRASQNVFNLAHWYQQKPGQAPRLLIYDASNRAITGVPARFSGSGS GTDFTLTITSSLEPEDFAVYYCQQTKNRPPTFGQGTKVEIK	
SEQ ID NO: 36	DNA VH	CAGGTGCAATTTGGTTCAGTCTGGCGCGGAAGTGAACCAACCGGCAGCAGCGTGAAAGTGAG CTGCAAGCCTCCGGAGGCATTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAGCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCCGGTGACCATACCGCGGATGAAGCACCAGCACCCTGATATGGAAGTCTGAGCAG CCTGCGTAGCAAGATACGGCCGTGATTATTGCGCGCGTAATTGGCCTTATTATTATATGAGATT TTTGGGCGCAAGGCACCTGGTGACGGTTAGCTCA	
SEQ ID NO: 37	DNA VL	GATATCGTGTGACCCAGAGCCCGGCGACCCCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCTTGGTACCAGCAGAAACCAAGGTCAAG CACCCTGCTCTATTAATTTATGATGCTTCTAATCTGTGCAACTGGGGTCCCGGCGCGTTTTAGCGGC TCTGGATCCGGCAGCGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGACTAAGAATCGTCTCTCTACCTTTGGCCAGGGTACGAAAGTTGAAATTAAC	
SEQ ID NO: 38	Heavy Chain	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMGLIIPRYGKARYAQKFG GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSSATKGPS	

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
		VFPLAPSSKSTSGGTAALGLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK KDTLMISRTEPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDNLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMHLEALH NHYTQKSLSLSPGK
SEQ ID NO: 39	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRLLIYDASNRATGVPARFSGSGS GTDFTLTLSISLEPEDFAVYYCQQTKNRPPTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKS GTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKAD YEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 40	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGA AAAAACCGGCAGCAGCGTGAAAGTGAG CTGCAAGCCTCCGGAGGCAC TTTAGCAGCTATGCGATTAGCTGGGTGCGCCAGCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAGTT TCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACC CGGTATATGGAAGTCTGAGCAG CCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCC CCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGGCGCCCTGACCAGCGCGCTGCACACC TTCCCGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACCAAGGTGGAC AAGAGAGTTGAGCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCAAGGACACCCCTCATGATCTCCCGG ACCCCTGAGGTACATGCGTGGTGGTGAGCGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAAC TGGTACGTGGAGCGCGTGAGGTGCATAATGCCAAGACAAAGCCGCGGAGGAGCAGTACAA CAGCACGTACCGGTGGTGACGCTCTCACCCTCTGCACAGGACTGGCTGAATGGCAAGGA GTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCTCATCGAGAAAACATCTCCAAGGCC AAAGGGCAGCCCCGAGAACCAAGGTGTACACCTGCCCTCCATCCCGGAGGAGATGACCAAG AACCAGGTGACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCAGCCCTCCCGTGTGGACTCCGACGGCT CCTTCTTCTCTACAGCAAGCTCACCCTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAGACCTCTCCCTGTCTCCG GGTAA
SEQ ID NO: 41	DNA Light Chain	GATATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAG CACCGCTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCGCGCGTTTATAGCGG TCTGGATCCGGCAGCGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGACTAAGAATCGTCTCTTACCTTTGGCCAGGGTACGAAAGTTGAAATTA ACGTACGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGC ACCGCCAGCGTGGTGTGCTGCTGAACAACCTTCTACCCCGGGAGGCCAAGGTGCAGTGAAG GTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTACCCGAGCAGGACAGCAAGGA CTCCACCTACAGCTGAGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAAGCACCAAGGT GTACGCTTGCAGGTGACCCACCAGGGCTGTCCAGCCCGTGACCAAGAGCTTCAACCGGGG CGAGTGT
MOR12604		
SEQ ID NO: 42 (Kabat)	HCDR1	SYAIS
SEQ ID NO: 43 (Kabat)	HCDR2	LIIPRYGKARYAQKFQG
SEQ ID NO: 44 (Kabat)	HCDR3	NWPYYMDF
SEQ ID NO: 45 (Chothia)	HCDR1	GGTFSSY
SEQ ID NO: 46 (Chothia)	HCDR2	IPRYGK
SEQ ID NO: 47 (Chothia)	HCDR3	NWPYYMDF
SEQ ID NO: 48 (Kabat)	LCDR1	RASQNIVFNLA
SEQ ID NO: 49 (Kabat)	LCDR2	DASN RAT
SEQ ID NO: 50 (Kabat)	LCDR3	QQKKSMLPT
SEQ ID NO: 51 (Chothia)	LCDR1	SQNIVFN
SEQ ID NO: 52 (Chothia)	LCDR2	DAS
SEQ ID NO: 53 (Chothia)	LCDR3	KKSMPL
SEQ ID NO: 54	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSY AISWVRQAPGQGLEWMGLIIPRYGKARYAQKFQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSS

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
SEQ ID NO: 55	VL	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRL LIYDASNRATGVPARFSGSGS GTDFTLT ISSLEPEDFAVYYCQQKKSMLTFGQGTKVEIK
SEQ ID NO: 56	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAG CTGCAAAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTCGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCGGGTGACCATACCGCGGATGAAAGCACCAGCACCGCGTATATGGAAGTGAAGT CCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCTAATTGGCCTTATTATATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCA
SEQ ID NO: 57	DNA VL	GATATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGAAGCTGCGACCCCTG AGCTGCGAGCGAGCCAGAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAG CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGTCCCGCGCGCTTTAGCGGC TCTGGATCCGGCAGCGATTTTACCTGACCATAGCAGCCTGGAACTGAAGACTTTGCGGTGT ATTATTGCCAGCAGAAAGTCTATGCCTCTTACCTTTGGCCAGGGTACGAAAGTTGAAATTA
SEQ ID NO: 58	Heavy Chain	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAI SWVRQAPGQGLEWMGLIIPRYGKARYAQKFKQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYIMDFWGQGLTVTVSSASTKG PSVFP LAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYI CNVNHKPSNTKVDKRVPEPKSCDKHTHTCPPCPAPELLGGPVSVF LFPFKPKDTLMI SRTPEVTVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNV FSCSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 59	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRL LIYDASNRATGVPARFSGSGS GTDFTLT ISSLEPEDFAVYYCQQKKSMLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKLS GTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSITYLSSTLTLSKAD YEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 60	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAG CTGCAAAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTCGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCGGGTGACCATACCGCGGATGAAAGCACCAGCACCGCGTATATGGAAGTGAAGT CCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCTAATTGGCCTTATTATATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCC CCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCTTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCCTGACCAGCGGGCTGCACACC TTCCCGGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGAG AAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCTTGGGGGACCGGTGAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCATGATCTCCCCG ACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAAGACCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA CAGCAGCTACCGGGTGGTCAGCGTCTCACCCTCCTGCACAGGACTGGCTGAATGGCAAGGA GTACAAGTGCAAGTCTTCAACAAAGCCCTCCAGCCCCATCGAGAAAACCTTCCAAAGCC AAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCATCCCGGGAGGAGATGACCAAG AACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAACAACCTACAAGACCAAGCCTCCCGTGTGGACTCCGACGGCT CCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTC ATGCTCCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAGAGCCTCTCCCTGTCTCCG GGTAAA
SEQ ID NO: 61	DNA Light Chain	GATATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGAAGCTGCGACCCCTG AGCTGCGAGCGAGCCAGAAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAG CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGTCCCGCGCGCTTTAGCGGC TCTGGATCCGGCAGCGATTTTACCCTGACCATAGCAGCCTGGAACTGAAGACTTTGCGGTGT ATTATTGCCAGCAGAAAGTCTATGCCTCTTACCTTGGCCAGGGTACGAAAGTTGAAATTA ACGTACGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGC ACCGCCAGCGTGGTGTGCTGTGTAACAACCTTACCCCGGGAGGCCAAGGTGAGTGGAAAG GTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTCACCGAGCAGGACAGCAAGGA CTCCACCTACAGCTGAGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAAGCACAAGGT GTACCGCTGAGGAGTGACCCACAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGG CGAGTGT
MOR12605		
SEQ ID NO: 62 (Kabat)	HCDR1	SYAIS
SEQ ID NO: 63 (Kabat)	HCDR2	LIIPRYGKARYAQKFKQ
SEQ ID NO: 64 (Kabat)	HCDR3	NWPYYIMDF
SEQ ID NO: 65 (Chothia)	HCDR1	GGTFSSY

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
SEQ ID NO: 66 (Chothia)	HCDR2	IPRYGK
SEQ ID NO: 67 (Chothia)	HCDR3	NWPYYMDF
SEQ ID NO: 68 (Kabat)	LCDR1	RASQNIVFNLA
SEQ ID NO: 69 (Kabat)	LCDR2	DASNRAT
SEQ ID NO: 70 (Kabat)	LCDR3	QQFRRKSNT
SEQ ID NO: 71 (Chothia)	LCDR1	SQNIVFN
SEQ ID NO: 72 (Chothia)	LCDR2	DAS
SEQ ID NO: 73 (Chothia)	LCDR3	FRRKSNN
SEQ ID NO: 74	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAIISWVRQAPGQGLEWMGLIIPRYGKARYAQKFKQGRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSS
SEQ ID NO: 75	VL	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRLLIYDASNRRATGVPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQFRRKSNTFGQGTKVEIK
SEQ ID NO: 76	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGA AAAAAACGGGCAGCAGCGTGAAAGTGAGCTGCA AAGCCTCCGAGGCACTTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGGCAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTTTCAGGGTCGGGTGACCATACCGCGGATGAAAGCAC CAGCACCGCGTATATGGAACGAGCAGCCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCA
SEQ ID NO: 77	DNA VL	GATATCGTGCTGACCCAGAGCCCGCGACCCCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTGAGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCCTTGGTACCAGCAGAAACAGGTC AAGCACCGCTCTATTAAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCCGGCGGTTTTAGCGGCTCTGGATCCGGCAGGATTTTACCCTGACCATAGCAGCTGGAACCTGAAGACATTTGCGGTGTATTATTGCCAGCAGTTTCGTCGTAAGTCTAATACCTTTGGCCAGGGTACGAAAGTTGAAATTTAA
SEQ ID NO: 78	Heavy Chain	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAIISWVRQAPGQGLEWMGLIIPRYGKARYAQKFKQGRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSSASTKGPSVPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVKRVEPKSCDKHTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDVGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDSGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNYHTQKSLSLSPGK
SEQ ID NO: 79	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRLLIYDASNRRATGVPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQFRRKSNTFGQGTKVEIKRTVAAPS FIFPPSPDEQLKSGTASVVCCLNNFYPREAKVQWKVDNALQSNLSQESVTEQDSKDSSTYLSSTLTLSKADYEEKH VYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 80	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGA AAAAAACGGGCAGCAGCGTGAAAGTGAGCTGCA AAGCCTCCGAGGCACTTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGGCAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTTTCAGGGTCGGGTGACCATACCGCGGATGAAAGCAC CAGCACCGCGTATATGGAACGAGCAGCCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCCCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTCGCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGCGCCCTGACCAGGGCGGTGCACACCTTCCCGGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGAC AAGAGAGTTGAGCCAAATCTTGTGACAAAACCTCACACATGCCACCGCTGCCAGCAGCCTGAACCTCTGGGGGGACCGTCACTCTCTCTCTTCCCCCAAAACCAAGGACACCCCTCATGATCTCCCGGAGCCCTGAGGTACATCGTGGTGGTGGACGTGAGCCACGAAGCCCTGAGGTGAGGTCAAGTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAGCCCGCGGAGGAGCAGTACAA CAGCAGTACCGGGTGTGACGCTCTCACCGTCTGCAACAGGACTGGTGAATGGCAAGGA GTACAAGTGCAAGTCTTCCAACAAGCCCTCCAGCCCCATCGAGAAACCATCTCCAAAGCC AAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGAGGAGATGACCAAG AACAGGTCAGCCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGACCGCGGAGAACAACCTACAAGACACGCTCCCGTGTGGAACCTCCGAGCGCT CTTCTCTCTCTACAGCAAGCTACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTCTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCGAAGAGCCTCTCCCTGTCTCCG GTAAA
SEQ ID NO: 81	DNA Light Chain	GATATCGTGCTGACCCAGAGCCCGCGACCCCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTGAGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCCTTGGTACCAGCAGAAACAGGTC AAG

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.			
			CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCGGCGCGTTTTAGCGGC TCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGTTTCGTGCTAAGTCTAATACCTTTGGCCAGGGTACGAAAGTTGAAATTAA CGTACGGTGGCCGCTCCACAGCGTGTTCATCTTCCCCCAGCGACGAGCAGTGAAGAGCGGCA CCGCCAGCGTGGTGTGCTGCTGAACAACCTTACCCCCGGGAGGCCAAGGTGCAGTGAAGG TGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTACCGAGCAGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAAGCACAAAGGTG TACGCTGCGAGGTGACCACAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGC GAGTGT
MOR12606			
SEQ ID NO: 82 (Kabat)	HCDR1	SYAIS	
SEQ ID NO: 83 (Kabat)	HCDR2	LIIPRYGKARYAQKPFQ	
SEQ ID NO: 84 (Kabat)	HCDR3	NWPYYMDF	
SEQ ID NO: 85 (Chothia)	HCDR1	GGTFSSY	
SEQ ID NO: 86 (Chothia)	HCDR2	IPRYGK	
SEQ ID NO: 87 (Chothia)	HCDR3	NWPYYMDF	
SEQ ID NO: 88 (Kabat)	LCDR1	RASQNIVFNLA	
SEQ ID NO: 89 (Kabat)	LCDR2	DASNRA	
SEQ ID NO: 90 (Kabat)	LCDR3	QQTSKSPST	
SEQ ID NO: 91 (Chothia)	LCDR1	SQNIVFN	
SEQ ID NO: 92 (Chothia)	LCDR2	DAS	
SEQ ID NO: 93 (Chothia)	LCDR3	TKSKPSP	
SEQ ID NO: 94	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMGLIIPRYGKARYAQKPFQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTSS	
SEQ ID NO: 95	VL	DIVLTQSPATLSLSPGERATLSCRASQNIVFNLAHWYQQKPGQAPRLLIYDASNRA	
SEQ ID NO: 96	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAACAAACCGGCAGCAGCGTGAAGTGAG CTGCAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCCGGTGACCATACCGCGGATGAAAGCACCAGCACC	
SEQ ID NO: 97	DNA VL	GATATCGTGTGACCCAGAGCCCGCGACCCCTGAGCCTGTCTCCGGCGAAGCTGCGACCCCTG AGCTGACAGCGAGCCAGAATATTGTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAG CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCGGCGCGTTTTAGCGGC TCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGACTAAGTCTAAGCCTTCTCTACCTTTGGCCAGGGTACGAAAGTTGAAATT AAA	
SEQ ID NO: 98	Heavy Chain	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMGLIIPRYGKARYAQKPFQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTSSASTKG PSVFPPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKSCDKHTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDLNGLKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFCSCVMHEALHNHYTQKSLSLSPGK	
SEQ ID NO: 99	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNIVFNLAHWYQQKPGQAPRLLIYDASNRA	
SEQ ID NO: 100	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAACAAACCGGCAGCAGCGTGAAGTGAG CTGCAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCCGGTGACCATACCGCGGATGAAAGCACCAGCACC	

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
		TTTGGGGCCAAGGCACCTTGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCC CCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGTGGAATCAGGCGCCCTGACCAGCGCGGTGCACACC TTCCCGGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCAGCAACACCAAGGTGGAC AAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCTCATGATCTCCCCG ACCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTC AAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA CAGCAGTACCGGGTGGTGAGCGTCTCACCGTCTGCACAGGACTGGGTGAATGGCAAGGA GTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCATCTCCAAGCC AAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCGGGAGGAGATGACCAAG AACCAGGTACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCAGCCCTCCGTGTGGACTCCGACGGCT CCTTCTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGAGGGGAACGTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAGAGCCCTCTCCCTGTCTCCG GGTAAG
SEQ ID NO: 101	DNA Light Chain	GATATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAG CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCGCGCGCTTTTAGCGGG TCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGACTAAGTCTAAGCCTTCTCTACCTTTGGCCAGGGTACGAAAGTTGAAATT AAACGTACGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGAGCAGCAGCTGAAGAGCG GCACCGCCAGCGTGGTGTGCTGTGAACAACCTTCTACCCCGGGAGGCCAAGGTGCAAGTGA AGGTGGAACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTACCGAGCAGGACAGCAAG GACTCCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAGCACAAG GTGTACGCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCGTGACCAAGAGCTTCAACCGG GGGGAGTGT
MOR12607		
SEQ ID NO: 102 (Kabat)	HCDR1	SYAIS
SEQ ID NO: 103 (Kabat)	HCDR2	LIIPRYGKARYAQKFQ
SEQ ID NO: 104 (Kabat)	HCDR3	NWPYYMDF
SEQ ID NO: 105 (Chothia)	HCDR1	GGTFSSY
SEQ ID NO: 106 (Chothia)	HCDR2	IPRYGK
SEQ ID NO: 107 (Chothia)	HCDR3	NWPYYMDF
SEQ ID NO: 108 (Kabat)	LCDR1	RASQNI VFNL A
SEQ ID NO: 109 (Kabat)	LCDR2	DASN RAT
SEQ ID NO: 110 (Kabat)	LCDR3	QQVKRPFT
SEQ ID NO: 111 (Chothia)	LCDR1	SQNI VFN
SEQ ID NO: 112 (Chothia)	LCDR2	DAS
SEQ ID NO: 113 (Chothia)	LCDR3	VKKRPF
SEQ ID NO: 114	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSY AISWVRQAPGQGLEWMGLIIPRYGKARYAQKFQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPPYYMDFWGQGLTVTVSS
SEQ ID NO: 115	VL	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLAWYQQKPGQAPRLLIYDASN RATGVPARFSGSGS GTDFTLTITSSLEPEDFAVYYCQQVKRPFTFGQGTKVEIK
SEQ ID NO: 116	DNA VH	CAGGTGCAATTGGTTCACTGTGGCGCGGAAGTGAAAAACCGGCAGCAGCGTGAAAGTGAG CTGCAAAAGCCTCCGAGGCACTTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAGGCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTTCGGGTGACCATACCGCGGATGAAAGCACCAAGCCGCTATATGGAAGTCTGAGCAG CCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTAATTGCGCCTTATTATTATATGAGTT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCA
SEQ ID NO: 117	DNA VL	GATATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAG CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGGTCCCGCGCGCTTTTAGCGGG TCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGGTTAAGAAGCGTCCTTTTACCTTTGGCCAGGGTACGAAAGTTGAAATTAA

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.			
SEQ ID NO: 118	Heavy Chain	QVQLVQSGAEVKKPGSSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGLIIPRYGKARYAQKFPQGRVITITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	
SEQ ID NO: 119	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNIIVFNLAWYQQKPGQAPRLLIYDASNRATGVPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQVKKRPFTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
SEQ ID NO: 120	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAGCTGCAAAAGCCTCCGGAGGCACTTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAAGCCCTCGGCAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTTTTCAGGGTCCGGTGACCATTACCGCGGATGAAAGCACCCAGCACCCGCTATATGGAAGTCTGAGCAGCCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTAATTGGCCTTATTATATATGGATTTTTGGGGCCAAGGCACCTCGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCCCTGGGCACCTCTCCAAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAAGTCTAGGCGCCCTGACCAGCGCGGTGCACACCTTCCCGGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAAGCCACGACCAACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCACAGCACCTGAACTCCTGGGGGACCGTCAAGTCTTCTCTTCCCCCAAACCAAGGACACCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAAGCAGTACCGGGTGGTCAAGCTCCTCACCCTCTGCACCAAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCCAAGGCCAAAGGGCAGCCCCGAGAACACAGGTGTACACCTTGCCCCCATCCCGGGAGGAGATGACCAAGAACAGGTACAGCCTGACCTGACCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGAGAGACAATGGGCAGCCGGAGAACACTACAAGACCAAGCCTCCCGTGTCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTTCTCTATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGTAAA	
SEQ ID NO: 121	DNA Light Chain	GATATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGAAGCTGCGACCCCTGAGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAGCACCGCTCTATTAATTTATGATGCTTCTAATCTGTGCAACTGGGGTCCCGGCGCGTTTTAGCGGCTCTGGATTCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGTATTATTGCCAGCAGGTTAAGAAGCGTCTCTTTACCTTTGGCCAGGGTACGAAAGTTGAATTTAAACGTACCGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGCACCGCACGCTGGTGTGCTGCTGAACAACCTTACCCCCGGGAGGCCAAGGTGCAAGTGGAAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTACCGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCACCTGACCCCTGAGCAAGGCCGACTACGAGAAGCACAAAGGTGTACCGCCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGGCGAGTGT	
MOR12608			
SEQ ID NO: 122 (Kabat)	HCDR1	SYAIS	
SEQ ID NO: 123 (Kabat)	HCDR2	LIIPRYGKARYAQKFPQ	
SEQ ID NO: 124 (Kabat)	HCDR3	NWPYYMDF	
SEQ ID NO: 125 (Chothia)	HCDR1	GGTFSSY	
SEQ ID NO: 126 (Chothia)	HCDR2	IPRYGK	
SEQ ID NO: 127 (Chothia)	HCDR3	NWPYYMDF	
SEQ ID NO: 128 (Kabat)	LCDR1	RASQNIIVFNLA	
SEQ ID NO: 129 (Kabat)	LCDR2	DASNRAT	
SEQ ID NO: 130 (Kabat)	LCDR3	QQSYTRPTT	
SEQ ID NO: 131 (Chothia)	LCDR1	SQNIIVFN	
SEQ ID NO: 132 (Chothia)	LCDR2	DAS	
SEQ ID NO: 133 (Chothia)	LCDR3	SYTRPT	

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
SEQ ID NO: 134	VH	QVQLVQSGAEVKKPGSSSVKVSCKASGGTFSSYAIISWVRQAPGQGLEWMGLIIPRYGKARYAQKFP GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWQGGLTVTVSS
SEQ ID NO: 135	VL	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRLLIYDASNRATGVPARFSGSGS GTDFTLTISLLEPEDFAVYYCQQSYTRPTTFGQGTKVEIK
SEQ ID NO: 136	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAG CTGCAAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAAGCCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACC CGCTATATGGAAGT GAGCAG CCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATT TTTGGGCCAAGGCACCTTGGTGACGGTTAGCTCA
SEQ ID NO: 137	DNA VL	GATATCGTGTGACCCAGAGCCCGCGACCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAATATTGTTTTAATCTGGCTTGGTACCAGCAGAAAC CAGGTCAAG CACC CGCTCTATTAATTTATGATGCTTCTAATCTGTCACCTGGGGTCCCCGCGCGTTTTAGCGGC TCTGGATCCGCGACGGATTTTACCCTGACCATTAGCAGCCTGGAACTGGAAGACTTTGCGGTGT ATTATTGCCAGCAGTCTTATACTCGTCTACTACCTTTGGCCAGGGTACGAAAGTTGAAATAA
SEQ ID NO: 138	Heavy Chain	QVQLVQSGAEVKKPGSSSVKVSCKASGGTFSSYAIISWVRQAPGQGLEWMGLIIPRYGKARYAQKFP GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWQGGLTVTVSSASTK GPSVFP LAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKHTCPPCPAPPELLGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDNLNGKEYKKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSR WQQGNVSCSVMHEALHNHYTQKLSLSLSPGK
SEQ ID NO: 139	Light Chain	DIVLTQSPATLSLSPGERATLSCRASQNI VFNLA WYQQKPGQAPRLLIYDASNRATGVPARFSGSGS GTDFTLTISLLEPEDFAVYYCQQSYTRPTTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKS GTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKAD YEKKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 140	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAG CTGCAAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAAGCCCCTGGG CAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACC CGCTATATGGAAGT GAGCAG CCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTAATTGGCCTTATTATTATATGGATT TTTGGGCCAAGGCACCTTGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCC CCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGGCGCCCTGACCAGCGCGCTGCACACC TTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACCAAGGTGGAC AAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGACACCCCTCATGATCTCCCGG ACCCCTGAGGTACATGCGTGGTGGTGAGCGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAAC TGGTACGTGGAGCGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGGAGCAGTACAA CAGCACGTACCGGTGGT CAGCGTCTCACCCTCCTGCACCAGGACTGGCTGAATGGCAAGGA GTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCATCTCCAAGGCC AAAGGGCAGCCCCGAGAACCAAGGTGTACACCTGCCCCCATCCCGGAGGAGATGACCAAG AACCAGGTACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGAGAACCACTACAAGACCAGCCCTCCCGTGTGGACTCCGACGGCT CCTTCTTCTCTACAGCAAGCTCACCGTGACAAGAGCAGGTGGCAGCAGGGGAACGCTCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAGAGCCTCTCCCTGTCTCCG GGTAAA
SEQ ID NO: 141	DNA Light Chain	GATATCGTGTGACCCAGAGCCCGCGACCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAATATTGTTTTAATCTGGCTTGGTACCAGCAGAAAC CAGGTCAAG CACC CGCTCTATTAATTTATGATGCTTCTAATCTGTCACCTGGGGTCCCGCGCGTTTTAGCGGC TCTGGATCCGGCAGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGCTTATACTCGTCTACTACCTTTGGCCAGGGTACGAAAGTTGAAATAA CGTACGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGACAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGCTGCTGAACAACCTTACCCCGGGAGGC CAGGTG CAGTGAAGG TGGACAACGCCCTGCAGAGCGGAACAGCCAGGAAAGCGTCAACGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAAGCACAGAGTG TACGCCGTGCGAGGTGACCCACAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGGC GAGTGT
MOR14533		
SEQ ID NO: 142 (Kabat)	HCDR1	SYAIS
SEQ ID NO: 143 (Kabat)	HCDR2	LIIPRYGKARYAQKFPQ
SEQ ID NO: 144 (Kabat)	HCDR3	NWPYYMDF

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
SEQ ID NO: 145 (Chothia) HCDR1		GGTFSSY
SEQ ID NO: 146 (Chothia) HCDR2		IPRYGK
SEQ ID NO: 147 (Chothia) HCDR3		NWPYYMDF
SEQ ID NO: 148 (Kabat) LCDR1		RASQNIVFNLA
SEQ ID NO: 149 (Kabat) LCDR2		DASN RAT
SEQ ID NO: 150 (Kabat) LCDR3		QQTKSKPSPT
SEQ ID NO: 151 (Chothia) LCDR1		SQNIVFN
SEQ ID NO: 152 (Chothia) LCDR2		DAS
SEQ ID NO: 153 (Chothia) LCDR3		TKSKPSP
SEQ ID NO: 154	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSY AISWVRQAPGQGLEWMGLIIPRYGKARYAQKFKQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSS
SEQ ID NO: 155	VL	EIVLTQSPATLSLSPGERATLSCRASQNIVFNLA WYQQKPGQAPRLLIYDASN RATGIPARFS GSGSGTDFTLTISSLEPEDFAVYYCQQTKSKPSPTFGQGTKVEIK
SEQ ID NO: 156	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAG CTGCAAGACCTCCGGAGGCACTTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAGGCCCTCGGG CAGGGTCTCGAGTGGAATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACC CGGTATATGGAAC TGAGCAG CCTGCGTAGCGAAGATACGGCCGTGTATTATGCGCGCGTAATTGGCCCTTATTATATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCA
SEQ ID NO: 157	DNA VL	GAGATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGCGGAACGTGCGACCCCTG AGCTGCGAGCGAGCCAGAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAAC CAGGTCAAG CACCGCGTCTATTAAATTTATGATGCTTCTAATCGTGCAACTGGGATCCCGGCGCGTTTTAGCGGC TCTGGATCCGGCAGGATTTTACCTGACCATTAGCAGCCTGGAACCTGAGACTTTGCGGTGT ATTATTGCCAGCAGACTAAGTCTAAGCCTTCTCTACCTTTGGCCAGGTCAGAAAGTTGAAATT AAA
SEQ ID NO: 158	Heavy Chain	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSY AISWVRQAPGQGLEWMGLIIPRYGKARYAQKFKQ GRVTITADESTSTAYMELSSLRSEDTAVYYCARNWPYYMDFWGQGLTVTVSSASTKG PSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKSCDKHTHTCPPCPAPPELLGGPSVFP LFPPPKDITLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYITLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSLKLTVDKSRWQ QGNVFSYCMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 159	Light Chain	EIVLTQSPATLSLSPGERATLSCRASQNIVFNLA WYQQKPGQAPRLLIYDASN RATGIPARFSGS GSGTDFTLTISSLEPEDFAVYYCQQTKSKPSPTFGQGTKVEIKRTVAAPSVFIFPPSDEQL KSGTASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSTLTLSKA DYEKHVYACEVTHQGLSPVTKSFNRGEC
SEQ ID NO: 160	DNA Heavy Chain	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGGCAGCAGCGTGAAAGTGAG CTGCAAGACCTCCGGAGGCACTTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAGGCCCTCGGG CAGGGTCTCGAGTGGAATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTT TCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACC CGGTATATGGAAC TGAGCAG CCTGCGTAGCGAAGATACGGCCGTGTATTATGCGCGCGTAATTGGCCCTTATTATATATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCAGCCTCCACCAAGGTCCTCAGGCTCTCC CCTGGCACCCCTCCTCCAAGGACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTAGGCGCCCTGACCAGCGCGCTGCACACC TTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGACCGTCCCTCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGAC AAGAGAGTTGAGCCCAAACTCTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCCTGGGGGACCGTCACTCTCTCTCTCCCCCAAACCAAGGACACCTCATGATCTCCCGG ACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTC AAC TGGTACGTGGACGGCTGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAA CAGCAGTACCGGTGGTCAGCGTCTCACCCTCTGCACCAGGACTGGCTGAATGGCAAGGA GTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCTCATCGAGAAAACCATCTCCAAGGCC AAAGGGCAGCCCCGAGAACCAAGGTGTACACCTGCCCCCATCCCGGGAGGAGATGACCAAG AACCAGTCAAGCTGACCTGCCTGGTCAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGAGAACAACTACAAGACCAGCCCTCCCGTGTGACTCCGACGGCT CCTTCTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTCTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAAGACCTCTCCCTGTCTCCG GGTAAA

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.			
SEQ ID NO: 161	DNA Light Chain	GAGATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTGAGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCTTGGTACCAGCAGAAACCAGGTCAAGCACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGATCCCGGCGCGTTTTAGCGGCTCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGTATTATTGCCAGCAGACTAAGTCTAAGCCTTCTCTACCTTTGGCCAGGGTACGAAAGTTGAAATTAAACGTACGGTGGCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCACCTGACCCTGAGCAAGGCCGACTACGAGAAGCACAAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGCGAGTGT	
MOR14534			
SEQ ID NO: 162 (Kabat)	HCDR1	SYAIS	
SEQ ID NO: 163 (Kabat)	HCDR2	LIIPRYGKARYAQKFQ	
SEQ ID NO: 164 (Kabat)	HCDR3	NWPYYMDF	
SEQ ID NO: 165 (Chothia)	HCDR1	GGTFSSY	
SEQ ID NO: 166 (Chothia)	HCDR2	IPRYGK	
SEQ ID NO: 167 (Chothia)	HCDR3	NWPYYMDF	
SEQ ID NO: 168 (Kabat)	LCDR1	RASQNIVFNLA	
SEQ ID NO: 169 (Kabat)	LCDR2	DASNRA	
SEQ ID NO: 170 (Kabat)	LCDR3	QQTKNRPT	
SEQ ID NO: 171 (Chothia)	LCDR1	SQNIVFN	
SEQ ID NO: 172 (Chothia)	LCDR2	DAS	
SEQ ID NO: 173 (Chothia)	LCDR3	TKNRPP	
SEQ ID NO: 174	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMGLIIPRYGKARYAQKFGRTITADESTSTAYMELSSLRSEDTAVYYCARNWPIYYMDFWGQGLTVTVSS	
SEQ ID NO: 175	VL	EIVLTQSPATLSLSPGERATLSCRASQNIVFNLAWYQQKPGQAPRLLIYDASNRAIGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQTKNRPTTFGQGTKVEIK	
SEQ ID NO: 176	DNA VH	CAGGTGCAATTGGTTCAGTCTGGCGCGGAAGTGAAAAACCGGCAGCAGCGTGAAAGTGAGCTGCAAGCCTCCGGAGGCACCTTTAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCTGGGCAGGGTCTCGAGTGGATGGGCCTTATTATTCCTCGTTATGGTAAGGCTCGTTATGCTCAGAAGTTTCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACCCTATATGGAAGTACGAGCAGCCTGCGTAGCAAGATACGCCCGTGATTATTGCGCGGTAATTGGCCTTATTATTATATGGATTTTTGGGCCAAGGCACCTTGGTGACGGTTAGCTCA	
SEQ ID NO: 177	DNA VL	GAGATCGTGTGACCCAGAGCCCGGCGACCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTGAGCTGCAGAGCGAGCCAGAATATTGTTTTTAATCTGGCTTGGTACCAGCAGAAACCAGGTCAAGCACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGATCCCGGCGCGTTTTAGCGGCTCTGGATCCGGCACGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGTATTATTGCCAGCAGACTAAGAATCGTCTCTACCTTTGGCCAGGGTACGAAAGTTGAAATTAAATTGGGCGAGGCTGAG	

TABLE 1-continued

Examples of HER3 antibodies that bind to a non-linear epitope within domain 3 of HER3.		
		TCAGGGTCGGGTGACCATTACCGCGGATGAAAGCACCAGCACCGCTATATGGAAGTGGAGCAG CCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTAATTGGCCTTATTATTATGGATT TTTGGGGCCAAGGCACCTGGTGACGGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCC CCTGGCACCCCTCTCCAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGGCGCCCTGACCAGCGCGTGCACACC TTCCCGGTCTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG CAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCAGCAACCAAGGTGGAC AAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCTGAAC TCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGACACCCATGATCTCCCGG ACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCGTGAGGTCAAGTTCAAC TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGGAGCAGTACAA CAGCACGTACCGGTGGTCAAGCTCTCACCCTCTGCACAGGACTGGCTGAATGGCAAGGA GTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACATCTCCAAAGCC AAAGGGCAGCCCCGAGAACCAAGGTGTACACCTGCCCCATCCGGGAGGAGATGACCAAG AACCAGGTACGCTGACCTGCTGGTCAAGGCTTCTATCCAGCGATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCAAGCCCTCCCGTGTGGACTCCGACGGCT CCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTTCTC ATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAAGAGCCTCTCCCTGTCTCCG GGTAAA
SEQ ID NO: 181	DNA Light Chain	GAGATCGTGTGACCCAGAGCCCGCGACCCCTGAGCCTGTCTCCGGGCGAACGTGCGACCCCTG AGCTGCAGAGCGAGCCAGAATATGTTTTTAATCTGGCTTGGTACCAGCAGAAACAGGTCAAG CACCGCGTCTATTAATTTATGATGCTTCTAATCGTGCAACTGGGATCCCGCGCGTTTTAGCGGG TCTGGATCCGGCAGGATTTTACCCTGACCATTAGCAGCCTGGAACCTGAAGACTTTGCGGTGT ATTATTGCCAGCAGACTAAGAATCGTCTCTTACCTTTGGCCAGGGTACGAAAGTTGAAATTAA ACGTACGGTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGC ACCGCCAGCGTGGTGTGCTGCTGAACAACCTTCTACCCCGGAGGCCAAGGTGAGTGGGAAG GTGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTACCCGAGCAGGACAGCAAGGA CTCCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGCCGACTACGAGAAGCACAAGGT GTACGCTGCGAGGTGACCCACAGGGCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGG CGAGTGT

TABLE 2

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
MOR12514		
SEQ ID NO: 182 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 183 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 184 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 185 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 186 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 187 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 188 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 189 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 190 (Kabat)	LCDR3	QVRDMSLFVDV
SEQ ID NO: 191 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 192 (Chothia)	LCDR2	GVS
SEQ ID NO: 193 (Chothia)	LCDR3	RDMSLFD
SEQ ID NO: 194	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTRDTSISITAYMELSRLESEDVAVYYCARGSFYTRDSYFDVWQGGLTVTVSS
SEQ ID NO: 195	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCQVRDMSLFDVFGGGTKLTVL
SEQ ID NO: 196	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACTACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGGTATATGGAAGTGAAGCC

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		GTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCA
SEQ ID NO: 197	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAACTGATGATCTACGGTGTCTTAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGGTTTCGTGACATGTCTCTGTTTCGACGTGTTTGGCGGCGGCACGA AGTTAACCGTCCCTA
SEQ ID NO: 198	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTTRDTSISTAYMELSLRLSEDTAVYYCARGSFYTRDSYFDVWQGTLLVTSSASTKGPSVFP LAPSSKSTSGGTAAALGLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSSGLYSLSVVTVPPSSSL GTQTYICNVNHHKPSNTHKVDKRVPEKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMHEALHNNHYTQKSLSLSPGK
SEQ ID NO: 199	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTIISGLQAEDEADYYCQVRDMSLFDVFGGGTKLTVLGQPKAAPSVTLFPPSSSEELQANKA TLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKSHRSYSCQVTH EGSTVEKTVAPTECS
SEQ ID NO: 200	DNA Heavy Chain	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGTGCGCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAATGAGCC GTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCTCTCTCAAGAGCACTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACCTCAGGCGCCCTGACCAGCGG CGTGACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCAAATCTTGTGACAAAACCTCACACATGCCACCCTGCCCCA GCACCTGAACTCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCTTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGCTACCGGTGGTCAGCGTCTCACCCTCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCCGACGGCTCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGCTTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 201	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAACTGATGATCTACGGTGTCTTAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATAGCGGCCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGGTTCTGTGACATGTCTCTGTTTCGACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTTAGGTACAGCCAAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGAG GAGCTTCAAGCCAAACAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGA CAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACACACCTCCA AACAAAGCAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGAAGT CCACAGAGCTACAGCTGCCAGGTACGCATGAAGGAGCACCGTGGAGAAGACAGTGGCC CCTACAGAAATGTTCA
MOR12515		
SEQ ID NO: 202 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 203 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 204 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 205 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 206 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 207 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 208 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 209 (Kabat)	LCDR2	GVSKRPS

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 210 (Kabat)	LCDR3	YSRDSMPDQV
SEQ ID NO: 211 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 212 (Chothia)	LCDR2	GVS
SEQ ID NO: 213 (Chothia)	LCDR3	RDSMPDQ
SEQ ID NO: 214	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTTRDTSISTAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWQGQTLVTVSS
SEQ ID NO: 215	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCYSRDSPMDQVFGGKLTVL
SEQ ID NO: 216	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGAGCC GTCTGCGTAGCGAAGATACGGCCGTGATATTATGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 217	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCGCGAAACTGATGATCTACGGTGTTTCTAAACGTCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTACTCTCGTGACTCTCCGATGGACCAGGTGTTTGGCGGCGGCACGA AGTTAACCGTCCTA
SEQ ID NO: 218	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTTRDTSISTAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWQGQTLVTVSSASTKGPSVFP LAPSSKSTSGGTAALGLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSS SLGTQTYICNVNHPKPSNTKVDKRVPEPKSCDKHTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDNLNGKEYKC KVSINKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ PENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMHREALHNYHTQKSLSLSPGK
SEQ ID NO: 219	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCYSRDSPMDQVFGGKLTVLGQPKAASVTLFPPSSSEELQANKA TLVCLISDFYPGAVTVAWKADSSPVKAGVETTPSKQSNNKYAASSYLSLTPEQWKSHRYSYSCQVTH EGSTVEKTVAPTECS
SEQ ID NO: 220	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGAGCC GTCTGCGTAGCGAAGATACGGCCGTGATATTATGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCTCCAAGAGCACTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGAACCAGGTGACGGTGTCTGGAACCTAGCGGCCCTGACCAGCGG CGTGACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTACACATGCCCCACCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAGACCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGCTACCGGTGGTCAGCGTCTTACCCTCTGACACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGAAGGTCTCCAACAAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGGAAGAACACTACAAGACCACGCCCTCCCGTGTGGA CTCCGACGGCTCTTCTTCTCTACAGCAAGCTCACCGTGACAAAGAGCAGGTGGCAGCAGGG GAACGCTCTTCTATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 221	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGACCCGGCACAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCGCGAAACTGATGATCTACGGTGTTTCTAAACGTCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTACTCTCGTGACTCTCCGATGGACCAGGTGTTTGGCGGCGGCACGA AGTTAACCGTCTAGGTACGCCCAAGGCTGCCCTCGGTCACTGTGTTCCCGCCTCTCTGAG GAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGAGCCGTGA

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
			CAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCACACCTCCA AACAAAGCAACAACAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGAAAGT CCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCC CCTACAGAATGTTCA
MOR12516			
SEQ ID NO: 222 (Kabat)	HCDR1		SYDIH
SEQ ID NO: 223 (Kabat)	HCDR2		RIDPYSGNTNYAQKFQG
SEQ ID NO: 224 (Kabat)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 225 (Chothia)	HCDR1		GYTFTSY
SEQ ID NO: 226 (Chothia)	HCDR2		DPYSGN
SEQ ID NO: 227 (Chothia)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 228 (Kabat)	LCDR1		TGTSSDVGTYNQVS
SEQ ID NO: 229 (Kabat)	LCDR2		GVSKRPS
SEQ ID NO: 230 (Kabat)	LCDR3		QSRDITYRPVKV
SEQ ID NO: 231 (Chothia)	LCDR1		TSSDVGTYNQ
SEQ ID NO: 232 (Chothia)	LCDR2		GVS
SEQ ID NO: 233 (Chothia)	LCDR3		RDITYRPVK
SEQ ID NO: 234	VH		QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTTRDTSISTAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 235	VL		DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCQSRDITYRPVKVFGGGTKLTVL
SEQ ID NO: 236	DNA VH		CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCAGCGGTATATGGAAGTGGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 237	DNA VL		GATATCGCGGTGACCCAGCCGGCGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACACGACGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCGAAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGTCTCGTGACACTTACCGTCCGGTTAAAGTGTTTGGCGCGGCA CGAAGTTAACCGTCCTA
SEQ ID NO: 238	Heavy Chain		QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYA QKFGGRVTMTTRDTSISTAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSSAST KGPSVFLPAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SVVTVPSSSLGTQYICNVNHKPSNTKVDKRVPEPKSCDKHTKCPPCPAPPELLGGPSVFLFPPK KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQCSVMHEALHNH YTQKSLSLSPGK
SEQ ID NO: 239	Light Chain		DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCQSRDITYRPVKVFGGGTKLTVLQPKAAPSVTLFPPSSEEL QANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPSKQSNKNYAASSYLSLTPEQWKSH RSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 240	DNA Heavy Chain		CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCAGCGGTATATGGAAGTGGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGTTGACCT CGGTCTTCCCCCTGGCACCCCTCTCCAAAGAGCACTCTGGGGGCACAGCGGCCCTGGCTGCCT GGTCAAGGACTACTTCCCGAACCAGGTGACGGGTGCTGGAAGTCAAGCGCCCTGACAGCGG CGTGACACCTTCCCGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGGTGGTGACCG TGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCAGCAACAC

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
			CAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCCA GCACCTGAACTCCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAAGACCCGTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGGTGGTCAGCGTCTCACCCTCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCGAGCCGGAGAACACTACAAGACCACGCCTCCCGTGTCTGGA CTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCCTGGACAAGAGCAGGTGGCAGCAGGG GAACGCTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 241	DNA Light Chain		GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCGACGCGATGTGGGCACCTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGCTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGTCTCGTGACACTTACCGTCCGGTTAAAGTGTCTGGCGGCGGCA CGAAGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCTCCTCT GAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCC GTGACAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCAACACC CTCCAACAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTG GAAGTCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAAGACAG TGGCCCCACAGAATGTTCA
MOR12615			
SEQ ID NO: 242 (Kabat)	HCDR1		SYDIH
SEQ ID NO: 243 (Kabat)	HCDR2		RIDPYSGNTNYAQKFGQ
SEQ ID NO: 244 (Kabat)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 245 (Chothia)	HCDR1		GYTFTSY
SEQ ID NO: 246 (Chothia)	HCDR2		DPYSGN
SEQ ID NO: 247 (Chothia)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 248 (Kabat)	LCDR1		TGTSSDVGTYNQVS
SEQ ID NO: 249 (Kabat)	LCDR2		GVSKRPS
SEQ ID NO: 250 (Kabat)	LCDR3		SSRDLIGHTYV
SEQ ID NO: 251 (Chothia)	LCDR1		TSSDVGTYNQ
SEQ ID NO: 252 (Chothia)	LCDR2		GVS
SEQ ID NO: 253 (Chothia)	LCDR3		RDLIGHTY
SEQ ID NO: 254	VH		QVQLVQSGAEVKKPGASVKVSKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTRDTSISTAYMELSRLRSEDTAVYVCARGSFYTRDSYFDVWQGTLVTVSS
SEQ ID NO: 255	VL		DIALTQPASVSGSPGQSIITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCSSRDLIGHTYVFGGKLTVL
SEQ ID NO: 256	DNA VH		CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGA AAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAATACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCTATATGGAACGTAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCAAGGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 257	DNA VL		GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCGACGCGATGTGGGCACCTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGCTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTCGTGACCTGATCGGTCTATTACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTCA
SEQ ID NO: 258	Heavy Chain		QVQLVQSGAEVKKPGASVKVSKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNY AQKFGQGRVTMTRDTSISTAYMELSRLRSEDTAVYVCARGSFYTRDSYFDVWQGTLVTVSSAS TKGPSVFPLAPSSKSTSGGTAALGLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSYL SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 259	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSN RFGSGSKSGNTASLTISGLQAEDADYYC SSRDLIGHYVFGGGTKLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPSKQSNKYAASSYLSTLTPQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 260	DNA Heavy Chain	CAGGTGCAATTGGTGACAGACGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAAAGCGTCCGGATATACCTTCACCTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAAGGCCGGGTGACCATGACCCGTGATACCGCATTAGCACCGCGTATATGGAACGTAGCC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCCAAGGCACCCCTGGTGACTGTAGCTCAGCCTCCACCAAGGGTCCAT CGGCTTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGCTGTGGAACCTCAGCGCCCTGACCAGCGG CGTGACACCTTCCCCGGCTGTCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCCAAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTGTGACAAAACCTACACATGCCCCACCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGGTGGTGACGCTCCTCACCGTCTGCACACGAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCTCCCGTGTGGA CTCCGACGGCTCCTTCTCTCTACAGCAAGCTCACCGTGACAAAGACAGGTGGCAGCAGGG GAACGCTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 261	DNA Light Chain	GATATCGCGCTGACCCAGCCGCGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACACGACGCGATGTGGGCACTTACAACCAAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCGCAAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTCGTGACCTGATCGGTCTATTACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCGCGCCTCCTCTGAG GAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCGGTGA CAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCAACCCCTCCA AACAAAGCAACAACAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGAAAGT CCCACAGAAGCTACAGTGCCAGGTACGCATGAAGGAGCACCGTGGAGAAGACAGTGGCC CTTACAGAAATGTTCA
MOR12920		
SEQ ID NO: 262 (Kabat)	HCDR1	GYVMH
SEQ ID NO: 263 (Kabat)	HCDR2	DIEPYHGKPLYAQKFQG
SEQ ID NO: 264 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 265 (Chothia)	HCDR1	GYTFTGY
SEQ ID NO: 266 (Chothia)	HCDR2	EPYHGK
SEQ ID NO: 267 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 268 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 269 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 270 (Kabat)	LCDR3	SSRDLIGHYV
SEQ ID NO: 271 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 272 (Chothia)	LCDR2	GVS
SEQ ID NO: 273 (Chothia)	LCDR3	RDIGHY
SEQ ID NO: 274	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTGYMHVVRQAPGQGLEWMGDI EPYHGKPLYAQK FQGRVTMTTRDTSISTAYMELSRLSSEDTAVYYCARGSFYTRDSYFDVWGQGLTVVSS

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 275	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGNAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSRDLIGHYVFGGGTKLTVL
SEQ ID NO: 276	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGCGAAAGCTGAAAATTAG CTGCAAAGGCTCCGGATATAGCTTCACTAACTCTTGGGTGCTTGGGTGCGCCAGATGCCGGGC AAAGGTCTCGAGTGGATGGGCATCATCTACCCGGGTAAACAGCGACACCATCTATAGCCCGAGCT TTCAGGGCCAGGTGACCATTAGCGCGGATAAAAGCATCAGCACCAGCTATCTGCAATGGAGCA GCCTGAAAGCGAGCGATACCGCGATGTATTATTGCGCGCTGTTTCATATCATCCAGCGCCGCTC TGCTTGGTCTTACAACGCTATGGATGTTTGGGGCCAAGGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 277	DNA VL	GATATCCAGATGACCCAGAGCCCAGCAGCCTGAGCGCCAGCGTGGGCGATCGCGTGACCATT ACCTGCAGAGCCAGCCAGTCTATTTCTACTTACCTGAACTGGTACCAGCAGAAACCGGGCAAG CGCCGAACTATTAACTCTCGGTGCTTCTAACCTGCAAAGCGCGTGGCCAGCCGCTTTAGCGG CAGCGGATCCGGCACCAGATTTCACCTGACCATTAGCTCTCTGCAACCGGAAGACTTTGCGACCT ATTATTGCCAGCAGTCTATCACTGAACGTTCACCTTTGGCCAGGGCAGCAAAGTTGAAATTA
SEQ ID NO: 278	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTGYMHVWRQAPGQGLEWMGDI EPHYGKPK LYAQKFQGRVTMRDTSISITAYMELSRLEDTAVYYCARGSFYTRDSYFDVWGGTLLVTVS SASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 279	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGNAPKLMYGVSKRPSGVSNR FSGSKSGNTASLTISGLQAEDEADYYCSSRDLIGHYVFGGGTKLTVLQPKAAPSVTLFPPSSE ELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQWK SHRSYSQCVTHEGSTVEKTVAPTECS
SEQ ID NO: 280	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGCGAAAGCTGAAAATTAG CTGCAAAGGCTCCGGATATAGCTTCACTAACTCTTGGGTGCTTGGGTGCGCCAGATGCCGGGC AAAGGTCTCGAGTGGATGGGCATCATCTACCCGGGTAAACAGCGACACCATCTATAGCCCGAGCT TTCAGGGCCAGGTGACCATTAGCGCGGATAAAAGCATCAGCACCAGCTATCTGCAATGGAGCA GCCTGAAAGCGAGCGATACCGCGATGTATTATTGCGCGCTGTTTCATATCATCCAGCGCCGCTC TGCTTGGTCTTACAACGCTATGGATGTTTGGGGCCAAGGCACCCCTGGTGACTGTTAGCTCAGCC TCCACCAAGGTCCTCGGTCTTCCCTTGGCACCTCTCCCAAGAGCACCTCTGGGGGCACAG CGGCCCTGGGCTGCTGGTCAAGGACTACTTCCCGAACCGGTGACCGTGTCGTGGAAGTCTAG GCGCCCTGACCAGCGCGTGCACACCTTCCCGGTGTCTCTACAGTCTCTCAGGACTCTACTCCCTC AGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATC ACAAGCCAGCAACACCAAGGTGACAAGAGAGTTGAGCCCAAATCTTGTGACAAACTCACA CATGCCACCGTGCCAGCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAA CCCAAGGACACCTCATGATCTCCCGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCC ACGAAGACCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCAGCTACCGGGTGGTCAGCGTCTCTACCGTCTGTC ACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCC CCATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCCCGAGAACCCAGAGTGTACACCTGTC CCCCATCCCGGGAGGAGATGACCAAGAACCAGGTGACGCTGACCTGGTCAAGGCTTCT ATCCAGCGACATCCGCGTGGAGTGGGAGAGCAATGGGCAGCCGAGAGAACACTACAAGACC ACGCTTCCCGTGTGGACTCCGACGGCTCTTCTCTCTACAGCAAGCTCACCGTGACCAAGA GCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAAGAGCCTCTCCCTGTCTCCGGTAA
SEQ ID NO: 281	DNA Light Chain	GATATCCAGATGACCCAGAGCCCAGCAGCCTGAGCGCCAGCGTGGGCGATCGCGTGACCATT ACCTGCAGAGCCAGCCAGTCTATTTCTACTTACCTGAACTGGTACCAGCAGAAACCGGGCAAAG CGCCGAACTATTAACTCTCGGTGCTTCTAACCTGCAAAGCGCGTGGCCAGCCGCTTTAGCGG CAGCGGATCCGGCACCAGATTTACCCCTGACCATTAGCTCTCTGCAACCGGAAGACTTTGCGACCT ATTATTCCCAGCAGTCTATCACTGAACTGTTACCTTTGGCCAGGGCAGCAAGTTGAAATTA CGTACGTTGGCCGCTCCAGCGTGTTCATCTTCCCCCAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGCTGCTGAACAACCTTCTACCCCGGGAGGCCAAGGTGCAAGTGAAGG TGGACAACGCCCTGCAGAGCGGCAACAGCCAGGAAAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCTGACCTGAGCAAGGCCGACTACGAGAAGCACAGGTG TACGCTGCGAGGTGACCCACAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACCGGGG GAGTGT
MOR12921		
SEQ ID NO: 282 (Kabat)	HCDR1	GYMH
SEQ ID NO: 283 (Kabat)	HCDR2	DIDPHSGNAVYAQKFQG
SEQ ID NO: 284 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 285 (Chothia)	HCDR1	GYFTGY

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 286 (Chothia) HCDR2	DPHSGN	
SEQ ID NO: 287 (Chothia) HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 288 (Kabat) LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 289 (Kabat) LCDR2	GVSKRPS	
SEQ ID NO: 290 (Kabat) LCDR3	SSRDLIGHYV	
SEQ ID NO: 291 (Chothia) LCDR1	TSSDVGTYNQ	
SEQ ID NO: 292 (Chothia) LCDR2	GVS	
SEQ ID NO: 293 (Chothia) LCDR3	RDIGHY	
SEQ ID NO: 294	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTGYMHVWRQAPGQGLEWMGDIDPHSGNAVYAQ KFQGRVTMTDRDTSISTAYMELSLRSEDVAVYYCARGSFYTRDSYFDVWVGQGTTLTVSS
SEQ ID NO: 295	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCSSRDLIGHYVFGGGTKLTVL
SEQ ID NO: 296	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACCGGCTATTACATGCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCGACATCGACCCGCTTCTGGCAACGCTGTTTACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGACC GTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCTGGTGACTGTTAGCTCA
SEQ ID NO: 297	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCAACCGGCACCGAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTCGTGACCTGATCGGTCTATTACGTGTTTGGCGGCGGCACGA AGTTAACCGTCCTA
SEQ ID NO: 298	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTGYMHVWRQAPGQGLEWMGDIDPHSG NAVYAQKFQGRVTMTDRDTSISTAYMELSLRSEDVAVYYCARGSFYTRDSYFDVWVGQGTTLTVSS SASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSVGHVTPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKHTHTCPPCPAPELLGGPSVFLFPPK PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNNHYT QKSLSLSPGK
SEQ ID NO: 299	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGV VSKRPSGVSNRFGSGSKGNTASLTISGLQAEDEADYYCSSRDLIGHYVFGGGTKLTVLGQPKAA PSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKNKYAASS YLSLTPEQWKSHRYSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 300	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACCGGCTATTACATGCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCGACATCGACCCGCTTCTGGCAACGCTGTTTACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGACC GTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGCAACCGGTGACGGTGTCTGGAACCTCAGCGCCCTGACCAGCGG CGTGACACCTTCCCCGTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGTTGGGCACCCAGACCTACATCTGCAACGTGAATCAAGACCCACAGAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTGTGACAAAACCTACACATGCCCCACCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGTTGATGAGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGGTGGTACGCTCTCACCCTCTGCACCAGGACTGGCTGA ATGGCAAGGAGTACAAGTGAAGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTTGCCCCATCCCGGGAGG GATGACCAAGAACCAGGTGACCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCGAGCGGAGAACACTACAAGACCACGCCTCCCGTGTGGA CTCCGACGGCTCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGCTTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAAGAGCCTC TCCCTGTCTCCGGGTAAA

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
SEQ ID NO: 301	DNA Light Chain	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAGCAGCGATGTGGGCACCTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTCGTGACCTGATCGGTCATTACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGAG GAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGA CAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCACACCTCCA AACAAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGAAAGT CCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGATGGCC CCTACAGAATGTTCA	
MOR12922			
SEQ ID NO: 302 (Kabat)	HCDR1	GYVMH	
SEQ ID NO: 303 (Kabat)	HCDR2	VIDPYSGWTEYAQKFQG	
SEQ ID NO: 304 (Kabat)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 305 (Chothia)	HCDR1	GYTFTGY	
SEQ ID NO: 306 (Chothia)	HCDR2	DPYSGW	
SEQ ID NO: 307 (Chothia)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 308 (Kabat)	LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 309 (Kabat)	LCDR2	GVSKRPS	
SEQ ID NO: 310 (Kabat)	LCDR3	SSRDIGHYV	
SEQ ID NO: 311 (Chothia)	LCDR1	TSSDVGTYNQ	
SEQ ID NO: 312 (Chothia)	LCDR2	GVS	
SEQ ID NO: 313 (Chothia)	LCDR3	RDLIGHY	
SEQ ID NO: 314	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYMHVVRQAPGQGLEWMGVDPYSGWTEYAQK FQGRVTMTDRTSISTAYMELSRLRSEDVAVYYCARGSFYTRDSYFDVWGQTLTVTSS	
SEQ ID NO: 315	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSRDIGHYVFGGGTKLTVL	
SEQ ID NO: 316	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACCGGCTATTACATGCATTGGGTGCGCCAGGCCCCGGGC CAGGGCCTCGAGTGGATGGGCGTTATTGACCCGTACTCTGGCTGGACTGAATACGCGCAGAAA TTTCAGGCGCGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAAGTGAAGC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAGGCACCTGGTGACTGTTAGCTCA	
SEQ ID NO: 317	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAGCAGCGATGTGGGCACCTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTCGTGACCTGATCGGTCATTACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTCA	
SEQ ID NO: 318	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYMHVVRQAPGQGLEWMGVDPYSGWTEYAQKFPQGRVTMTDRTSISTAYMELSRLRSEDVAVYYCARGSFYTRDSYFDVWGQGLTLTVTSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPPELLGGPSVFLFPPPKPDTLMISRTEPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRREEQYNSTYRVVSVLTVLHQDNLNGLKEYKKVSNKALPAPIEKTISKAKGQPREPQVYTLTPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGGSFFLYSKLTVDKSRWQQGNVFPSCSVMHEALHNHYTQKSLSLSPGK	
SEQ ID NO: 319	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSRDIGHYVFGGGTKLTVLQPKAAPSVTLFPPSSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTTPSKQSNNKYAASSYLSLTPEQWKSHRYSYSCQVTHEGSTVEKTVAPTECS	
SEQ ID NO: 320	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACCGGCTATTACATGCATTGGGTGCGCCAGGCCCCGGGC	

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		CAGGGCCTCGAGTGGATGGGCGTTATTGACCCGTACTCTGGCTGGACTGAATACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAAGTGAAGC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCCAAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGTGACGGTGCTGTGGAAGTCAAGCGCCTGACAGCGG CGTGACACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTACACATGCCCCCGTGCCCA GCACCTGAAGTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCCTCACCCTCCTGACCAGGACTGGTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAGAACAACTACAAGACCACGCCCTCCGCTGTGGA CTCCGACGGCTCCTTCTCTCTACAGCAAGCTCACCCTGGACAAAGAGCAGGTGGCAGCAGGG GAACGCTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGTAAA
SEQ ID NO: 321	DNA Light Chain	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCGCAAACTGATGATCTACGGTGTCTTAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTCGTGACCTGATCGGTCTATTACGTGTTGGCGGCGGCACGA AGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCTCGGTCACTCTGTTCCGCGCTCCTCTGAG GAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGA CAGTGGCCTGGAAGGCAGATAGCAGCCCGTCAAGGCGGGAGTGGAGACCACCAACCCCTCCA AACAAAGCAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGAAGT CCCAAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAAGACAGTGGCC CCTACAGAATGTTCA
MOR13654		
SEQ ID NO: 322 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 323 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQ
SEQ ID NO: 324 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 325 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 326 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 327 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 328 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 329 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 330 (Kabat)	LCDR3	QSRGEYRPGWV
SEQ ID NO: 331 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 332 (Chothia)	LCDR2	GVS
SEQ ID NO: 333 (Chothia)	LCDR3	RGEYRPGW
SEQ ID NO: 334	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVMTMRDTSISITAYMELSRLESEDVAVYICARGSFYTRDSYFDVWQGGLTVTVSS
SEQ ID NO: 335	VL	DIALTQPASVSGSPGQSITISCTGSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYICQSRGEYRPGWVFGGGLKLTVL
SEQ ID NO: 336	DNA VH	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAAGTGAAGC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTTCGATGTTTGGGGCCAAGGCACCTCGTGACTGTTAGCTCA
SEQ ID NO: 337	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCAACCGGCACCCAGCAGCATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCGCAAACTGATGATCTACGGTGTCTTAACGTCCGAGCGCGGTGAGCAACCGT

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 338	Heavy Chain	TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGTCTCGTGGTGAATACCGTCCGGGTGGGTGTTTGGCGGCGGC ACGAAGTTAACCGTCCTA
SEQ ID NO: 339	Light Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGN TNYAQKFQGRVTMTDRDTSISTAYMELSLRSEDVAVYFCARGSFYTRDSYFDPVWGQGL VTVSSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKHTHTCPPCPAPE LLGSPSVFLFPPPKDKTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 340	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGGTATATGGAACAGAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAGGCACCTCGTGACTGTAGCTCAGCCTCCACCAGGGTCCAT CGGTCTTCCCGCTGGCACCTCTCCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGAACCGGTGACGGTGTCTGTGGAACAGGCGCCCTGACCAGCGG CGTGACACACCTTCCCGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACC TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTTGTGACAAAACACACATGCCACCCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG AGCAGTACAACAGCACGTACCGGTGGTACGCTCCTCACCGTCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGAAGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCGAGCGGAGAACACTACAAGACCACGCCTCCCGTGTCTGA CTCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACCAACCACTACACGCAGAAGAGCCTC TCCTGTCTCCGGGTAAA
SEQ ID NO: 341	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACACGACGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCGCAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGTCTCTGGTGAATACCGTCCGGGTGGGTGTTTGGCGGCGGC ACGAAGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTC TGAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTCTCATAAGTGACTTCTACCCGGGAGCC GTGACAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGAGTGGAGACCACCAACAC CTCCAAACAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACCGCTGAGCAGTG GAAGTCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAG TGGCCCTACAGAATGTTCA
MOR13655		
SEQ ID NO: 342 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 343 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 344 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 345 (Chothia)	HCDR1	GYFTTSY
SEQ ID NO: 346 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 347 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 348 (Kabat)	LCDR1	TGSSDVGTYNQVS
SEQ ID NO: 349 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 350 (Kabat)	LCDR3	SSATQKPDVTV
SEQ ID NO: 351 (Chothia)	LCDR1	TSSDVGTYNQ

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 352 (Chothia) LCDR2	GVS	
SEQ ID NO: 353 (Chothia) LCDR3	ATQKPDVT	
SEQ ID NO: 354	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTTRDTSISTAYMELSLRSEDVAVYVCARGSFYTRDSYFDVWQGGLTVTVSS
SEQ ID NO: 355	VL	DIALTQPASVSGSPGQSIITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSKSGNTASLTISGLQAEDEADYYCSSATQKPDVTVFVGGGKLTVL
SEQ ID NO: 356	DNA VH	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGCTCCGGATATACCTTCACCTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAAATTCAGGGCCGGGTGACCATGACCCGTGATACCGCATTAGCACCAGCGGTATATGGAACCTGAGCCGTCTGCGTAGCGAAGATACGCGCGTGATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCA
SEQ ID NO: 357	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCCGGGCCAGAGCATTACCATTAGCTGACCCGGCACCAGCAGCGATGTGGGCACCTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGCGCGCGAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGACGAAGCGGATTATTACTGCTCTTCTGCTACTCAGAAACCGGACGTTACTGTGTTTGGCGCGGCAAGAAGTTAACCGTCCTA
SEQ ID NO: 358	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTTRDTSISTAYMELSLRSEDVAVYVCARGSFYTRDSYFDVWQGGLTVTVSSASTKGPSVFPPLAPSSKSTSGGTAALGLVVDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKHTHTCPPCPAPPELLGGPSVFLFPPKPKDLMISRTPTEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTIVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 359	Light Chain	DIALTQPASVSGSPGQSIITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGKSGNTASLTISGLQAEDEADYYCSSATQKPDVTVFVGGGKLTVLVGGPKAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNINKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 360	DNA Heavy Chain	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGCTCCGGATATACCTTCACCTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAAATTCAGGGCCGGGTGACCATGACCCGTGATACCGCATTAGCACCAGCGGTATATGGAACCTGAGCCGTCTGCGTAGCGAAGATACGCGCGTGATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCCCCTGGCACCCCTCCTCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCGAACCGGTGACGGTGTCTGGAACTCAGCGCCCTGACCAGCGCGTGCACACCTTCCCGGTCTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACACAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTACACATGCCCAACCGTGCCCAACCTGAACTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGTCAAGTTCACTGGTACGTGGACGGCTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGGAGCAGTACAACAGCACGTACCGGTGGTACGCTCCTCACCCTCTGCACCAGGACTGGCTGATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTGACCTGCTGGTCAAAGGCTTCTATCCAGCGCATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGAGAGAACAACTACAAGACCACGCTCTCCGTGTGACCTCCGACGGCTCTTCTCTCTACAGCAAGCTCACCCTGGACAAAGAGCAGGTGGCAGCAGGGGAACGCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGAGAAGAGCCTCTCCCTGTCTCCGGTAA
SEQ ID NO: 361	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCCGGGCCAGAGCATTACCATTAGCTGACCCGGCACCAGCAGCGATGTGGGCACCTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGCGCGCGAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGACGAAGCGGATTATTACTGCTCTTCTGCTACTCAGAAAACCGGACGTTACTGTGTTTGGCGCGGCAAGAAGTTAACCGTCTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCTCTCTGAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAGTGGCTTGGAAAGGAGATAGCAGCCCGTCAAGGCGGGAGTGGAGACCAACCACTCTCCAACAAGCAACAACAAGTACCGCGCCAGCAGCTATCTGAGCTGACGCTGAGCAGTGAAGTCCCAAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGTGCCCTTACAGAATGTTCA

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
MOR13656		
SEQ ID NO: 362 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 363 (Kabat)	HCDR2	RIDPYSGNTNYAQKFG
SEQ ID NO: 364 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 365 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 366 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 367 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 368 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 368 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 370 (Kabat)	LCDR3	AVRDSVWHV
SEQ ID NO: 371 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 372 (Chothia)	LCDR2	GVS
SEQ ID NO: 373 (Chothia)	LCDR3	RDSVWH
SEQ ID NO: 374	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTTRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 375	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGSKGNTASLTISGLQAEDEADYYCAVRDSVWHVFGGGTKLTVL
SEQ ID NO: 376	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAATTTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGCCGTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 377	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCGGTAGCCCGGGCCAGAGCATTACCATAGCTGACACCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGGCGCCGAAACGTATGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCGTGCAAGCGGAAGACGAAGCGGATTATTACTGCGGTGTTCGTGACTCCGTTTGGCATGTGTTTGGCGGCGGCACGAAGTTAACCGTCCTA
SEQ ID NO: 378	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFGQGRVTMTTRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWVGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 379	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGSKGNTASLTISGLQAEDEADYYCAVRDSVWHVFGGGTKLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPPSKQSNKYYASSYLSLTPEQWQKSHRSYSCQVTHEGSTEVEKTVAPTECS
SEQ ID NO: 380	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAATTTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGCCGTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGCTGGAACCTCAGCGGCCCTGACCAGCGCGTGTCACACCTTCCCCGCTGTCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAATCTGTGACAAAACCTCACACATGCCACCGGTGCCACGCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAACTGTTACGTGACGCGGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
			AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCAAAGGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCCTCCCGTGTGGGA CTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 381	DNA Light Chain		GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCGCTGTTCTGTGACTCCGTTTGGCATGTGTTTGGCGGCGGCACGAAGT TAACCGTCTTAGGTGAGCCCAAGGCTGCCCTCGGTCACTCTGTTCCCGCCCTCTCTGAGGAG CTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTTACCCGGGAGCCGTGACAG TGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCAACACCTCCAAAC AAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGAAGTCCC ACAGAAGCTACAGCTGCCAGGTACGCATGAAGGAGACCGTGGAGAAGACAGTGGCCCCCT ACAGAATGTTCA
MOR13657			
SEQ ID NO: 382 (Kabat)	HCDR1		SYDIH
SEQ ID NO: 383 (Kabat)	HCDR2		RIDPYSGNTNYAQKFQG
SEQ ID NO: 384 (Kabat)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 385 (Chothia)	HCDR1		GYTFTSY
SEQ ID NO: 386 (Chothia)	HCDR2		DPYSGN
SEQ ID NO: 387 (Chothia)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 388 (Kabat)	LCDR1		TGTSSDVGTYNQVS
SEQ ID NO: 389 (Kabat)	LCDR2		GVSKRPS
SEQ ID NO: 390 (Kabat)	LCDR3		SARDGWSEYV
SEQ ID NO: 391 (Chothia)	LCDR1		TSSDVGTYNQ
SEQ ID NO: 392 (Chothia)	LCDR2		GVS
SEQ ID NO: 393 (Chothia)	LCDR3		RDGWSEY
SEQ ID NO: 394	VH		QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVMTTRDTSISITAYMELSRLRSEDVAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 395	VL		DIALTPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSARDGWSEYVFGGGTKLTVL
SEQ ID NO: 396	DNA VH		CAGGTGCAATTGGTGACAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACTACGCGCAGAAA TTTCAGGCCCCGGGTGACCATGACCCGTGATACCGCATTAGCACCGCGTATATGGAAGTGAAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACTACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTCGGTGACTGTTAGCTCA
SEQ ID NO: 397	DNA VL		GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTGCTCGTGACGGTTGGTCTGAATACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTTA
SEQ ID NO: 398	Heavy Chain		QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNT NYAQKFQGRVMTTRDTSISITAYMELSRLRSEDVAVYYCARGSFYTRDSYFDVWGQGLTVTVSS ASTKGPSVFPFLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKHTCTPPCPAPPELLGGPSVFLFPPKPK KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKS LSLSPGK

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 399	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSG VSNRFGSGKSGNTASLTISGLQAEDEADYYCSARDGWSYVFGGGTKLTVLGQPKAAPSVTLF PPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPSKQSNKNKYAASSYLSLTP EQWKSRSYSQVTHEGSTVEKTVAPTECS
SEQ ID NO: 400	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAACAGACC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGGCACCTGGTGACTGTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGAACCAGGTGACGGTGTCTGGAACTCAGGCGCCCTGACCAGCGG CGTGACACACCTTCCCGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTGTGACAAAACACACATGCCACCCCTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAAGCCGCGGAGG AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCTCACCCTCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCATCCCGGGAGGA GATGACCAGAACCAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCCGACGGCTCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGATGAGGCTCTGCACAACTACTACAGCAGAAGAGCCTC TCCCTGTCTCCGGTAAA
SEQ ID NO: 401	DNA Light Chain	GATATCGCGTGAACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCGAAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTGCTCGTGACGGTTGGTCTGAATACGTGTTTGGCGGCGGCACGA AGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTCTGAG GAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCGGTGA CAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACACACCTCCA AACAAAGCAACAACAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGAAAGT CCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGAGCACCGTGGAGAAGACAGTGGCC CCTACAGAATGTTCA
MOR13658		
SEQ ID NO: 402 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 403 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 404 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 405 (Chothia)	HCDR1	GYFTTSY
SEQ ID NO: 406 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 407 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 408 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 409 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 410 (Kabat)	LCDR3	ASADHSYHTV
SEQ ID NO: 411 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 412 (Chothia)	LCDR2	GVS
SEQ ID NO: 413 (Chothia)	LCDR3	ADHSYHT
SEQ ID NO: 414	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTRDTSISITAYMELSRRLSEDAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 415	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSG KSGNTASLTISGLQAEDEADYYCASADHSYHTVFGGGTKLTVL
SEQ ID NO: 416	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 417	DNA VL	CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAAGTACGCGCAGAAA TTTTCAGGGCCGGGTGACCATGACCCGTGATACCCAGCATTAGCACCAGCTATATGGAAGTACGCGC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 418	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYS GNTNYAKKFQGRVTMTDRDTSISTAYMELSLRSEDVAVYYCARGSFYTRDSYFDVWVGQGLTV TVSSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSG SGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPELGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL TCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDGSFPLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 419	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKR PSGVSNRFSGSKGNTASLTISGLQAEDEADYYCASADHSYHTVFGGGTKLTVLQGPKAAPSV TLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPPSKQSNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 420	DNA Heavy Chain	CAGGTGCAATTGGTGACAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAAGTACGCGCAGAAA TTTTCAGGGCCGGGTGACCATGACCCGTGATACCCAGCATTAGCACCAGCTATATGGAAGTACGCGC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAGAGCACCCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGCGCCCTGACCAGCGG CGTGACACACCTTCCCGGCTGTCTTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCACGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTCACACATGCCACCCTGCCCCA GCACCTGAACTCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGCTACCGGGTGGTACGCGTCTCACCCTCTGACACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGCATCGCC GTGGAGTGGGAGGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCGACGGCTCTTCTTCTCTACAGCAAGCTCACCGTGGAACAAGAGCAGGTGGCAGCAGGG GAACGCTTTCTCATGCTCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 421	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCGCTTCTGCTGACCATTTTACCATACTGTGTTTGGCGGCGGCACGAA GTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTCTGAGG AGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCAACCGGGAGCCGTGAC AGTGGCTTGAAGGCAGATAGCAGCCCCGTCAAGCGGGAGTGGAGACCACACACCCCTCCAA ACAAGACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCAGTGGAGTGC CCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCCC CTACAGAATGTTCA
MOR13659		
SEQ ID NO: 422 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 423 (Kabat)	HCDR2	RIDPYSGNTNYAKKFQ
SEQ ID NO: 424 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 425 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 426 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 427 (Chothia)	HCDR3	GSFYTRDSYFDV

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 428 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 429 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 430 (Kabat)	LCDR3	GSRTSHNVV
SEQ ID NO: 431 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 432 (Chothia)	LCDR2	GVS
SEQ ID NO: 433 (Chothia)	LCDR3	RTSHNV
SEQ ID NO: 434	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPQGLEWMGRIDPYSGNNTNYAQKFQGRVTMTDRDTSISTAYMELSLRLSEDTAVYYCARGSFYTRDSYFDVWVGQGLTVTVSS
SEQ ID NO: 435	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCGSRTSHNVVFGGGTKLTVL
SEQ ID NO: 436	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGCCGTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 437	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCGGTAGCCCGGGCCAGAGCATTACCATTAGCTGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACGTATGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGGCTCAACGCGGAAGAC GAAGCGGATTATTACTGCGGTTCTCGTACTTCTATAACTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 438	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPQGLEWMGRIDPYSGNNTNYAQKFQGRVTMTDRDTSISTAYMELSLRLSEDTAVYYCARGSFYTRDSYFDVWVGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKHTHTCP PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREQYNYSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSQSVMHREALHNYTQKSLSLSPGK
SEQ ID NO: 439	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCGSRTSHNVVFGGGTKLTVLGGQPKAAPS VTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAA SYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 440	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGCCGTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCCCCTGGCACCCTCCTCCCAAGAGCACCTCTGGGGGCACAGCGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGCTGGAACCTCAGGCGCCTGACCAGCGGCGTGACACACCTTCCCCGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACAC CAAGGTGGACAAGAGATTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCCGTGCCA GCACCTGAACCTCTGGGGGACCGTCACTCTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTCAATGCGTGGTGGTGACGTGAGCCACGAAGACCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG AGCAGTACAACAGCAGTACCGGGTGGTACGCTCCTCACCCTCCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTCAAGGTCTCCAACAAGCCCTCCAGCCCTCCAGCAAGACCTGAGGT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGGAGAACAACTACAAGACACCGCTCCCGTGGTGA CTCCGAGGGCTCCTTCTCTCTCTACAGCAAGCTCACCGTGGACAAAGAGCAGGTGGCAGCAGGG GAACGCTTCTCTATGCTCGTGATGCATGAGGCTCTGCACAACCACTACACGCAAGAGCCCT TCCCTGTCTCCGGGTAAA
SEQ ID NO: 441	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCGGTAGCCCGGGCCAGAGCATTACCATTAGCTGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACGTATGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTTCAAGCGGAAGAC GAAGCGGATTATTACTCGGTTCTCGTACTTCTATAACTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTAGGTACGCCAAGGCTGCCCTCTCGGTACTCTGTTCCCGCCCTCTCTGAGGAG

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		CTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAG TGGCCTGGAAGGCAGATAGCAGCCCCGTCAGGCGGGAGTGGAGACCACCACACCTCCAAAC AAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGAAGTCCC ACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCCCCCT ACAGAATGTTCA
MOR13660		
SEQ ID NO: 442 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 443 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 444 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 445 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 446 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 447 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 448 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 449 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 450 (Kabat)	LCDR3	AVRGSQTLV
SEQ ID NO: 451 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 452 (Chothia)	LCDR2	GVS
SEQ ID NO: 453 (Chothia)	LCDR3	RGSQTL
SEQ ID NO: 454	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTDRDTSISTAYMELSRLRSEDVAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 455	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCAVRGSQTLVFGGGTKLTVL
SEQ ID NO: 456	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCCAGGCCCGGGC CAGGGCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAACGTAGACC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCA
SEQ ID NO: 457	DNA VL	GATATCGCGCTGACCCAGCCGCGGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCGGTGTTCTGCGTGTCTCAGACTCTGGTGTTTGGCGGCGGACGCAAGT TAACCGTCCTA
SEQ ID NO: 458	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYS GNTNYAQKFQGRVTMTDRDTSISTAYMELSRLRSEDVAVYYCARGSFYTRDSYFDVWGQ TLTVTVSSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSVHTFP AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKCDKTHTCPPCPAPE LLGGPSVFLFPPPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSR EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFPLYSKLTVDKSR WQQGNVPSFCSVMHEALHNHYTQKLSLSLSPGK
SEQ ID NO: 459	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSG VSNRFGSGKSGNTASLTISGLQAEDEADYYCAVRGSQTLVFGGGTKLTVLQPKAAP VTLPFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPPSKQSNINKYAA SSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 460	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCCAGGCCCGGGC CAGGGCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAACGTAGACC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCAGCCTCCACCAGGGTCCAT CGGTCTTCCCCCTGGCACCTCTCCAAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGAACCAGGTGACGGTGTCTGGAACCTCAGCGCCCTGACCAAGG CGTGACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
			TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTTGTGACAAAACACACATGCCCACCGTGCCCA GCACCTGAATCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGACACCCCTCAT GATCTCCCGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCCTCACCGTCTGCACCAAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCGTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTGGA CTCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGTCTCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGTAAA
SEQ ID NO: 461	DNA Light Chain		GATATCGCGCTGACCCAGCCGGCGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTTCAAGCGGAAGAC GAAGCGGATTATTACTGCGCTGTTCGTGGTCTCAGACTCTGGTGTCTGGCGCGGCGCACGAAGT TAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTCTGAGGAG CTTCAGCCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAG TGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACACCCCTCCAAC AAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGAAGTCCC ACAGAAGCTACAGCTGCCAGGTACGCATGAAGGAGCACCGTGGAGAAGACAGTGGCCCCCT ACAGAATGTTCA
MOR13661			
SEQ ID NO: 462 (Kabat)	HCDR1	SYDIH	
SEQ ID NO: 463 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQ	
SEQ ID NO: 464 (Kabat)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 465 (Chothia)	HCDR1	GYTFTSY	
SEQ ID NO: 466 (Chothia)	HCDR2	DPYSGN	
SEQ ID NO: 467 (Chothia)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 468 (Kabat)	LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 469 (Kabat)	LCDR2	GVSKRPS	
SEQ ID NO: 470 (Kabat)	LCDR3	GSRDSWAHV	
SEQ ID NO: 471 (Chothia)	LCDR1	TSSDVGTYNQ	
SEQ ID NO: 472 (Chothia)	LCDR2	GVS	
SEQ ID NO: 473 (Chothia)	LCDR3	RDSWAH	
SEQ ID NO: 474	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWGQGLTVTVSS	
SEQ ID NO: 475	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCGSRDSWAHVFGGGTKLTVL	
SEQ ID NO: 476	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATAGCACCGCGTATATGGAAGTGGCC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCA	
SEQ ID NO: 477	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTTCAAGCGGAAGAC GAAGCGGATTATTACTGCGGTCTCTGCTGACTCTTGGGCTCATGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA	
SEQ ID NO: 478	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTFTSYDIHWVRQAPGQGLEWMGRIDPYSG NTNYAQKFQGRVTMTRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWGQGL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTPFAV	

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYITLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFPLYSKLTVDKSRWQQ GNVFCSSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 479	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSG VSNRFGSGKSGNTASLTISGLQAEDEADYYCGSRDSWAHVFGGGTKLTVLQPKAAPSVTL FPPSSEELQANKATLVCLISDFYPGAVTVANKADSSPVKAGVETTPPSKQSNKNKYAASSYL LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 480	DNA Heavy Chain	CAGGTGCAATTGGTGACAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTTGGGGCCAGGCACCCTGGTGACTGTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAGAGCACCCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGGAACCTCAGCGGCCCTGACCAGCGG CGTGACACCTTCCCGGCTGTCTTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCACGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTCACACATGCCACCGTGCCCA GCACCTGAACTCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGTACCGGGTGGTCAGCGTCTCACCCTCTGCACACGAGTGGTCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAAGGTGAGCTGACCTGCTGGTCAAAGGCTTCTATCCAGCGCATCGCC GTGGAGTGGGAGGACATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 481	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACACGACGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTTTCTAAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCGGTTCTCGTGACTCTTGGGCTCATGTGTTTGGCGGCGGCACGAAGT TAACCGTCTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGAGGAG CTTCAAGCCAAACAGGCCCACTGGTGTGTCATAAGTGACTTCTACCCGGGAGCCGTGACAG TGGCTTGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACACACCCCTCCAAC AAAGCAACAACAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGAAGTCCC ACAGAAGCTACAGCTGCGAGGTACGCATGAAGGAGCACCCTGGAGAGACAGTGGCCCT ACAGAATGTTC
MOR13662		
SEQ ID NO: 482 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 483 (Kabat)	HCDR2	RIDPYSGNTNYAQKFG
SEQ ID NO: 484 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 485 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 486 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 487 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 488 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 489 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 490 (Kabat)	LCDR3	YSRAKTHWTDV
SEQ ID NO: 491 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 492 (Chothia)	LCDR2	GVS
SEQ ID NO: 493 (Chothia)	LCDR3	RAKTHWTD
SEQ ID NO: 494	VH	QVQLVQSGAEVKKPGASVKVSKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTDRDTSISTAYMELSRLESDTAVYYCARGSFYTRDSYFDVWQGLTVTVSS

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 495	VL	DIALTPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCYSRAKTHWTDVFGGGTKLTVL
SEQ ID NO: 496	DNA VH	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCCGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 497	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCAGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAGCGCAACACCGCGAGCGTACCATAGCGGCGCTGCAAGCGCGGAAGTGN GAAGCGGATTATTACTGCTACTCTCGTGCTAAACTCATTGGACTGACGTGTTTGGCGCGGCA CGAAGTTAACCGTCTCA
SEQ ID NO: 498	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYS GNTNYAQKQGRVMTDRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWVGQT LVTVSSASTKGPVFPPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSLSLTQTYICNVNHPKSNKVDKRVPEPKSCDKTHTCPPCPAPPELLG GPSVFLFPPPKPDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN TYRVVSVLTIVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSRREEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSLKTVDKSRWQQGNVF SCSVMHEALHNYHQSLSLSPGK
SEQ ID NO: 499	Light Chain	DIALTPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCYSRAKTHWTDVFGGGTKLTVLQPKAAPSVLTLPSPSEELQANK ATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPSKQSNKYYAASSYLSLTPEQWKSHRYSYSCQVT HEGSTVEKTVAPTECS
SEQ ID NO: 500	DNA Heavy Chain	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCCGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCTCTCCTCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCGT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGCTGTGGAACCTCAGCGCCCTGACAGCGG CGTGACACCTTCCCCGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTTGTGACAAAACCTCACACATGCCACCCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCACTCTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGTACCGGTGGTCAGCGTCTCACCCTCCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGGAGAACATAAGACACACCCCTCCCGTGTGGG CTCCGACGGCTCCTTCTCTCTACAGCAAGCTCACCGTGACAAAGAGCAGGTGGCAGCAGGG GAACGCTCTCTCATGCTCCGTGATGATGAGGCTCTGCACAAACCTACACGCAAGAGCCTC TCCCTGTCTCCGGTAAA
SEQ ID NO: 501	DNA Light Chain	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCAGAGCGCGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTACTCTCGTGCTAAACTCATTGGACTGAGCTGTTTGGCGCGGCA CGAAGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCTCCTGGTCACTCTGTTCCTGCGCTCTCT GAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTATAAGTACTTCTACCCGGGAGCC GTGACAGTGGCTGGAAAGGAGATAGCAGCCCGTCAAGGCGGGAGTGGAGACCAACACAC CTCCAACAAGCAACAAAGTACGCGGCCAGCAGTATCTGAGCTTGACGCTTGAGCAGTG GAAGTCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAG TGCCCCCTACAGAATGTTCA
MOR13663		
SEQ ID NO: 502 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 503 (Kabat)	HCDR2	RIDPYSGNTNYAQKFGQ
SEQ ID NO: 504 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 505 (Chothia)	HCDR1	GYFTSY

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 506 (Chothia) HCDR2	DPYSGN	
SEQ ID NO: 507 (Chothia) HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 508 (Kabat) LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 509 (Kabat) LCDR2	GVSKRPS	
SEQ ID NO: 510 (Kabat) LCDR3	SVWTSIKVVF	
SEQ ID NO: 511 (Chothia) LCDR1	TSSDVGTYNQ	
SEQ ID NO: 512 (Chothia) LCDR2	GVS	
SEQ ID NO: 513 (Chothia) LCDR3	WTSIKVF	
SEQ ID NO: 514	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTDRDTSISTAYMELSRLRSEDVAVYCARGSFYTRDSYFDVWQGGLTVTVSS
SEQ ID NO: 515	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGSKSGNTASLTISGLQAEDEADYYCSVWTSIKVVFVGGGKLTVL
SEQ ID NO: 516	DNA VH	CAGGTGCAATTGGTGCGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGGCAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA
		TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGAGCGTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 517	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGCTGCACCGGCACCCAGCAGCATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCGGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAAGCGGCAACCCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGACGAAGCGGATTATTACTGCTCTGTTTGGACTTCTATCAAAGTTTTCGTGTTTGGCGGCGGCACGAA
		GTTAACCGTCCTA
SEQ ID NO: 518	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTDRDTSISTAYMELSRLRSEDVAVYCARGSFYTRDSYFDVWQGGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSYRVSFVLTVLHQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 519	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGSKSGNTASLTISGLQAEDEADYYCSVWTSIKVVFVGGGKLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPPSKQSNKYYAASSYLSLTPEQWKSHRYSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 520	DNA Heavy Chain	CAGGTGCAATTGGTGCGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGGCAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA
		TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGTAGAGCGTCTGCGTAGCGAAGATACGGCCGTGATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCGCAACCGGTGACGGTGTCTGGAACCTCAGCGCCCTGACCAGCGGCGTGACACACCTTCCCCGTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCAAGACCCAGCAACAC
		CAAGGTGGACAAGAGAGTTGAGCCAAATCTGTGACAAAACCTACACATGCCCCACCGTGCCCA
		GCACCTGAATCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGTGGTACGCTCCTCACCGTCTGCACCAGGACTGGCTGA
		ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCATCTCCAAGGCCAAAGGGCAGGCCCGGAGAACCAAGGTGTACACCTTGCCCCATCCCGGGAGGATGACCAAGAACCAGGTGACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACACTACAAGACCACGCCTCCCGTGTGGA
		CTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGCTTTCTCATGCTGATGATGAGGCTCTGCACAACCACTACACGAGAAGAGCCCTC
		TCCCTGTCTCCGGGTAAA

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
SEQ ID NO: 521	DNA Light Chain	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCGCAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTGTTTGGACTTCTATCAAAGTTTTCGTGTTTGGCGGCGGCACGAA GTTAACCGTCTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGAGG AGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGAC AGTGGCTTGAAGGCAGATAGCAGCCCCGTCAAGCGGGAGTGGAGACCACACACCCCTCCAA ACAAAGCAACAACAAGTACGCGGCGCAGCAGTATCTGAGCCTGACGCTGAGCAGTGAAGTC CCACAGAAGCTACAGCTGCCAGGTCACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCCC CTACAGAATGTTC	
MOR13664			
SEQ ID NO: 522 (Kabat)	HCDR1	SYDIH	
SEQ ID NO: 523 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG	
SEQ ID NO: 524 (Kabat)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 525 (Chothia)	HCDR1	GYTFTSY	
SEQ ID NO: 526 (Chothia)	HCDR2	DPYSGN	
SEQ ID NO: 527 (Chothia)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 528 (Kabat)	LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 529 (Kabat)	LCDR2	GVSKRPS	
SEQ ID NO: 530 (Kabat)	LCDR3	SAYDASTQVV	
SEQ ID NO: 531 (Chothia)	LCDR1	TSSDVGTYNQ	
SEQ ID NO: 532 (Chothia)	LCDR2	GVS	
SEQ ID NO: 533 (Chothia)	LCDR3	YDASTQV	
SEQ ID NO: 534	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWGQGLTVTVSS	
SEQ ID NO: 535	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRPSGS KSGNTASLTISGLQAEDEADYYCSAYDASTQVVFGGGKLTVL	
SEQ ID NO: 536	DNA VH	CAGGTGCAATTTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGTGCCAGCGTGAAAGTTAG CTGCAAGCGCTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAATACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGGTATATGGAAGTGAAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCCCTGGTGACTGTTAGCTCA	
SEQ ID NO: 537	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCGCAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTGCTTACGACGCTTCTACTCAGGTTGTGTTTGGCGGCGGCACGA AGTTAACCGTCTCA	
SEQ ID NO: 538	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGN TNYAQKFQGRVTMTRDTSISTAYMELSLRSEDYAVYYCARGSFYTRDSYFDVWGQGLTV TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVTSWNSGALTSGVHTFPAVL QSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSR WQQGNVPSFCSVMHEALHNHYTQKSLSLSPGK	
SEQ ID NO: 539	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGV SNRPSGSKSGNTASLTISGLQAEDEADYYCSAYDASTQVVFGGGKLTVLGQPKAAPS VTLFPPSSEELQANKATLVCLISDFYPGAVTVANKADSSPVKAGVETTPSKQSNKNYA ASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS	
SEQ ID NO: 540	DNA Heavy Chain	CAGGTGCAATTTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC	

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 541	DNA Light Chain	CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACCTACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCGCATTAGCACCGCGTATATGGAACCTGAGCC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCCAAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGTGACGGTGCTGTGGAACCTCAGCGCCCTGACAGCGG CGTGACACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTACACATGCCCCCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCCTCACCCTCCTGACCAGGACTGGTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGGGAGAACAACTACAAGACCACGCCCTCCGCTGCTGGA CTCCGACGGCTCCTTCTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGCTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
MOR13665		
SEQ ID NO: 542 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 543 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQ
SEQ ID NO: 544 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 545 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 546 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 547 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 548 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 549 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 550 (Kabat)	LCDR3	QSAAIATSV
SEQ ID NO: 551 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 552 (Chothia)	LCDR2	GVS
SEQ ID NO: 553 (Chothia)	LCDR3	AAIATS
SEQ ID NO: 554	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTDRDTSISITAYMELSRLESEDVAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 555	VL	DIALTQPASVSGSPGQSITISCTGSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCQSAAIATSVFPGGKLTVL
SEQ ID NO: 556	DNA VH	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACCTACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCGCATTAGCACCGCGTATATGGAACCTGAGCC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTCGTGACTGTTAGCTCA
SEQ ID NO: 557	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCAACCGGCACCGACGCGATGTGGGCACTTACAACCAAGGTGCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAACCTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGTGAGCAACCGT

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGTCTGCTGCTATCGTACTTCTGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 558	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSG NTNYAQKFQGRVTMTRDTSISTAYMELSRLEDVAVYVCARGSFYTRDSYFDVWGQGLT VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 559	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSG VSNRFGSGKSGNTASLTISGLQAEDEADYVCSAAIATSVFGGGTKLTVLQPKAAPSVTL FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKNKYAASSYL SLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 560	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATAGCACCGCGTATATGGAACAGAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGGCACCTCGTGACTGTAGCTCAGCCTCCACCAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACACAGGCGCCTGACCAGCGG CGTGACACACCTTCCCGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACC TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACACACATGCCACCCGTCGCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCCTCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG AGCAGTACAACAGCACGTACCGGTGGTCAGCGTCTCACCCTCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCGAGCGGAGAACAACTACAAGACCACGCCTCCCGTGTCTGA CTCCGACGGCTCTTCTTCTCTACAGCAAGCTCACCCTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 561	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGTCTGCTGCTATCGCTACTTCTGTGTTTGGCGGCGGCACGAAGT TAACCGTCTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTCTGAGGAG CTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAG TGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGAGTGGAGACCACACCCCTCCAAC AAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGAAAGTCCC ACAGAAGCTACAGCTGCCAGGTACGCATGAAGGAGCACCGTGGAGAAGACAGTGGCCCCCT ACAGAATGTTCA
MOR13666		
SEQ ID NO: 562 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 563 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 564 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 565 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 566 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 567 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 568 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 569 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 570 (Kabat)	LCDR3	STTYSFHMV
SEQ ID NO: 571 (Chothia)	LCDR1	TSSDVGTYNQ

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 572 (Chothia) LCDR2	GVS	
SEQ ID NO: 573 (Chothia) LCDR3	TTYSFHM	
SEQ ID NO: 574	VH	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTTRDTSISTAYMELSLRSEDVAVYVCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 575	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSKSGNTASLTISGLQAEDEADYYCSTTTYSFHMFVGGGKLTVL
SEQ ID NO: 576	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAAAGCGTCCGGATATACCTTCACCTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA
SEQ ID NO: 577	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGCTGACCCGGCACCAGCAGCGATGTGGGCACCTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAAGCGGCAACCCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGACGAAGCGGATTATTACTGCTCTACTACTACTACTCTTCCATATGGTGTGTTGGCGGCGGCACGAA
SEQ ID NO: 578	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTTRDTSISTAYMELSLRSEDVAVYVCARGSFYTRDSYFDVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVKDKRVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 579	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSKSGNTASLTISGLQAEDEADYYCSTTTYSFHMFVGGGKLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKNKYAASSYL
SEQ ID NO: 580	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAAAGCGTCCGGATATACCTTCACCTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA
SEQ ID NO: 581	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGCTGACCCGGCACCAGCAGCGATGTGGGCACCTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAAGCGGCAACCCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGACGAAGCGGATTATTACTGCTCTACTACTACTACTCTTCCATATGGTGTGTTGGCGGCGGCACGAA

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
MOR13667			
SEQ ID NO: 582 (Kabat)	HCDR1	SYDIH	
SEQ ID NO: 583 (Kabat)	HCDR2	RIDPYSGNTNYAQKFG	
SEQ ID NO: 584 (Kabat)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 585 (Chothia)	HCDR1	GYTFTSY	
SEQ ID NO: 586 (Chothia)	HCDR2	DPYSGN	
SEQ ID NO: 587 (Chothia)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 588 (Kabat)	LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 589 (Kabat)	LCDR2	GVSKRPS	
SEQ ID NO: 590 (Kabat)	LCDR3	QAWDYRQTIV	
SEQ ID NO: 591 (Chothia)	LCDR1	TSSDVGTYNQ	
SEQ ID NO: 592 (Chothia)	LCDR2	GVS	
SEQ ID NO: 593 (Chothia)	LCDR3	WDYRQTI	
SEQ ID NO: 594	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFG QGRVTMTTRDTSISTAYMELSLRSEDYAVYVCARGSFYTRDSYFDVWGQGLVTVSS	
SEQ ID NO: 595	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCQAWDYRQTIVFGGGTKLTVL	
SEQ ID NO: 596	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCA	
SEQ ID NO: 597	DNA VL	GATATCGCGTGACCCAGCCGGCGAGCGGTAGCCCGGGCCAGAGCATTACCATAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACGTATGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCCGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGGCTTGGGACTACCGTCAGACTATCGTGTTTGGCGCGCGCAGC AAGTTAACCGTCCTA	
SEQ ID NO: 598	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSG NTNYAQKFGQGRVTMTTRDTSISTAYMELSLRSEDYAVYVCARGSFYTRDSYFDVWGQ TLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVHLQDQLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFPLYSKLTV DKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK	
SEQ ID NO: 599	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCQAWDYRQTIVFGGGTKLTVLGQPKAAPSVTLFPPSSSEELQANKA TLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQWKSRSYSQCQVTH EGSTVEKTVAPTECS	
SEQ ID NO: 600	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAACGAGCC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACCTCAGCGGCCCTGACCAGCGG CGTGACACCTTCCCCGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTCACACATGCCACCCGTGCCA GCACCTGAACCTCTGGGGGACCGTCACTCTCTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGTTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG	

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
			AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAGGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGACGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCCTCCCGTGTGGG CTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGACAAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 601	DNA Light Chain		GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGGCTTGGGACTACCGTCAGACTATCGTGTTTGGCGGCGGCACG AAGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGA GGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTG ACAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCAACCCCTCC AAACAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGGAG TCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGAGCACCGTGGAGAAGACAGTGGCC CCTACAGAATGTTCA
MOR13668			
SEQ ID NO: 602 (Kabat)	HCDR1		SYDIH
SEQ ID NO: 603 (Kabat)	HCDR2		RIDPYSGNTNYAQKFQG
SEQ ID NO: 604 (Kabat)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 605 (Chothia)	HCDR1		GYTFTSY
SEQ ID NO: 606 (Chothia)	HCDR2		DPYSGN
SEQ ID NO: 607 (Chothia)	HCDR3		GSFYTRDSYFDV
SEQ ID NO: 608 (Kabat)	LCDR1		TGTSSDVGTYNQVS
SEQ ID NO: 609 (Kabat)	LCDR2		GVSKRPS
SEQ ID NO: 610 (Kabat)	LCDR3		QVWDSQAMV
SEQ ID NO: 611 (Chothia)	LCDR1		TSSDVGTYNQ
SEQ ID NO: 612 (Chothia)	LCDR2		GVS
SEQ ID NO: 613 (Chothia)	LCDR3		WDSQAM
SEQ ID NO: 614	VH		QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMRDTSISTAYMELSLRSEDVAVYYCARGSFYTRDSYFDVWQGGLTVTVSS
SEQ ID NO: 615	VL		DIALTPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFGSGS KSGNTASLTISGLQAEDEADYYCQVWDSQAMVFGGGTKLTVL
SEQ ID NO: 616	DNA VH		CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACTACGCGCAGAAA TTTCAGGCGCGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAAGTGAAGC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACTCTGTGACTCT TACTTCGATGTTTGGGCCAAGGCACCTGGTGACTGTTAGCTCA
SEQ ID NO: 617	DNA VL		GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCCAGCAGCATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTAACGTCCGAGCGGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGGTTTGGGACTCTGACCAGGCTATGGTGTTTGGCGGCGGCACG AAGTTAACCGTCCTA
SEQ ID NO: 618	Heavy Chain		QVQLVQSGAEVKKPGASVKVSKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSG NTNYAQKFQGRVTMRDTSISTAYMELSLRSEDVAVYYCARGSFYTRDSYFDVWQGGLTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVTVPSLSLTQTYICNVNHKPSNTKVDKRVPEKSCDKHTCPCPPAPELLGGPSVF LFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL LVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSSFLLYSKLTVDKSRWQQGNVFPSCSVM HEALHNHYTQKSLSLSPGK

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
SEQ ID NO: 619	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTIISGLQAEDEADYYCQVWSDQAMVFGGGTKLTVLGQPKAAPSVTLFPPSSEELQANK ATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYYAASSYLSLTPEQWKSRSYSYSCQVT HEGSTVEKTVAPTECS	
SEQ ID NO: 620	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACATACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACCAGCATTAGCACCGCGTATATGGAACGTAGACC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTCTTCTTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGGCACCTGGTGACTGTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGGCGCCCTGACCAGCGG CGTGCAACACTTCCCGGTGTCTTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTTGTGACAAAACCTACACATGCCACCCAGCTGCCCA GCACCTGAACCTCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCTCACCCTCTGCACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTTGCCCCATCCCGGGAGGA GATGACCAGAACCAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCCGACGGCTCTTCTTCTCTACAGCAAGCTCACCGTGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGTCATGAGGCTCTGCACAACTACTACACGAGAAGAGCCTC TCCCTGTCTCCGGTAAA	
SEQ ID NO: 621	DNA Light Chain	GATATCGCGCTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCCAGGTTTGGGACTCTGACCAGGCTATGGTGTGGCGGCGGCACG AAGTTAACCGTCTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGA GGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTG ACAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACACACCTCC AAACAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGGAAG TCCACAGAAGCTACAGTGGCAGGTACGCATGAAGGAGCACCGTGGAGAAGCAGTGGCC CCTACAGAATGTTCA	
MOR13669			
SEQ ID NO: 622 (Kabat)	HCDR1	SYDIH	
SEQ ID NO: 623 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG	
SEQ ID NO: 624 (Kabat)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 625 (Chothia)	HCDR1	GYTFTSY	
SEQ ID NO: 626 (Chothia)	HCDR2	DPYSGN	
SEQ ID NO: 627 (Chothia)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 628 (Kabat)	LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 629 (Kabat)	LCDR2	GVSKRPS	
SEQ ID NO: 630 (Kabat)	LCDR3	STATAMTVSLV	
SEQ ID NO: 631 (Chothia)	LCDR1	TSSDVGTYNQ	
SEQ ID NO: 632 (Chothia)	LCDR2	GVS	
SEQ ID NO: 633 (Chothia)	LCDR3	ATAMTVSL	
SEQ ID NO: 634	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTTRDTSISITAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSS	
SEQ ID NO: 635	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGS KSGNTASLTIISGLQAEDEADYYCSTATAMTVSLVFGGGTKLTVL	
SEQ ID NO: 636	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGC	

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 637	DNA VL	CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAAGTACGCGCAGAAA TTTCAAGGCGCGGTGACCATGACCCGTGATACCGCATTAGCACCGCGTATATGGAAGTACGCGC GTCTGCGTAGCGAAGATACGCGCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 638	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYS GNTNYAQKFQGRVTMTDRDTSISTAYMELSLRSEDVAVYYCARGSFYTRDSYFDVWVGQ TLVTVSSASTKGPSVFPLAPSSKSTSGGTALGLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPA PELLGGPSVFLPFPKPKDTLMISRTPEVTVVVDVSHEDPEVKFNWYVDGEVHNAAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY LPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFPLYSK LTVDKSRWQGNVPSVMSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 639	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQHPGKAPKLMYGVSKRPSG VSNRFSGSKSGNTASLTISGLQAEDEADYYCSTATAMTVSLVFGGGTKLTVLGQPKAAPSVTL FPPSSEELQANKATLVCLISDFYPGAVTVANKADSSPVKAGVETTPPSKQSNNKYAASSYLSL TPEQWKSHRYSYCSQVTHEGSTVEKTVAPTECS
SEQ ID NO: 640	DNA Heavy Chain	CAGGTGCAATTGGTGACAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCCGGGC CAGGGCTTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAAGTACGCGCAGAAA TTTCAAGGCGCGGTGACCATGACCCGTGATACCGCATTAGCACCGCGTATATGGAAGTACGCGC GTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTAGCTCAGCCTCCACCAAGGGTCCAT CGGTCTTCCCCCTGGCACCCCTCCTCCAAAGAGCACTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGCGCCCTGACCAGCGG CGTGACACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAGCCACGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAAATCTGTGACAAAACCTCACACATGCCACCCTGCCCCA GCACCTGAACTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAGACCCCTGAGGT CAAGTTCACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGCTACCGGTGGTCAGCGTCTCACCCTCTGACACAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGCATCGCC GTGGAGTGGGAGAGCAATGGGCAGCGGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCGACGGCTCTCTTCTCTACAGCAAGCTCACCCTGGACAAGAGCAGGTGGCAGCAGGG GAACGCTTTCTCATGCTCGTGATGACGTGAGGCTCTGCACAACCACTACACGAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 641	DNA Light Chain	GATATCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGTGAGCAACCGT TTTAGCGGATCCAAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTACTGCTACTGCTATGACTGTTTCTCTGGTGTGGCGCGCGGCAC GAAGTTAACCGTCTAGGTGAGCCAAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTCTG AGGAGCTTCAAGCCAAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCGCT GACAGTGGCCTGGAAGGACAGATAGCAGCCCGTCAAGGCGGGAGTGGAGACCACCAACCCCT CCAACAAAGCAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCAGTGGGA AGTCCCAAGAAAGTACAGTGCAGGTGACGATGAAGGAGCACCGTGGAGAGACAGT GCGCCCTACAGAATGTTCA
MOR13670		
SEQ ID NO: 642 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 643 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 644 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 645 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 646 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 647 (Chothia)	HCDR3	GSFYTRDSYFDV

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
SEQ ID NO: 648 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 649 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 650 (Kabat)	LCDR3	QVADQGWQHV
SEQ ID NO: 651 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 652 (Chothia)	LCDR2	GVS
SEQ ID NO: 653 (Chothia)	LCDR3	ADQGWQHV
SEQ ID NO: 654	VH	QVQLVQSGAEVKKPGASVKVSKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTDRDTSISTAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 655	VL	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCQVADQGWQHVFGGGLTKLTVL
SEQ ID NO: 656	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAAATTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGCCGTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCA
SEQ ID NO: 657	DNA VL	GATATCGCGCTGACCCAGCCGGCGAGCGGTAGCGGTAGCCCGGGCCAGAGCATTACCATAGCTGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGGCGCCGAAACGTATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGGCTCAGCAAGCGAAGCGGATTATTACTGCCAGGTGCTGACCAAGGTTGGCATCAGGTGTTTGGCGCGCGCACGAAGTTAACCGTCCTA
SEQ ID NO: 658	Heavy Chain	QVQLVQSGAEVKKPGASVKVSKASGYTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKFQGRVTMTDRDTSISTAYMELSRRLSEDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVQLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTVCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDLNGLKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFPLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 659	Light Chain	DIALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCQVADQGWQHVFGGGLTKLTVLQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKSHRYSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 660	DNA Heavy Chain	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACCAACCGGGTGCCAGCGTGAAAGTTAGCTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAAATTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGCCGTCTGCGTAGCGAAGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCTTACTTCGATGTTTGGGGCCAGGCACCCCTGGTGACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGTCTTCCCCCTGGCACCCCTCCTCCCAAGAGCACCTCTGGGGGCACAGCGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACCGGTGCTGGAACCTCAGGCGCCTGACCAGCGGCGTGACACACCTTCCCCGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAATCTTGTGACAAAACCTCACACATGCCACCGGTGCCCAACACCTGAACCTCTGGGGGACCGTCACTCTCTCTCTTCCCCCAAAACCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTCAATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGTGGTCAAGCTCCTCACCCTCTGCAACAGGACTGGGTGATGGCAAGGAGTACAAGTCAAGTCTCCAACAAGCCCTCCAGCCCTCCAGAGAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTTGCCCATCCCGGGAGGAGATGACCAAGAACCAGGTACGCTGACCTGCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAAGCCGAGAGAACAACTACAAGACACCCCTCCCGTGGTGGACTCCGAGCGGCTCTCTCTCTCTCTACAGCAAGCTCACCGTGGACAAAGAGCAGGTGGCAGCAGGGGAACGCTCTCTCATGCTCCGTGATGTCATGAGGCTCTGCACAACCACTACACGCAAGAGCCTCTCCTGTCTCCGGTAAA
SEQ ID NO: 661	DNA Light Chain	GATATCGCGCTGACCCAGCCGGCGAGCGGTAGCGGTAGCCCGGGCCAGAGCATTACCATAGCTGACCCGGCACCAGCAGCGATGTGGGCACTTACAACAGGTGTCTTGGTACCAGCAGCATCCGGCAAGGCGCCGAAACGTATGATCTACGGTGTCTTAAACGTCCGAGCGCGGTGAGCAACCGTTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGACGAAGCGGATTATTACTGCCAGGTGCTGACCAAGGTTGGCATCAGGTGTTTGGCGCGCGCACGAAGTTAACCGTCTAGGTGAGCCCAAGGCTGCCCCCTGGTGACTCTGTTCCCGCCCTCTCTGA

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		GGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTG ACAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCACACCTTCC AAACAAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCAGTGGAG TCCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCC CCTACAGAATGTTCA
MOR14537		
SEQ ID NO: 662 (Kabat)	HCDR1	SYDIH
SEQ ID NO: 663 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQG
SEQ ID NO: 664 (Kabat)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 665 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 666 (Chothia)	HCDR2	DPYSGN
SEQ ID NO: 667 (Chothia)	HCDR3	GSFYTRDSYFDV
SEQ ID NO: 668 (Kabat)	LCDR1	TGTSSDVGTYNQVS
SEQ ID NO: 669 (Kabat)	LCDR2	GVSKRPS
SEQ ID NO: 670 (Kabat)	LCDR3	SSATQKPDVTV
SEQ ID NO: 671 (Chothia)	LCDR1	TSSDVGTYNQ
SEQ ID NO: 672 (Chothia)	LCDR2	GVS
SEQ ID NO: 673 (Chothia)	LCDR3	ATQKPDVT
SEQ ID NO: 674	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTSDTSISTAYMELSLRLSDDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSS
SEQ ID NO: 675	VL	QSALTQPASVSGSPGQSITISCTGSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSG SKSGNTASLTISGLQAEDEADYYCSSATQKPDVTVFGGGTKLTVL
SEQ ID NO: 676	DNA VH	CAGGTGCAATTGGTGCGAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCCAGGCCCGGGC CAGGGCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGACC GTCTGCGTAGCGACGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCA
SEQ ID NO: 677	DNA VL	CAGAGCGCGCTGACCCAGCCGGCGAGCGGTAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCAACGGCACCGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAACTGATGATCTACGGTGTCTTAACAGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAAGCGCAACACCGCGAGCCTGACCATTAGCGGCTGCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTGCTACTCAGAAACCGGACGTTACTGTGTTTGGCGCGCGCA CGAAGTTAACCGTCTCA
SEQ ID NO: 678	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTSYDIHWVRQAPGQGLEWMGRID PYSGNTNYAQKFQGRVTMTSDTSISTAYMELSLRLSDDTAVYYCARGSFYTRDSYFDV WGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVKRVEPKSCDKTH TCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSVCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 679	Light Chain	QSALTQPASVSGSPGQSITISCTGSSDVGTYNQVSWYQQHPGKAPKLMYGVSK RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSATQKPDVTVFGGGTKLTVLGPQK AAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPSKQSNK YAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 680	DNA Heavy Chain	CAGGTGCAATTGGTGCGAGCGGTGCGGAAGTGAAAAACCGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCCAGGCCCGGGC CAGGGCTCGAGTGGATGGGCCGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCGCGTATATGGAACGTAGACC GTCTGCGTAGCGACGATACGGCCGTGTATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAGGCACCTGGTGACTGTTAGCTCAGCCTCCACCAGGGTCCAT CGGTCTTCCCCCTGGCACCTCTCCAAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGAACCAGGTGACGGTGTCTGGAACCTCAGCGCCCTGCACAGCGG CGTGACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.			
			TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTTGAGCCCAATCTTGTGACAAAACACACATGCCCACCGTGCCCA GCACCTGAATCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGACACCCCTCAT GATCTCCCGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGT CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGG AGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCCTCACCGTCTGCACCAAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACCAT CTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCGTGCCCCATCCCGGGAGGA GATGACCAAGAACCAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGCTGGA CTCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 681	DNA Light Chain		CAGAGCGCGTGAACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTTCAAGCGGAAGAC GAAGCGGATTATTACTGCTCTTCTGCTACTCAGAAACCGGACGTTACTGTGTTTGGCGGGCGCA CGAAGTTAACCGTCTTAGGTGAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCTCTCT GAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTATAAGTGACTTCTACCCGGGAGCC GTGACAGTGGCTTGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGACCACCAACC CTCCAAACAAGCAACAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCAGTG GAAGTCCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAG TGCCCTTACAGAATGTTCA
MOR14538			
SEQ ID NO: 682 (Kabat)	HCDR1	SYDIH	
SEQ ID NO: 683 (Kabat)	HCDR2	RIDPYSGNTNYAQKFQ	
SEQ ID NO: 684 (Kabat)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 685 (Chothia)	HCDR1	GYTFTSY	
SEQ ID NO: 686 (Chothia)	HCDR2	DPYSGN	
SEQ ID NO: 687 (Chothia)	HCDR3	GSFYTRDSYFDV	
SEQ ID NO: 688 (Kabat)	LCDR1	TGTSSDVGTYNQVS	
SEQ ID NO: 689 (Kabat)	LCDR2	GVSKRPS	
SEQ ID NO: 690 (Kabat)	LCDR3	ASADHSYHTV	
SEQ ID NO: 691 (Chothia)	LCDR1	TSSDVGTYNQ	
SEQ ID NO: 692 (Chothia)	LCDR2	GVS	
SEQ ID NO: 693 (Chothia)	LCDR3	ADHSYHT	
SEQ ID NO: 694	VH	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTSYDIHWVRQAPGQGLEWMGRIDPYSGNTNYAQKF QGRVTMTRDTSISTAYMELSLRLSDDTAVYYCARGSFYTRDSYFDVWGQGLTVTVSS	
SEQ ID NO: 695	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMYGVSKRPSGVSNRFSG SKSGNTASLTISGLQAEDADYICASADHSYHTVFGGGTKLTVL	
SEQ ID NO: 696	DNA VH	CAGGTGCAATTGGTGCAGAGCGGTGCGGAAGTGAACAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCCGGGC CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAACACGCGCAGAAA TTTCAAGGCGGGTGACCATGACCCGTGATACCGCATAGCACCGCGTATATGGAAGTGGAGCC GTCTGCGTAGCGACGATACGCGCGTGTATTATTGCGCGCGTGGTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCAAAGCACCCCTGGTGACTGTTAGCTCA	
SEQ ID NO: 697	DNA VL	CAGAGCGCGTGAACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGCACCGGCACCAGCAGCGATGTGGGCACTTACAACCAGGTGTCTTGGTACCAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTCTAAACGTCCGAGCGCGGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATTAGCGGCTTCAAGCGGAAGAC GAAGCGGATTATTACTGCGCTTCTGCTGACCATTTCTACCATACTGTGTTTGGCGGGCGGCACGAA GTTAACCGTCTTA	
SEQ ID NO: 698	Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYFTFTSYDIHWVRQAPGQGLEWMGRIDPYSG NTNYAQKFQGRVTMTRDTSISTAYMELSLRLSDDTAVYYCARGSFYTRDSYFDVWGQ TLTVSSASTKGPSVFLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTF	

TABLE 2-continued

Examples of HER3 antibodies that bind to amino acids within domains 3-4 of HER3.		
		PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHTCPPCPA PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFPLYSKL TVDKSRWQQGNVFCSCVMHEALHNNHYTQKLSLSLSPGK
SEQ ID NO: 699	Light Chain	QSALTQPASVSGSPGQSITISCTGTSSDVGTYNQVSWYQQHPGKAPKLMIIYGVSKRPS GVSNRFGSGKSGNTASLTISGLQAEDEADYICASADHSYHTVFGGGTKLTVLGQPKAAPSVTLFPP SSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPPSKQNNKYAASSYLSLTPEQW KSHRSYSQCVTHEGSTVEKTVAPTECS
SEQ ID NO: 700	DNA Heavy Chain	CAGGTGCAATTGGTGACAGAGCGGTGCGGAAGTGAAAAACCGGGTGCCAGCGTGAAAGTTAG CTGCAAAAGCGTCCGGATATACCTTCACTTCTTACGACATCCATTGGGTGCGCCAGGCCCGGGG CAGGGCCTCGAGTGGATGGGCGGTATCGACCCGTACTCTGGCAACACGAATACGCGCAGAAA TTTCAGGGCCGGGTGACCATGACCCGTGATACAGCATTAGCACCAGCGTATATGGAATGAGCC GTCTGCGTAGCGACGATACGGCCGTGATTATTGCGCGCGTGGTTCTTTCTACACTCGTGACTCT TACTTCGATGTTTGGGGCCCAAGGCACCCTGGTGACTGTAGCTCAGCCTCCACCAAGGTCAT CGGTCTTCCCTTGGCACCCTCCTCCAGAGCACCCTGCGGGGCACAGCGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCGAACCGGTGACGGTGTCGTGGAACCTCAGCGCCCTGACCAGCGG CGTGACACCTTCCCGGTGTCTTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG TGCCCTCCAGCAGCTTGGGCACCAGACCTACATCTGCAACGTGAATCACAGCCACGCAACAC CAAGGTGGACAAGAGAGTTGAGCCAAATCTGTGACAAAACCTCACACATGCCACCGTGCCCA GCACCTGAACCTCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAAACCAAGGACACCCCTCAT GATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACGTGAGCCACGAAGCCCTGAGGT CAAGTTCACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGG AGCAGTACAACAGCAGCTACCGGTGGTCAGCGTCTCACCCTCTGCACCAAGGACTGGCTGA ATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCAGCCTCCATCGAGAAAACCAT CTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCCGGGAGGA GATGACCAAGAACAGGTACGCCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCC GTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTCTGGA CTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTC TCCCTGTCTCCGGGTAAA
SEQ ID NO: 701	DNA Light Chain	CAGAGCGCGTGACCCAGCCGGCGAGCGTGAGCGGTAGCCCGGGCCAGAGCATTACCATTAGC TGACCCGGCACCAGCAGCATGTGGGCACTTACAACAGGTGTCTTGTACAGCAGCATCCG GGCAAGGCGCCGAAACTGATGATCTACGGTGTCTTAAACGTCCGAGCGCGTGAGCAACCGT TTTAGCGGATCCAAAGCGGCAACACCGCGAGCCTGACCATAGCGGCTCGCAAGCGGAAGAC GAAGCGGATTATTACTGCGCTTCTGTGACCATTTCTACCATCTGTGTTTGGCGGGCGCACGAA GTTAACCGTCTTAGTTCAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCGCCCTCTCTGAGG AGCTTCAAGCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGAC AGTGGCTTGAAGGCAGATAGCAGCCCGTCAAGGCGGAGTGGAGACCACACACCTCCAA ACAAAGCAACAAGTACGCGGCCAGCAGCTATCTGAGCTGACGCCTGAGCAGTGAAGTCTC CCACAGAAGCTACAGCTGCCAGGTACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCCC CTACAGAATGTTCA

[0148] In one aspect, the present invention provides antibodies that specifically bind to domain 3 of HER3 protein (e.g., human and/or cynomologus HER3), the antibodies comprising a VH domain having an amino acid sequence of SEQ ID NO: 14, 34, 54, 74, 94, 114, 134, 154, and 174. In another, the present invention provides antibodies that specifically bind specifically bind to domain 3 of HER3 protein (e.g., human and/or cynomologus HER3), the antibodies comprising a VL domain having an amino acid sequence of SEQ ID NO: 15, 35, 55, 75, 95, 115, 135, 155, and 175.

[0149] In one aspect, the present invention provides antibodies that specifically bind to domains 3-4 of HER3 protein (e.g., human and/or cynomologus HER3), the antibodies comprising a VH domain having an amino acid sequence of SEQ ID NO: 194, 214, 234, 254, 274, 294, 314, 334, 354, 374, 394, 414, 434, 454, 474, 494, 514, 534, 554, 574, 594, 614, 634, 654, 674, and 694. In another aspect, the present invention provides antibodies that specifically bind specifically bind to domain 3 of HER3 protein (e.g., human and/or cynomologus HER3), the antibodies comprising a VL domain having an amino acid sequence of SEQ ID NO: 195, 215, 235, 255, 275, 295, 315, 335, 355, 375, 395, 415, 435, 455, 475, 495, 515, 535, 555, 575, 595, 615, 635, 655, 675, and 695.

[0150] Since each of these antibodies or fragments thereof can bind to HER3, the VH, VL, full length light chain, and full length heavy chain sequences (amino acid sequences and the nucleotide sequences encoding the amino acid sequences) can be “mixed and matched” to create other HER3 antibodies of the invention. Such “mixed and matched” HER3 antibodies can be tested using the binding assays known in the art (e.g., ELISAs, and other assays described in the Example section). When these chains are mixed and matched, a VH sequence from a particular VH/VL pairing should be replaced with a structurally similar VH sequence. Likewise a full length heavy chain sequence from a particular full length heavy chain/full length light chain pairing should be replaced with a structurally similar full length heavy chain sequence. Likewise, a VL sequence from a particular VH/VL pairing should be replaced with a structurally similar VL sequence. Likewise a full length light chain sequence from a particular full length heavy chain/full length light chain pairing should be replaced with a structurally similar full length light chain sequence.

[0151] Accordingly, in one aspect, the invention provides an isolated monoclonal antibody or fragment thereof having:

a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 14, 34, 54, 74, 94, 114, 134, 154, and 174; and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 15, 35, 55, 75, 95, 115, 135, 155, and 175; wherein the antibody specifically binds to domain 3 of HER3 (e.g., human and/or cynomolgus).

[0152] Accordingly, in one aspect, the invention provides an isolated monoclonal antibody or fragment thereof having: a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 194, 214, 234, 254, 274, 294, 314, 334, 354, 374, 394, 414, 434, 454, 474, 494, 514, 534, 554, 574, 594, 614, 634, 654, 674, and 694; and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 195, 215, 235, 255, 275, 295, 315, 335, 355, 375, 395, 415, 435, 455, 475, 495, 515, 535, 555, 575, 595, 615, 635, 655, 675, and 695; wherein the antibody specifically binds to domain 3 of HER3 (e.g., human and/or cynomolgus).

[0153] In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO. 14 and VL of SEQ ID NO: 15. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 34 and VL of SEQ ID NO: 35. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 54 and VL of SEQ ID NO: 55. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a SEQ ID NO: 74 and VL of SEQ ID NO: 75. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 94 and VL of SEQ ID NO: 95. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 114 and VL of SEQ ID NO: 115. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 134 and VL of SEQ ID NO: 135. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 154 and VL of SEQ ID NO: 155. In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a VH of SEQ ID NO: 174 and VL of SEQ ID NO: 175.

[0154] In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO. 194 and VL of SEQ ID NO: 195. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 214 and VL of SEQ ID NO: 215. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 234 and VL of SEQ ID NO: 235. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a SEQ ID NO: 254 and VL of SEQ ID NO: 255.

[0155] In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 274 and VL of SEQ ID NO: 275. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 294 and VL of SEQ ID NO: 295. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 314 and VL of SEQ ID NO: 315. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 334 and VL of SEQ ID NO: 335. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 354 and VL of SEQ ID NO: 355. In a specific

embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 374 and VL of SEQ ID NO: 375. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 394 and VL of SEQ ID NO: 395. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 414 and VL of SEQ ID NO: 415. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 434 and VL of SEQ ID NO: 435. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 454 and VL of SEQ ID NO: 255. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 474 and VL of SEQ ID NO: 475. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 494 and VL of SEQ ID NO: 495. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 514 and VL of SEQ ID NO: 515. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 534 and VL of SEQ ID NO: 535. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 554 and VL of SEQ ID NO: 555. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 574 and VL of SEQ ID NO: 575. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 594 and VL of SEQ ID NO: 595. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 614 and VL of SEQ ID NO: 615. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 634 and VL of SEQ ID NO: 635. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 654 and VL of SEQ ID NO: 655. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 674 and VL of SEQ ID NO: 675. In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a VH of SEQ ID NO: 694 and VL of SEQ ID NO: 695.

[0156] In another aspect, the present invention provides HER3 antibodies that bind to domain 3 that comprise the heavy chain and light chain CDR1s, CDR2s and CDR3s as described in Table 1, or combinations thereof. The amino acid sequences of the VH CDR1s of the antibodies are shown in SEQ ID NOs: 2, 22, 42, 62, 82, 102, 122, 142, and 162. The amino acid sequences of the VH CDR2s of the antibodies and are shown in SEQ ID NOs: 3, 23, 43, 63, 83, 103, 123, 143, and 163. The amino acid sequences of the VH CDR3s of the antibodies are shown in SEQ ID NOs: 4, 24, 44, 64, 84, 104, 124, 144, and 164. The amino acid sequences of the VL CDR1s of the antibodies are shown in SEQ ID NOs: 8, 28, 48, 68, 88, 108, 128, 148, and 168. The amino acid sequences of the VL CDR2s of the antibodies are shown in SEQ ID NOs: 9, 29, 49, 69, 89, 109, 129, 149, and 169. The amino acid sequences of the VL CDR3s of the antibodies are shown in SEQ ID NOs: 10, 30, 50, 70, 90, 110, 130, 150, and 170. The CDR regions are delineated using the Kabat system (Kabat et al., (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia et al., (1987) J. Mol. Biol. 196:901-917; Chothia et al., (1989) Nature 342: 877-883; and Al-Lazikani et al., (1997) J. Mol. Biol. 273, 927-948).

[0157] In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a heavy chain variable region CDR1 of SEQ ID NO: 142; a CDR2 of SEQ ID NO: 143; a CDR3 of SEQ ID NO: 144; a light chain variable region CDR1 of SEQ ID NO: 148; a CDR2 of SEQ ID NO: 149; and a CDR3 of SEQ ID NO: 150.

[0158] In a specific embodiment, an antibody that binds to domain 3 of HER3 comprises a heavy chain variable region CDR1 of SEQ ID NO: 162; a CDR2 of SEQ ID NO: 163; a CDR3 of SEQ ID NO: 164; a light chain variable region CDR1 of SEQ ID NO: 168; a CDR2 of SEQ ID NO: 169; and a CDR3 of SEQ ID NO: 170.

[0159] In another aspect, the present invention provides HER3 antibodies that bind to domains 3-4 that comprise the heavy chain and light chain CDR1s, CDR2s and CDR3s as described in Table 2, or combinations thereof. The amino acid sequences of the VH CDR1s of the antibodies are shown in SEQ ID NOs: 182, 202, 222, 242, 262, 282, 302, 322, 342, 362, 382, 402, 422, 442, 462, 482, 502, 522, 542, 562, 582, 602, 622, 642, 662, and 682. The amino acid sequences of the VH CDR2s of the antibodies are shown in SEQ ID NOs: 183, 203, 223, 243, 263, 283, 303, 323, 343, 363, 383, 403, 423, 443, 463, 483, 503, 523, 543, 563, 583, 603, 623, 643, 663, and 683. The amino acid sequences of the VH CDR3s of the antibodies are shown in SEQ ID NOs: 184, 204, 224, 244, 264, 284, 304, 324, 344, 364, 384, 404, 424, 444, 464, 484, 504, 524, 544, 564, 584, 604, 624, 644, 664, and 684. The amino acid sequences of the VL CDR1s of the antibodies are shown in SEQ ID NOs: 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, and 688. The amino acid sequences of the VL CDR2s of the antibodies are shown in SEQ ID NOs: 189, 209, 229, 249, 269, 289, 309, 329, 349, 369, 389, 409, 429, 449, 469, 489, 509, 529, 549, 569, 589, 609, 629, 649, 669, and 689. The amino acid sequences of the VL CDR3s of the antibodies are shown in SEQ ID NOs: 190, 210, 230, 250, 270, 290, 310, 330, 350, 370, 390, 410, 430, 450, 470, 490, 510, 530, 550, 570, 590, 610, 630, 650, 670, and 690. The CDR regions are delineated using the Kabat system (Kabat et al., (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia et al., (1987) J. Mol. Biol. 196:901-917; Chothia et al., (1989) Nature 342: 877-883; and Al-Lazikani et al., (1997) J. Mol. Biol. 273, 927-948).

[0160] In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a heavy chain variable region CDR1 of SEQ ID NO: 662; a CDR2 of SEQ ID NO: 663; a CDR3 of SEQ ID NO: 664; a light chain variable region CDR1 of SEQ ID NO: 668; a CDR2 of SEQ ID NO: 669; and a CDR3 of SEQ ID NO: 670.

[0161] In a specific embodiment, an antibody that binds to domains 3-4 of HER3 comprises a heavy chain variable region CDR1 of SEQ ID NO: 682; a CDR2 of SEQ ID NO: 683; a CDR3 of SEQ ID NO: 684; a light chain variable region CDR1 of SEQ ID NO: 688; a CDR2 of SEQ ID NO: 689; and a CDR3 of SEQ ID NO: 690.

[0162] Other antibodies of the invention include amino acids that have been mutated, yet have at least 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98% or 99% identity in the CDR regions with the CDR regions depicted in the sequences described in Table 1 or Table 2. In some embodiments, it includes mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the CDR

regions when compared with the CDR regions depicted in the sequence described Table 1 or Table 2, while still maintaining their specificity for the original antibody's epitope

[0163] Other antibodies of the invention include amino acids that have been mutated, yet have at least 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98% or 99% identity in the framework regions with the framework regions depicted in the sequences described in Table 1 or Table 2. In some embodiments, it includes mutant amino acid sequences wherein no more than 1, 2, 3, 4, 5, 6, or 7 amino acids have been mutated in the framework regions when compared with the framework regions depicted in the sequence described Table 1 or Table 2, while still maintaining their specificity for the original antibody's epitope. The present invention also provides nucleic acid sequences that encode VH, VL, the full length heavy chain, and the full length light chain of the antibodies that specifically bind to a HER3 protein (e.g., human and/or cynomolgus HER3).

[0164] Other antibodies of the invention include those where the amino acids or nucleic acids encoding the amino acids have been mutated, yet have at least 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98% or 99% identity to the sequences described in Table 1 or Table 2. In some embodiments, it include mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the variable regions when compared with the variable regions depicted in the sequence described in Table 1 or Table 2, while retaining substantially the same therapeutic activity.

[0165] As used herein, a human antibody comprises heavy or light chain variable regions or full length heavy or light chains that are "the product of" or "derived from" a particular germline sequence if the variable regions or full length chains of the antibody are obtained from a system that uses human germline immunoglobulin genes. Such systems include immunizing a transgenic mouse carrying human immunoglobulin genes with the antigen of interest or screening a human immunoglobulin gene library displayed on phage with the antigen of interest. A human antibody that is "the product of" or "derived from" a human germline immunoglobulin sequence can be identified as such by comparing the amino acid sequence of the human antibody to the amino acid sequences of human germline immunoglobulins and selecting the human germline immunoglobulin sequence that is closest in sequence (i.e., greatest % identity) to the sequence of the human antibody. A human antibody that is "the product of" or "derived from" a particular human germline immunoglobulin sequence may contain amino acid differences as compared to the germline sequence, due to, for example, naturally occurring somatic mutations or intentional introduction of site-directed mutations. However, in the VH or VL framework regions, a selected human antibody typically is at least 90% identical in amino acids sequence to an amino acid sequence encoded by a human germline immunoglobulin gene and contains amino acid residues that identify the human antibody as being human when compared to the germline immunoglobulin amino acid sequences of other species (e.g., murine germline sequences). In certain cases, a human antibody may be at least 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98% or 99% identical in amino acid sequence to the amino acid sequence encoded by the germline immunoglobulin gene. Typically, a recombinant human antibody will display no more than 10 amino acid differences from the amino acid sequence encoded by the human germline immunoglobulin gene in the VH or VL framework regions. In

certain cases, the human antibody may display no more than 5, or even no more than 4, 3, 2, or 1 amino acid difference from the amino acid sequence encoded by the germline immunoglobulin gene.

[0166] The antibodies disclosed herein can be derivatives of single chain antibodies, diabodies, domain antibodies, nanobodies, and unibodies. A “single-chain antibody” (scFv) consists of a single polypeptide chain comprising a VL domain linked to a VH domain, wherein VL domain and VH domain are paired to form a monovalent molecule. Single chain antibody can be prepared according to method known in the art (see, for example, Bird et al., (1988) *Science* 242: 423-426 and Huston et al., (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883). A “disbud” consists of two chains, each chain comprising a heavy chain variable region connected to a light chain variable region on the same polypeptide chain connected by a short peptide linker, wherein the two regions on the same chain do not pair with each other but with complementary domains on the other chain to form a bispecific molecule. Methods of preparing diabodies are known in the art (See, e.g., Holliger et al., (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448, and Poljak et al., (1994) *Structure* 2:1121-1123). Domain antibodies (dAbs) are small functional binding units of antibodies, corresponding to the variable regions of either the heavy or light chains of antibodies. Domain antibodies are well expressed in bacterial, yeast, and mammalian cell systems. Further details of domain antibodies and methods of production thereof are known in the art (see, for example, U.S. Pat. Nos. 6,291,158; 6,582,915; 6,593,081; 6,172,197; 6,696,245; European Patents 0368684 & 0616640; WO05/035572, WO04/101790, WO04/081026, WO04/058821, WO04/003019 and WO03/002609. Nanobodies are derived from the heavy chains of an antibody. A nanobody typically comprises a single variable domain and two constant domains (CH2 and CH3) and retains antigen-binding capacity of the original antibody. Nanobodies can be prepared by methods known in the art (See e.g., U.S. Pat. No. 6,765,087, U.S. Pat. No. 6,838,254, WO 06/079372). Unibodies consist of one light chain and one heavy chain of a IgG4 antibody. Unibodies may be made by the removal of the hinge region of IgG4 antibodies. Further details of unibodies and methods of preparing them may be found in WO2007/059782.

Homologous Antibodies

[0167] In yet another embodiment, the present invention provides an antibody or fragment thereof comprising amino acid sequences that are homologous to the sequences described in Table 1 or Table 2, and said antibody binds to a HER3 protein (e.g., human and/or cynomolgus HER3), and retains the desired functional properties of those antibodies described in Table 1 or Table 2.

[0168] For example, the invention provides an isolated monoclonal antibody (or a functional fragment thereof) comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence that is at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 34, 54, 74, 94, 114, 134, 154, and 174; the light chain variable region comprises an amino acid sequence that is at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 15, 35, 55, 75, 95, 115, 135, 155, and 175; wherein the

antibody binds to domain 3 of HER3 (e.g., human and/or cynomolgus HER3) and inhibits the signaling activity of HER3, which can be measured in a phosphorylation assay or other measure of HER signaling (e.g., phospho-HER3 assays, phospho-Akt assays, cell proliferation, and ligand blocking assays as described in the Examples). Also included within the scope of the invention are variable heavy and light chain parental nucleotide sequences; and full length heavy and light chain sequences optimized for expression in a mammalian cell. Other antibodies of the invention include amino acids or nucleic acids that have been mutated, yet have at least 60, 70, 80, 90, 95, 98, or 99% percent identity to the sequences described above. In some embodiments, it include mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated by amino acid deletion, insertion or substitution in the variable regions when compared with the variable regions depicted in the sequence described above.

[0169] For example, the invention provides an isolated monoclonal antibody (or a functional fragment thereof) comprising a heavy chain variable region and a light chain variable region,

[0170] wherein the heavy chain variable region comprises an amino acid sequence that is at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 194, 214, 234, 254, 274, 294, 314, 334, 354, 374, 394, 414, 434, 454, 474, 494, 514, 534, 554, 574, 594, 614, 634, 654, 674, and 694; the light chain variable region comprises an amino acid sequence that is at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 195, 215, 235, 255, 275, 295, 315, 335, 355, 375, 395, 415, 435, 455, 475, 495, 515, 535, 555, 575, 595, 615, 635, 655, 675, and 695; wherein the antibody binds to domains 3-4 of HER3 (e.g., human and/or cynomolgus HER3) and inhibits the signaling activity of HER3, which can be measured in a phosphorylation assay or other measure of HER signaling (e.g., phospho-HER3 assays, phospho-Akt assays, cell proliferation, and ligand blocking assays as described in the Examples). Also included within the scope of the invention are variable heavy and light chain parental nucleotide sequences; and full length heavy and light chain sequences optimized for expression in a mammalian cell. Other antibodies of the invention include amino acids or nucleic acids that have been mutated, yet have at least 60, 70, 80, 90, 95, 98, or 99% percent identity to the sequences described above. In some embodiments, it include mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated by amino acid deletion, insertion or substitution in the variable regions when compared with the variable regions depicted in the sequence described above.

[0171] In other embodiments, the VH and/or VL amino acid sequences may be 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98% or 99% identical to the sequences set forth in Table 1 or Table 2. In other embodiments, the VH and/or VL amino acid sequences may be identical except an amino acid substitution in no more than 1, 2, 3, 4 or 5 amino acid position. An antibody having VH and VL regions having high (i.e., 80% or greater) identity to the VH and VL regions of the antibodies described in Table 1 or Table 2 can be obtained by mutagenesis (e.g., site-directed or PCR-mediated mutagen-

esis), followed by testing of the encoded altered antibody for retained function using the functional assays described herein.

[0172] In other embodiments, the variable regions of heavy chain and/or light chain nucleotide sequences may be 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98% or 99% identical to the sequences set forth above.

[0173] As used herein, “percent identity” between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity equals number of identical positions/total number of positions $\times$ 100), taking into account the number of gaps, and the length of each gap, which needs to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm, as described in the non-limiting examples below.

[0174] Additionally or alternatively, the protein sequences of the present invention can further be used as a “query sequence” to perform a search against public databases to, for example, identify related sequences. For example, such searches can be performed using the BLAST program (version 2.0) of Altschul et al., (1990) *J. Mol. Biol.* 215:403-10.

Antibodies with Conservative Modifications

[0175] In certain embodiments, an antibody of the invention has a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences and a light chain variable region comprising CDR1, CDR2, and CDR3 sequences, wherein one or more of these CDR sequences have specified amino acid sequences based on the antibodies described herein or conservative modifications thereof, and wherein the antibodies retain the desired functional properties of the HER3 antibodies of the invention.

[0176] Accordingly, the invention provides an isolated HER3 monoclonal antibody, or a fragment thereof that bind to domain 3 of HER3, consisting of a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences and a light chain variable region comprising CDR1, CDR2, and CDR3 sequences, wherein: the heavy chain variable region CDR1 amino acid sequences are selected from the group consisting of SEQ ID NOs: 2, 22, 42, 62, 82, 102, 122, 142, and 162, and conservative modifications thereof; the heavy chain variable region CDR2 amino acid sequences are selected from the group consisting of SEQ ID NOs: 3, 23, 43, 63, 83, 103, 123, 143, and 163 and conservative modifications thereof; the heavy chain variable region CDR3 amino acid sequences are selected from the group consisting of SEQ ID NOs: 4, 24, 44, 64, 84, 104, 124, 144, and 164 and conservative modifications thereof; the light chain variable regions CDR1 amino acid sequences are selected from the group consisting of SEQ ID NOs: 8, 28, 48, 68, 88, 108, 128, 148, and 168 and conservative modifications thereof; the light chain variable regions CDR2 amino acid sequences are selected from the group consisting of SEQ ID NOs: 9, 29, 49, 69, 89, 109, 129, 149, and 169, and conservative modifications thereof; the light chain variable regions of CDR3 amino acid sequences are selected from the group consisting of SEQ ID NOs: 10, 30, 50, 70, 90, 110, 130, 150, and 170, and conservative modifications thereof; the antibody or fragment thereof specifically binds to HER3, and inhibits HER3 activity by inhibiting a HER3 signaling pathway, which can be measured in a phosphorylation assay or other measure of

HER signaling (e.g., phospho-HER3 assays, phospho-Akt assays, cell proliferation, and ligand blocking assays as described in the Examples).

[0177] Accordingly, the invention provides an isolated HER3 monoclonal antibody, or a fragment thereof that bind to domains 3-4 of HER3, consisting of a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences and a light chain variable region comprising CDR1, CDR2, and CDR3 sequences, wherein: the heavy chain variable region CDR1 amino acid sequences are selected from the group consisting of SEQ ID NOs: 182, 202, 222, 242, 262, 282, 302, 322, 342, 362, 382, 402, 422, 442, 462, 482, 502, 522, 542, 562, 582, 602, 622, 642, 662, and 682, and conservative modifications thereof; the heavy chain variable region CDR2 amino acid sequences are selected from the group consisting of SEQ ID NOs: 183, 203, 223, 243, 263, 283, 303, 323, 343, 363, 383, 403, 423, 443, 463, 483, 503, 523, 543, 563, 583, 603, 623, 643, 663, and 683 and conservative modifications thereof; the heavy chain variable region CDR3 amino acid sequences are selected from the group consisting of SEQ ID NOs: 184, 204, 224, 244, 264, 284, 304, 324, 344, 364, 384, 404, 424, 444, 464, 484, 504, 524, 544, 564, 584, 604, 624, 644, 664, and 684 and conservative modifications thereof; the light chain variable regions CDR1 amino acid sequences are selected from the group consisting of SEQ ID NOs: 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, and 688 and conservative modifications thereof; the light chain variable regions CDR2 amino acid sequences are selected from the group consisting of SEQ ID NOs: 189, 209, 229, 249, 269, 289, 309, 329, 349, 369, 389, 409, 429, 449, 469, 489, 509, 529, 549, 569, 589, 609, 629, 649, 669, and 689, and conservative modifications thereof; the light chain variable regions of CDR3 amino acid sequences are selected from the group consisting of SEQ ID NOs: 190, 210, 230, 250, 270, 290, 310, 330, 350, 370, 390, 410, 430, 450, 470, 490, 510, 530, 550, 570, 590, 610, 630, 650, 670, and 690, and conservative modifications thereof; the antibody or fragment thereof specifically binds to HER3, and inhibits HER3 activity by inhibiting a HER3 signaling pathway, which can be measured in a phosphorylation assay or other measure of HER signaling (e.g., phospho-HER3 assays, phospho-Akt assays, cell proliferation, and ligand blocking assays as described in the Examples).

Antibodies That Bind to the Same Epitope

[0178] The present invention provides antibodies that interact with (e.g., by binding, steric hindrance, stabilizing/desstabilizing, spatial distribution) the same epitope as do the HER3 antibodies described in Table 1 or Table 2. Additional antibodies can therefore be identified based on their ability to cross-compete (e.g., to competitively inhibit the binding of, in a statistically significant manner) with other antibodies of the invention in HER3 binding assays. The ability of a test antibody to inhibit the binding of antibodies of the present invention to a HER3 protein (e.g., human and/or cynomolgus HER3) demonstrates that the test antibody can compete with that antibody for binding to HER3; such an antibody may, according to non-limiting theory, bind to the same or a related (e.g., a structurally similar or spatially proximal) epitope on the HER3 protein as the antibody with which it competes. In a certain embodiment, the antibody that binds to the same epitope on HER3 as the antibodies of the present invention is

a human monoclonal antibody. Such human monoclonal antibodies can be prepared and isolated as described herein.

[0179] In one embodiment, the antibody or fragments thereof binds to domain 3 of HER3 and inhibits both ligand dependent and ligand-independent HER3 signal transduction. In one embodiment, the antibody or fragments thereof bind to domains 3-4 of HER3 and inhibits both ligand dependent and ligand-independent HER3 signal transduction.

[0180] The antibodies of the invention or fragments thereof inhibit both ligand dependent and independent activation of HER3 without preventing ligand binding. This is considered advantageous for the following reasons:

[0181] (i) The therapeutic antibody would have clinical utility in a broad spectrum of tumors than an antibody which targeted a single mechanism of HER3 activation (i.e. ligand dependent or ligand independent) since distinct tumor types are driven by each mechanism.

[0182] (ii) The therapeutic antibody would be efficacious in tumor types where both mechanisms of HER3 activation are simultaneously involved. An antibody targeting a single mechanism of HER3 activation (i.e. ligand dependent or ligand independent) would display little or no efficacy in these tumor types

[0183] (iii) The efficacy of an antibody which inhibits ligand dependent activation of HER3 without preventing ligand binding would be less likely to be adversely affected by increasing concentrations of ligand. This would translate to either increased efficacy in a tumor type driven by very high concentrations of HER3 ligand or a reduced drug resistance liability where resistance is mediated by up-regulation of HER3 ligands.

[0184] (iv) An antibody which inhibits HER3 activation by stabilizing the inactive form would be less prone to drug resistance driven by alternative mechanisms of HER3 activation.

[0185] Consequently, the antibodies of the invention may be used to treat conditions where existing therapeutic antibodies are clinically ineffective.

Engineered and Modified Antibodies

[0186] An antibody of the invention further can be prepared using an antibody having one or more of the VH and/or VL sequences shown herein as starting material to engineer a modified antibody, which modified antibody may have altered properties from the starting antibody. An antibody can be engineered by modifying one or more residues within one or both variable regions (i.e., VH and/or VL), for example within one or more CDR regions and/or within one or more framework regions. Additionally or alternatively, an antibody can be engineered by modifying residues within the constant region(s), for example to alter the effector function(s) of the antibody.

[0187] One type of variable region engineering that can be performed is CDR grafting. Antibodies interact with target antigens predominantly through amino acid residues that are located in the six heavy and light chain complementarity determining regions (CDRs). For this reason, the amino acid sequences within CDRs are more diverse between individual antibodies than sequences outside of CDRs. Because CDR sequences are responsible for most antibody-antigen interactions, it is possible to express recombinant antibodies that mimic the properties of specific naturally occurring antibodies by constructing expression vectors that include CDR sequences from the specific naturally occurring antibody

grafted onto framework sequences from a different antibody with different properties (see, e.g., Riechmann et al., (1998) Nature 332:323-327; Jones et al., (1986) Nature 321:522-525; Queen et al., (1989) Proc. Natl. Acad., U.S.A. 86:10029-10033; U.S. Pat. No. 5,225,539 to Winter, and U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al.)

[0188] Accordingly, another embodiment of the invention pertains to an isolated HER3 monoclonal antibody, or fragment thereof that binds to domain 3 of HER3, comprising a heavy chain variable region comprising CDR1 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 22, 42, 62, 82, 102, 122, 142, and 162; CDR2 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 33, 23, 43, 63, 83, 103, 123, 143, and 163; CDR3 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 24, 44, 64, 84, 104, 124, 144, and 164, respectively; and a light chain variable region having CDR1 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 28, 48, 68, 88, 108, 128, 148, and 168; CDR2 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 9, 29, 49, 69, 89, 109, 129, 149, and 169; and CDR3 sequences consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 10, 30, 50, 70, 90, 110, 130, 150, and 170, respectively.

[0189] Accordingly, another embodiment of the invention pertains to an isolated HER3 monoclonal antibody, or fragment thereof that bind to domains 3-4 of HER3, comprising a heavy chain variable region comprising CDR1 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 182, 202, 222, 242, 262, 282, 302, 322, 342, 362, 382, 402, 422, 442, 462, 482, 502, 522, 542, 562, 582, 602, 622, 642, 662, and 682; CDR2 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 183, 203, 223, 243, 263, 283, 303, 323, 343, 363, 383, 403, 423, 443, 463, 483, 503, 523, 543, 563, 583, 603, 623, 643, 663, and 683; CDR3 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 184, 204, 224, 244, 264, 284, 304, 324, 344, 364, 384, 404, 424, 444, 464, 484, 504, 524, 544, 564, 584, 604, 624, 644, 664, and 684, respectively; and a light chain variable region having CDR1 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, and 688; CDR2 sequences having an amino acid sequence selected from the group consisting of SEQ ID NOs: 189, 209, 229, 249, 269, 289, 309, 329, 349, 369, 389, 409, 429, 449, 469, 489, 509, 529, 549, 569, 589, 609, 629, 649, 669, and 689; and CDR3 sequences consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 190, 210, 230, 250, 270, 290, 310, 330, 350, 370, 390, 410, 430, 450, 470, 490, 510, 530, 550, 570, 590, 610, 630, 650, 670, and 690, respectively.

[0190] Such antibodies contain the VH and VL CDR sequences of monoclonal antibodies, yet may contain different framework sequences from these antibodies. Such framework sequences can be obtained from public DNA databases or published references that include germline antibody gene sequences. For example, germline DNA sequences for human heavy and light chain variable region genes can be found in the "Vbase" human germline sequence database (available on

the Internet at www.mrc-cpe.cam.ac.uk/vbase), as well as in Kabat et al., (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia et al., (1987) J. Mol. Biol. 196:901-917; Chothia et al., (1989) Nature 342:877-883; and Al-Lazikani et al., (1997) J. Mol. Biol. 273:927-948; Tomlinson et al., (1992) J. Mol. Biol. 227:776-798; and Cox et al., (1994) Eur. J. Immunol. 24:827-836; the contents of each of which are expressly incorporated herein by reference.

[0191] An example of framework sequences for use in the antibodies of the invention are those that are structurally similar to the framework sequences used by selected antibodies of the invention, e.g., consensus sequences and/or framework sequences used by monoclonal antibodies of the invention. The VH CDR1, 2 and 3 sequences, and the VL CDR1, 2 and 3 sequences, can be grafted onto framework regions that have the identical sequence as that found in the germline immunoglobulin gene from which the framework sequence derive, or the CDR sequences can be grafted onto framework regions that contain one or more mutations as compared to the germline sequences. For example, it has been found that in certain instances it is beneficial to mutate residues within the framework regions to maintain or enhance the antigen binding ability of the antibody (see e.g., U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al.).

[0192] Another type of variable region modification is to mutate amino acid residues within the VH and/or VL CDR1, CDR2 and/or CDR3 regions to thereby improve one or more binding properties (e.g., affinity) of the antibody of interest, known as "affinity maturation." Site-directed mutagenesis or PCR-mediated mutagenesis can be performed to introduce the mutation(s) and the effect on antibody binding, or other functional property of interest, can be evaluated in vitro or in vivo assays as described herein and provided in the Examples. Conservative modifications (as discussed above) can be introduced. The mutations may be amino acid substitutions, additions or deletions. Moreover, typically no more than one, two, three, four or five residues within a CDR region are altered.

[0193] Accordingly, in another embodiment, the invention provides isolated HER3 monoclonal antibodies, or fragment thereof that bind to domain 3 of HER3, consisting of a heavy chain variable region having: a VH CDR1 region consisting of an amino acid sequence selected from the group having SEQ ID NOs: 22, 22, 42, 62, 82, 102, 122, 142, and 162 or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 2, 22, 42, 62, 82, 102, 122, 142, and 162; a VH CDR2 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 23, 43, 63, 83, 103, 123, 143, and 163 or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 3, 23, 43, 63, 83, 103, 123, 143, and 163; a VH CDR3 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 24, 44, 64, 84, 104, 124, 144, and 164, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 4, 24, 44, 64, 84, 104, 124, 144, and 164; and a VL CDR1 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 28, 48, 68, 88, 108, 128, 148, and 168, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or

additions as compared to SEQ ID NOs: 8, 28, 48, 68, 88, 108, 128, 148, and 168; a VL CDR2 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 9, 29, 49, 69, 89, 109, 129, 149, and 169, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 9, 29, 49, 69, 89, 109, 129, 149, and 169; and a VL CDR3 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 10, 30, 50, 70, 90, 110, 130, 150, and 170, and 373, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 10, 30, 50, 70, 90, 110, 130, 150, and 170.

[0194] Accordingly, in another embodiment, the invention provides isolated HER3 monoclonal antibodies, or fragment thereof bind to domains 3-4 of HER3, consisting of a heavy chain variable region having: a VH CDR1 region consisting of an amino acid sequence selected from the group having SEQ ID NOs: 182, 202, 222, 242, 262, 282, 302, 322, 342, 362, 382, 402, 422, 442, 462, 482, 502, 522, 542, 562, 582, 602, 622, 642, 662, and 682 or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 182, 202, 222, 242, 262, 282, 302, 322, 342, 362, 382, 402, 422, 442, 462, 482, 502, 522, 542, 562, 582, 602, 622, 642, 662, and 682; a VH CDR2 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 183, 203, 223, 243, 263, 283, 303, 323, 343, 363, 383, 403, 423, 443, 463, 483, 503, 523, 543, 563, 583, 603, 623, 643, 663, and 683 or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 183, 203, 223, 243, 263, 283, 303, 323, 343, 363, 383, 403, 423, 443, 463, 483, 503, 523, 543, 563, 583, 603, 623, 643, 663, and 683; a VH CDR3 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 184, 204, 224, 244, 264, 284, 304, 324, 344, 364, 384, 404, 424, 444, 464, 484, 504, 524, 544, 564, 584, 604, 624, 644, 664, and 684, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 184, 204, 224, 244, 264, 284, 304, 324, 344, 364, 384, 404, 424, 444, 464, 484, 504, 524, 544, 564, 584, 604, 624, 644, 664, and 684; and a VL CDR1 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, and 688, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, and 688; a VL CDR2 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 189, 209, 229, 249, 269, 289, 309, 329, 349, 369, 389, 409, 429, 449, 469, 489, 509, 529, 549, 569, 589, 609, 629, 649, 669, and 689, or an amino acid sequence having one, two, three, four or five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 189, 209, 229, 249, 269, 289, 309, 329, 349, 369, 389, 409, 429, 449, 469, 489, 509, 529, 549, 569, 589, 609, 629, 649, 669, and 689; and a VL CDR3 region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 190, 210, 230, 250, 270, 290, 310, 330, 350, 370, 390, 410, 430, 450, 470, 490, 510, 530, 550, 570, 590, 610, 630, 650, 670, and 690, or an amino acid sequence having one, two, three, four or

five amino acid substitutions, deletions or additions as compared to SEQ ID NOs: 190, 210, 230, 250, 270, 290, 310, 330, 350, 370, 390, 410, 430, 450, 470, 490, 510, 530, 550, 570, 590, 610, 630, 650, 670, and 690.

Grafting Antibody Fragments Into Alternative Frameworks or Scaffolds

[0195] A wide variety of antibody/immunoglobulin frameworks or scaffolds can be employed so long as the resulting polypeptide includes at least one binding region which specifically binds to HER3. Such frameworks or scaffolds include the 5 main idiotypes of human immunoglobulins, or fragments thereof, and include immunoglobulins of other animal species, preferably having humanized aspects. Novel frameworks, scaffolds and fragments continue to be discovered and developed by those skilled in the art.

[0196] In one aspect, the invention pertains to generating non-immunoglobulin based antibodies using non-immunoglobulin scaffolds onto which CDRs of the invention can be grafted. Known or future non-immunoglobulin frameworks and scaffolds may be employed, as long as they comprise a binding region specific for the target HER3 protein (e.g., human and/or cynomolgus HER3). Known non-immunoglobulin frameworks or scaffolds include, but are not limited to, fibronectin (Compound Therapeutics, Inc., Waltham, Mass.), ankyrin (Molecular Partners AG, Zurich, Switzerland), domain antibodies (Domantis, Ltd., Cambridge, Mass., and Ablynx nv, Zwijnaarde, Belgium), lipocalin (Pieris Proteolab AG, Freising, Germany), small modular immunopharmaceuticals (Trubion Pharmaceuticals Inc., Seattle, Wash.), maxyodies (Avidia, Inc., Mountain View, Calif.), Protein A (Affibody AG, Sweden), and affilin (gamma-crystallin or ubiquitin) (Scil Proteins GmbH, Halle, Germany).

[0197] The fibronectin scaffolds are based on fibronectin type III domain (e.g., the tenth module of the fibronectin type III (¹⁰Fn3 domain)). The fibronectin type III domain has 7 or 8 beta strands which are distributed between two beta sheets, which themselves pack against each other to form the core of the protein, and further containing loops (analogous to CDRs) which connect the beta strands to each other and are solvent exposed. There are at least three such loops at each edge of the beta sheet sandwich, where the edge is the boundary of the protein perpendicular to the direction of the beta strands (see U.S. Pat. No. 6,818,418). These fibronectin-based scaffolds are not an immunoglobulin, although the overall fold is closely related to that of the smallest functional antibody fragment, the variable region of the heavy chain, which comprises the entire antigen recognition unit in camel and llama IgG. Because of this structure, the non-immunoglobulin antibody mimics antigen binding properties that are similar in nature and affinity to those of antibodies. These scaffolds can be used in a loop randomization and shuffling strategy in vitro that is similar to the process of affinity maturation of antibodies in vivo. These fibronectin-based molecules can be used as scaffolds where the loop regions of the molecule can be replaced with CDRs of the invention using standard cloning techniques.

[0198] The ankyrin technology is based on using proteins with ankyrin derived repeat modules as scaffolds for bearing variable regions which can be used for binding to different targets. The ankyrin repeat module is a 33 amino acid polypeptide consisting of two anti-parallel α -helices and a β -turn. Binding of the variable regions is mostly optimized by using ribosome display.

[0199] Avimers are derived from natural A-domain containing protein such as HER3. These domains are used by nature for protein-protein interactions and in human over 250 proteins are structurally based on A-domains. Avimers consist of a number of different "A-domain" monomers (2-10) linked via amino acid linkers. Avimers can be created that can bind to the target antigen using the methodology described in, for example, U.S. Patent Application Publication Nos. 20040175756; 20050053973; 20050048512; and 20060008844.

[0200] Affibody affinity ligands are small, simple proteins composed of a three-helix bundle based on the scaffold of one of the IgG-binding domains of Protein A. Protein A is a surface protein from the bacterium *Staphylococcus aureus*. This scaffold domain consists of 58 amino acids, 13 of which are randomized to generate affibody libraries with a large number of ligand variants (See e.g., U.S. Pat. No. 5,831,012). Affibody molecules mimic antibodies, they have a molecular weight of 6 kDa, compared to the molecular weight of antibodies, which is 150 kDa. In spite of its small size, the binding site of affibody molecules is similar to that of an antibody.

[0201] Anticalins are products developed by the company Pieris ProteoLab AG. They are derived from lipocalins, a widespread group of small and robust proteins that are usually involved in the physiological transport or storage of chemically sensitive or insoluble compounds. Several natural lipocalins occur in human tissues or body liquids. The protein architecture is reminiscent of immunoglobulins, with hyper-variable loops on top of a rigid framework. However, in contrast with antibodies or their recombinant fragments, lipocalins are composed of a single polypeptide chain with 160 to 180 amino acid residues, being just marginally bigger than a single immunoglobulin domain. The set of four loops, which makes up the binding pocket, shows pronounced structural plasticity and tolerates a variety of side chains. The binding site can thus be reshaped in a proprietary process in order to recognize prescribed target molecules of different shape with high affinity and specificity. One protein of lipocalin family, the bilin-binding protein (BBP) of *Pieris Brassicae* has been used to develop anticalins by mutagenizing the set of four loops. One example of a patent application describing anticalins is in PCT Publication No. WO 199916873.

[0202] Affilin molecules are small non-immunoglobulin proteins which are designed for specific affinities towards proteins and small molecules. New affilin molecules can be very quickly selected from two libraries, each of which is based on a different human derived scaffold protein. Affilin molecules do not show any structural homology to immunoglobulin proteins. Currently, two affilin scaffolds are employed, one of which is gamma crystalline, a human structural eye lens protein and the other is "ubiquitin" superfamily proteins. Both human scaffolds are very small, show high temperature stability and are almost resistant to pH changes and denaturing agents. This high stability is mainly due to the expanded beta sheet structure of the proteins. Examples of gamma crystalline derived proteins are described in WO200104144 and examples of "ubiquitin-like" proteins are described in WO2004106368.

[0203] Protein epitope mimetics (PEM) are medium-sized, cyclic, peptide-like molecules (MW 1-2 kDa) mimicking beta-hairpin secondary structures of proteins, the major secondary structure involved in protein-protein interactions.

[0204] In some embodiments, the Fabs are converted to silent IgG1 format by changing the Fc region. For example, antibodies in Table 1 or Table 2 can be converted to IgG format.

Human or Humanized Antibodies

[0205] The present invention provides fully human antibodies that specifically bind to a HER3 protein (e.g., human and/or cynomolgus/mouse/rat HER3). Compared to the chimeric or humanized antibodies, the human HER3 antibodies or fragments thereof, have further reduced antigenicity when administered to human subjects.

[0206] Human HER3 antibodies or fragments thereof can be generated using methods that are known in the art. For example, the humaneering technology used to converting non-human antibodies into engineered human antibodies. U.S. Patent Publication No. 20050008625 describes an in vivo method for replacing a nonhuman antibody variable region with a human variable region in an antibody while maintaining the same or providing better binding characteristics relative to that of the nonhuman antibody. The method relies on epitope guided replacement of variable regions of a non-human reference antibody with a fully human antibody. The resulting human antibody is generally unrelated structurally to the reference nonhuman antibody, but binds to the same epitope on the same antigen as the reference antibody. Briefly, the serial epitope-guided complementarity replacement approach is enabled by setting up a competition in cells between a “competitor” and a library of diverse hybrids of the reference antibody (“test antibodies”) for binding to limiting amounts of antigen in the presence of a reporter system which responds to the binding of test antibody to antigen. The competitor can be the reference antibody or derivative thereof such as a single-chain Fv fragment. The competitor can also be a natural or artificial ligand of the antigen which binds to the same epitope as the reference antibody. The only requirements of the competitor are that it binds to the same epitope as the reference antibody, and that it competes with the reference antibody for antigen binding. The test antibodies have one antigen-binding V-region in common from the nonhuman reference antibody, and the other V-region selected at random from a diverse source such as a repertoire library of human antibodies. The common V-region from the reference antibody serves as a guide, positioning the test antibodies on the same epitope on the antigen, and in the same orientation, so that selection is biased toward the highest antigen-binding fidelity to the reference antibody.

[0207] Many types of reporter system can be used to detect desired interactions between test antibodies and antigen. For example, complementing reporter fragments may be linked to antigen and test antibody, respectively, so that reporter activation by fragment complementation only occurs when the test antibody binds to the antigen. When the test antibody- and antigen-reporter fragment fusions are co-expressed with a competitor, reporter activation becomes dependent on the ability of the test antibody to compete with the competitor, which is proportional to the affinity of the test antibody for the antigen. Other reporter systems that can be used include the reactivator of an auto-inhibited reporter reactivation system (RAIR) as disclosed in U.S. patent application Ser. No. 10/208,730 (Publication No. 20030198971), or competitive activation system disclosed in U.S. patent application Ser. No. 10/076,845 (Publication No. 20030157579).

[0208] With the serial epitope-guided complementarity replacement system, selection is made to identify cells expresses a single test antibody along with the competitor, antigen, and reporter components. In these cells, each test antibody competes one-on-one with the competitor for binding to a limiting amount of antigen. Activity of the reporter is proportional to the amount of antigen bound to the test antibody, which in turn is proportional to the affinity of the test antibody for the antigen and the stability of the test antibody. Test antibodies are initially selected on the basis of their activity relative to that of the reference antibody when expressed as the test antibody. The result of the first round of selection is a set of “hybrid” antibodies, each of which is comprised of the same non-human V-region from the reference antibody and a human V-region from the library, and each of which binds to the same epitope on the antigen as the reference antibody. One of more of the hybrid antibodies selected in the first round will have an affinity for the antigen comparable to or higher than that of the reference antibody.

[0209] In the second V-region replacement step, the human V-regions selected in the first step are used as guide for the selection of human replacements for the remaining non-human reference antibody V-region with a diverse library of cognate human V-regions. The hybrid antibodies selected in the first round may also be used as competitors for the second round of selection. The result of the second round of selection is a set of fully human antibodies which differ structurally from the reference antibody, but which compete with the reference antibody for binding to the same antigen. Some of the selected human antibodies bind to the same epitope on the same antigen as the reference antibody. Among these selected human antibodies, one or more binds to the same epitope with an affinity which is comparable to or higher than that of the reference antibody.

[0210] Using one of the mouse or chimeric HER3 antibodies or fragments thereof described above as the reference antibody, this method can be readily employed to generate human antibodies that bind to human HER3 with the same binding specificity and the same or better binding affinity. In addition, such human HER3 antibodies or fragments thereof can also be commercially obtained from companies which customarily produce human antibodies, e.g., KaloBios, Inc. (Mountain View, Calif.).

Camelid Antibodies

[0211] Antibody proteins obtained from members of the camel and dromedary (*Camelus bactrianus* and *Camelus dromaderius*) family including new world members such as llama species (*Lama paccos*, *Lama glama* and *Lama vicugna*) have been characterized with respect to size, structural complexity and antigenicity for human subjects. Certain IgG antibodies from this family of mammals as found in nature lack light chains, and are thus structurally distinct from the typical four chain quaternary structure having two heavy and two light chains, for antibodies from other animals. See PCT/EP93/02214 (WO 94/04678 published 3 Mar. 1994).

[0212] A region of the camelid antibody which is the small single variable domain identified as VHH can be obtained by genetic engineering to yield a small protein having high affinity for a target, resulting in a low molecular weight antibody-derived protein known as a “camelid nanobody”. See U.S. Pat. No. 5,759,808 issued Jun. 2, 1998; see also Stijlemans et al., (2004) J Biol Chem 279:1256-1261; Dumoulin et al., (2003) Nature 424:783-788; Pleschberger et al., (2003) Bio-

conjugate Chem 14:440-448; Cortez-Retamozo et al., (2002) Int J Cancer 89:456-62; and Lauwereys et al., (1998) EMBO J. 17:3512-3520. Engineered libraries of camelid antibodies and antibody fragments are commercially available, for example, from Ablynx, Ghent, Belgium. (e.g., US20060115470; Domantis (US20070065440, US20090148434). As with other antibodies of non-human origin, an amino acid sequence of a camelid antibody can be altered recombinantly to obtain a sequence that more closely resembles a human sequence, i.e., the nanobody can be "humanized". Thus the natural low antigenicity of camelid antibodies to humans can be further reduced.

[0213] The camelid nanobody has a molecular weight approximately one-tenth that of a human IgG molecule, and the protein has a physical diameter of only a few nanometers. One consequence of the small size is the ability of camelid nanobodies to bind to antigenic sites that are functionally invisible to larger antibody proteins, i.e., camelid nanobodies are useful as reagents detect antigens that are otherwise cryptic using classical immunological techniques, and as possible therapeutic agents. Thus yet another consequence of small size is that a camelid nanobody can inhibit as a result of binding to a specific site in a groove or narrow cleft of a target protein, and hence can serve in a capacity that more closely resembles the function of a classical low molecular weight drug than that of a classical antibody.

[0214] The low molecular weight and compact size further result in camelid nanobodies being extremely thermostable, stable to extreme pH and to proteolytic digestion, and poorly antigenic. Another consequence is that camelid nanobodies readily move from the circulatory system into tissues, and even cross the blood-brain barrier and can treat disorders that affect nervous tissue. Nanobodies can further facilitated drug transport across the blood brain barrier. See U.S. patent application 20040161738 published Aug. 19, 2004. These features combined with the low antigenicity to humans indicate great therapeutic potential. Further, these molecules can be fully expressed in prokaryotic cells such as *E. coli* and are expressed as fusion proteins with bacteriophage and are functional.

[0215] Accordingly, a feature of the present invention is a camelid antibody or nanobody having high affinity for HER3. In certain embodiments herein, the camelid antibody or nanobody is naturally produced in the camelid animal, i.e., is produced by the camelid following immunization with HER3 or a peptide fragment thereof, using techniques described herein for other antibodies. Alternatively, the HER3-binding camelid nanobody is engineered, i.e., produced by selection for example from a library of phage displaying appropriately mutagenized camelid nanobody proteins using panning procedures with HER3 as a target as described in the examples herein. Engineered nanobodies can further be customized by genetic engineering to have a half life in a recipient subject of from 45 minutes to two weeks. In a specific embodiment, the camelid antibody or nanobody is obtained by grafting the CDRs sequences of the heavy or light chain of the human antibodies of the invention into nanobody or single domain antibody framework sequences, as described for example in PCT/EP93/02214. In one embodiment, the camelid antibody or nanobody binds to at least amino acids residue in domain 3 of HER3 selected from amino acid residues: 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), or a subset thereof. In one embodiment, the camelid antibody or nanobody binds to at least amino acids resi-

due in domain 3 of HER3 selected from amino acid residues: 571, 582-584, 596-597, 600-602, 609-615 (of domain 4), or a subset thereof.

Bispecific Molecules and Multivalent Antibodies

[0216] In another aspect, the present invention features biparatopic, bispecific or multispecific molecules comprising an antibody or a fragment thereof that binds to a non-linear or conformational epitope within domain 3 of HER3. In another aspect, the biparatopic, bispecific or multispecific molecules comprise an antibody or a fragment thereof that binds to an epitope within domain 4 of HER3. The antibody or fragment thereof can be derivatized or linked to another functional molecule, e.g., another peptide or protein (e.g., another antibody or ligand for a receptor) to generate a bispecific molecule that binds to at least two different binding sites or target molecules. The antibody or fragment thereof may in fact be derivatized or linked to more than one other functional molecule to generate biparatopic or multi-specific molecules that bind to more than two different binding sites and/or target molecules; such biparatopic or multi-specific molecules. To create a bispecific molecule, an antibody or fragment thereof can be functionally linked (e.g., by chemical coupling, genetic fusion, non-covalent association or otherwise) to one or more other binding molecules, such as another antibody, antibody fragment, peptide or binding mimetic, such that a bispecific molecule results.

[0217] Further clinical benefits may be provided by the binding of two or more antigens within one antibody (Coloma et al., (1997); Merchant et al., (1998); Alt et al., (1999); Zuo et al., (2000); Lu et al., (2004); Lu et al., (2005); Marvin et al., (2005); Marvin et al., (2006); Shen et al., (2007); Wu et al., (2007); Dimasi et al., (2009); Michaelson et al., (2009)). (Morrison et al., (1997) Nature Biotech. 15:159-163; Alt et al. (1999) FEBS Letters 454:90-94; Zuo et al., (2000) Protein Engineering 13:361-367; Lu et al., (2004) JBC 279:2856-2865; Lu et al., (2005) JBC 280:19665-19672; Marvin et al., (2005) Acta Pharmacologica Sinica 26:649-658; Marvin et al., (2006) Curr Opin Drug Disc Develop 9:184-193; Shen et al., (2007) J Immun Methods 218:65-74; Wu et al., (2007) Nat. Biotechnol. 11:1290-1297; Dimasi et al., (2009) J Mol. Biol. 393:672-692; and Michaelson et al., (2009) mAbs 1:128-141.

[0218] The bispecific molecules can be prepared by conjugating the constituent binding specificities, using methods known in the art. For example, each binding specificity of the bispecific molecule can be generated separately and then conjugated to one another, for example, a variety of coupling or cross-linking agents can be used for covalent conjugation. Examples of cross-linking agents include protein A, carbodiimide, N-succinimidyl-5-acetyl-thioacetate (SATA), 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB), o-phenylenedimaleimide (oPDM), N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP), and sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (sulfo-SMCC) (see e.g., Karpovsky et al., (1984) J. Exp. Med. 160:1686; Liu et al., (1985) Proc. Natl. Acad. Sci. USA 82:8648). Other methods include those described in Paulus (1985) Behring Ins. Mitt. No. 78:118-132; Brennan et al., (1985) Science 229:81-83, and Glennie et al., (1987) J. Immunol. 139: 2367-2375). Conjugating agents are SATA and sulfo-SMCC, both available from Pierce Chemical Co. (Rockford, Ill.).

[0219] With antibodies, they can be conjugated by sulfhydryl bonding of the C-terminus hinge regions of the two heavy chains. In a particularly embodiment, the hinge region is modified to contain an odd number of sulfhydryl residues, for example one, prior to conjugation.

[0220] Alternatively, both binding specificities can be encoded in the same vector and expressed and assembled in the same host cell. This method is particularly useful where the bispecific molecule is a mAbxmAb, mAbxFab, FabxF(ab')₂ or ligand x Fab fusion protein. A bispecific molecule of the invention can be a single chain molecule comprising one single chain antibody and a binding determinant, or a single chain bispecific molecule comprising two binding determinants. Bispecific molecules may comprise at least two single chain molecules. Methods for preparing bispecific molecules are described for example in U.S. Pat. No. 5,260,203; U.S. Pat. No. 5,455,030; U.S. Pat. No. 4,881,175; U.S. Pat. No. 5,132,405; U.S. Pat. No. 5,091,513; U.S. Pat. No. 5,476,786; U.S. Pat. No. 5,013,653; U.S. Pat. No. 5,258,498; and U.S. Pat. No. 5,482,858.

[0221] Binding of the bispecific molecules to their specific targets can be confirmed by, for example, enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (REA), FACS analysis, bioassay (e.g., growth inhibition), or Western Blot assay. Each of these assays generally detects the presence of protein-antibody complexes of particular interest by employing a labeled reagent (e.g., an antibody) specific for the complex of interest.

[0222] In another aspect, the present invention provides multivalent compounds comprising at least two identical or different fragments of the antibodies binding to HER3. The antibody fragments can be linked together via protein fusion or covalent or non covalent linkage. Tetravalent compounds can be obtained for example by cross-linking antibodies of the antibodies of the invention with an antibody that binds to the constant regions of the antibodies of the invention, for example the Fc or hinge region. Trimerizing domain are described for example in Borean patent EP 1012280B1. Pentamerizing modules are described for example in PCT/EP97/05897.

[0223] In one embodiment, the biparatopic/bispecific antibody binds to at least amino acids residue in domain 3 of HER3 selected from amino acid residues: 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), or a subset thereof. In one embodiment, the biparatopic/bispecific antibody binds to at least amino acids residue in domain 3 of HER3 selected from amino acid residues: 571, 582-584, 596-597, 600-602, 609-615 (of domain 4), or a subset thereof.

[0224] In another embodiment, the invention pertains to dual function antibodies in which a single monoclonal antibody has been modified such that the antigen binding site binds to more than one antigen, such as a dual function antibody which binds both HER3 and another antigen (e.g., HER1, HER2, and HER4). In another embodiment, the invention pertains to a dual function antibody that targets antigens having the same conformation, for example an antigen that has the same conformation of HER3 in the "closed" or "inactive" state. Examples of antigens with the same conformation of HER3 in the "closed" or "inactive" state include, but are not limited to, HER1 and HER4. Thus, a dual function antibody may bind to both HER3 and HER1; HER3 and HER4, or HER1 and HER4. The dual binding specificity of the dual function antibody may further translate into dual

activity, or inhibition of activity. (See e.g., Jenny Bostrom et al., (2009) Science: 323; 1610-1614).

Antibodies with Extended Half Life

[0225] The present invention provides for antibodies or fragments thereof that specifically bind to a non-linear or conformational epitope within domain 3 of HER3 which have an extended half-life in vivo. The present invention also provides for antibodies that specifically bind to an epitope within domain 4 of HER3 which have an extended half-life in vivo.

[0226] Many factors may affect a protein's half life in vivo. For examples, kidney filtration, metabolism in the liver, degradation by proteolytic enzymes (proteases), and immunogenic responses (e.g., protein neutralization by antibodies and uptake by macrophages and dendritic cells). A variety of strategies can be used to extend the half life of the antibodies of the present invention. For example, by chemical linkage to polyethyleneglycol (PEG), reCODE PEG, antibody scaffold, polysialic acid (PSA), hydroxyethyl starch (HES), albumin-binding ligands, and carbohydrate shields; by genetic fusion to proteins binding to serum proteins, such as albumin, IgG, FcRn, and transferring; by coupling (genetically or chemically) to other binding moieties that bind to serum proteins, such as nanobodies, Fabs, DARPins, avimers, affibodies, and anticalins; by genetic fusion to rPEG, albumin, domain of albumin, albumin-binding proteins, and Fc; or by incorporation into nanocarriers, slow release formulations, or medical devices.

[0227] To prolong the serum circulation of antibodies in vivo, inert polymer molecules such as high molecular weight PEG can be attached to the antibodies or a fragment thereof with or without a multifunctional linker either through site-specific conjugation of the PEG to the N- or C-terminus of the antibodies or via epsilon-amino groups present on lysine residues. To pegylate an antibody, the antibody, or fragment thereof, typically is reacted with polyethylene glycol (PEG), such as a reactive ester or aldehyde derivative of PEG, under conditions in which one or more PEG groups become attached to the antibody or antibody fragment. The pegylation can be carried out by an acylation reaction or an alkylation reaction with a reactive PEG molecule (or an analogous reactive water-soluble polymer). As used herein, the term "polyethylene glycol" is intended to encompass any of the forms of PEG that have been used to derivatize other proteins, such as mono (C1-C10) alkoxy- or aryloxy-polyethylene glycol or polyethylene glycol-maleimide. In certain embodiments, the antibody to be pegylated is an aglycosylated antibody. Linear or branched polymer derivatization that results in minimal loss of biological activity will be used. The degree of conjugation can be closely monitored by SDS-PAGE and mass spectrometry to ensure proper conjugation of PEG molecules to the antibodies. Unreacted PEG can be separated from antibody-PEG conjugates by size-exclusion or by ion-exchange chromatography. PEG-derivatized antibodies can be tested for binding activity as well as for in vivo efficacy using methods well-known to those of skill in the art, for example, by immunoassays described herein. Methods for pegylating proteins are known in the art and can be applied to the antibodies of the invention. See for example, EP 0 154 316 by Nishimura et al. and EP 0 401 384 by Ishikawa et al.

[0228] Other modified pegylation technologies include reconstituting chemically orthogonal directed engineering technology (ReCODE PEG), which incorporates chemically specified side chains into biosynthetic proteins via a reconstituted system that includes tRNA synthetase and tRNA.

This technology enables incorporation of more than 30 new amino acids into biosynthetic proteins in *E. coli*, yeast, and mammalian cells. The tRNA incorporates a normative amino acid any place an amber codon is positioned, converting the amber from a stop codon to one that signals incorporation of the chemically specified amino acid.

[0229] Recombinant pegylation technology (rPEG) can also be used for serum half-life extension. This technology involves genetically fusing a 300-600 amino acid unstructured protein tail to an existing pharmaceutical protein. Because the apparent molecular weight of such an unstructured protein chain is about 15-fold larger than its actual molecular weight, the serum half-life of the protein is greatly increased. In contrast to traditional PEGylation, which requires chemical conjugation and repurification, the manufacturing process is greatly simplified and the product is homogeneous.

[0230] Polysialylation is another technology, which uses the natural polymer polysialic acid (PSA) to prolong the active life and improve the stability of therapeutic peptides and proteins. PSA is a polymer of sialic acid (a sugar). When used for protein and therapeutic peptide drug delivery, polysialic acid provides a protective microenvironment on conjugation. This increases the active life of the therapeutic protein in the circulation and prevents it from being recognized by the immune system. The PSA polymer is naturally found in the human body. It was adopted by certain bacteria which evolved over millions of years to coat their walls with it. These naturally polysialylated bacteria were then able, by virtue of molecular mimicry, to foil the body's defense system. PSA, nature's ultimate stealth technology, can be easily produced from such bacteria in large quantities and with predetermined physical characteristics. Bacterial PSA is completely non-immunogenic, even when coupled to proteins, as it is chemically identical to PSA in the human body.

[0231] Another technology include the use of hydroxyethyl starch ("HES") derivatives linked to antibodies. HES is a modified natural polymer derived from waxy maize starch and can be metabolized by the body's enzymes. HES solutions are usually administered to substitute deficient blood volume and to improve the rheological properties of the blood. Hesylation of an antibody enables the prolongation of the circulation half-life by increasing the stability of the molecule, as well as by reducing renal clearance, resulting in an increased biological activity. By varying different parameters, such as the molecular weight of HES, a wide range of HES antibody conjugates can be customized.

[0232] Antibodies having an increased half-life in vivo can also be generated introducing one or more amino acid modifications (i.e., substitutions, insertions or deletions) into an IgG constant domain, or FcRn binding fragment thereof (preferably a Fc or hinge Fc domain fragment). See, e.g., International Publication No. WO 98/23289; International Publication No. WO 97/34631; and U.S. Pat. No. 6,277,375.

[0233] Further, antibodies can be conjugated to albumin in order to make the antibody or antibody fragment more stable in vivo or have a longer half life in vivo. The techniques are well-known in the art, see, e.g., International Publication Nos. WO 93/15199, WO 93/15200, and WO 01/77137; and European Patent No. EP 413,622.

[0234] The HER3 antibody or a fragment thereof may also be fused to one or more human serum albumin (HSA) polypeptides, or a portion thereof. HSA, a protein of 585 amino acids in its mature form, is responsible for a significant

proportion of the osmotic pressure of serum and also functions as a carrier of endogenous and exogenous ligands. The role of albumin as a carrier molecule and its inert nature are desirable properties for use as a carrier and transporter of polypeptides in vivo. The use of albumin as a component of an albumin fusion protein as a carrier for various proteins has been suggested in WO 93/15199, WO 93/15200, and EP 413 622. The use of N-terminal fragments of HSA for fusions to polypeptides has also been proposed (EP 399 666). Accordingly, by genetically or chemically fusing or conjugating the antibodies or fragments thereof to albumin, can stabilize or extend the shelf-life, and/or to retain the molecule's activity for extended periods of time in solution, in vitro and/or in vivo.

[0235] Fusion of albumin to another protein may be achieved by genetic manipulation, such that the DNA coding for HSA, or a fragment thereof, is joined to the DNA coding for the protein. A suitable host is then transformed or transfected with the fused nucleotide sequences, so arranged on a suitable plasmid as to express a fusion polypeptide. The expression may be effected in vitro from, for example, prokaryotic or eukaryotic cells, or in vivo e.g. from a transgenic organism. Additional methods pertaining to HSA fusions can be found, for example, in WO 2001077137 and WO 200306007, incorporated herein by reference. In a specific embodiment, the expression of the fusion protein is performed in mammalian cell lines, for example, CHO cell lines. Altered differential binding of an antibody to a receptor at low or high pHs is also contemplated to be within the scope of the invention. For example, the affinity of an antibody may be modified such that it remains bound to its receptor at a low pH, e.g., the low pH within a lysosome, by modifying the antibody to include additional amino acids such as a histidine in a CDR of the antibody (See e.g., Tomoyuki Igawa et al. (2010) Nature Biotechnology; 28, 1203-1207).

Antibody Conjugates

[0236] The present invention provides antibodies or fragments thereof that specifically bind to HER3 recombinantly fused or chemically conjugated (including both covalent and non-covalent conjugations) to a heterologous protein or polypeptide (or fragment thereof, preferably to a polypeptide of at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90 or at least 100 amino acids) to generate fusion proteins. In particular, the invention provides fusion proteins comprising an antibody fragment described herein (e.g., a Fab fragment, Fd fragment, Fv fragment, F(ab)₂ fragment, a VH domain, a VH CDR, a VL domain or a VL CDR) and a heterologous protein, polypeptide, or peptide. Methods for fusing or conjugating proteins, polypeptides, or peptides to an antibody or an antibody fragment are known in the art. See, e.g., U.S. Pat. Nos. 5,336,603, 5,622,929, 5,359,046, 5,349,053, 5,447,851, and 5,112,946; European Patent Nos. EP 307,434 and EP 367,166; International Publication Nos. WO 96/04388 and WO 91/06570; Ashkenazi et al., (1991) Proc. Natl. Acad. Sci. USA 88:10535-10539; Zheng et al., (1995) J. Immunol. 154:5590-5600; and Vil et al., (1992) Proc. Natl. Acad. Sci. USA 89:11337-11341.

[0237] Additional fusion proteins may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to alter the activities of antibodies of the invention or fragments

thereof (e.g., antibodies or fragments thereof with higher affinities and lower dissociation rates). See, generally, U.S. Pat. Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458; Patten et al., (1997) *Curr. Opin. Biotechnol.* 8:724-33; Harayama, (1998) *Trends Biotechnol.* 16(2):76-82; Hansson et al., (1999) *J. Mol. Biol.* 287:265-76; and Lorenzo and Blasco, (1998) *Biotechniques* 24(2):308-313 (each of these patents and publications are hereby incorporated by reference in its entirety). Antibodies or fragments thereof, or the encoded antibodies or fragments thereof, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. A polynucleotide encoding an antibody or fragment thereof that specifically binds to a HER3 protein may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

[0238] Moreover, the antibodies or fragments thereof can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide (SEQ ID NO: 702), such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, Calif., 91311), among others, many of which are commercially available. As described in Gentz et al., (1989) *Proc. Natl. Acad. Sci. USA* 86:821-824, for instance, hexa-histidine (SEQ ID NO: 702) provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the hemagglutinin ("HA") tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., (1984) *Cell* 37:767), and the "flag" tag.

[0239] In other embodiments, antibodies of the present invention or fragments thereof conjugated to a diagnostic or detectable agent. Such antibodies can be useful for monitoring or prognosing the onset, development, progression and/or severity of a disease or disorder as part of a clinical testing procedure, such as determining the efficacy of a particular therapy. Such diagnosis and detection can be accomplished by coupling the antibody to detectable substances including, but not limited to, various enzymes, such as, but not limited to, horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; prosthetic groups, such as, but not limited to, streptavidin/biotin and avidin/biotin; fluorescent materials, such as, but not limited to, umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; luminescent materials, such as, but not limited to, luminol; bioluminescent materials, such as but not limited to, luciferase, luciferin, and aequorin; radioactive materials, such as, but not limited to, iodine (^{131}I , ^{125}I , ^{123}I , and ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium (^{115}In , ^{113}In , ^{112}In , and ^{111}In), technetium (^{99}Tc), thallium (^{201}Tl), gallium (^{68}Ga , ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F), ^{153}Sm , ^{177}Lu , ^{159}Gd , ^{149}Pm , ^{140}La , ^{175}Yb , ^{166}Ho , ^{190}Y , ^{47}Sc , ^{186}Re , ^{188}Re , ^{142}Pr , ^{105}Rh , ^{97}Ru , ^{68}Ge , ^{57}Co , ^{65}Zn , ^{85}Sr , ^{32}P , ^{153}Gd , ^{169}Yb , ^{51}Cr , ^{54}Mn , ^{75}Se , ^{113}Sn , and ^{117}Te ; and positron emitting metals using various positron emission tomographies, and norradioactive paramagnetic metal ions.

[0240] The present invention further encompasses uses of antibodies or fragments thereof conjugated to a therapeutic moiety. An antibody or fragment thereof may be conjugated to a therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal

ion, e.g., alpha-emitters. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells.

[0241] Further, an antibody or fragment thereof may be conjugated to a therapeutic moiety or drug moiety that modifies a given biological response. Therapeutic moieties or drug moieties are not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein, peptide, or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, *pseudomonas* exotoxin, cholera toxin, or diphtheria toxin; a protein such as tumor necrosis factor, α -interferon, β -interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, an anti-angiogenic agent; or, a biological response modifier such as, for example, a lymphokine. In one embodiment, the HER3 antibody, or a fragment thereof is conjugated to a therapeutic moiety, such as a cytotoxin, a drug (e.g., an immunosuppressant) or a radiotoxin. Such conjugates are referred to herein as "immunoconjugates". Immunoconjugates that include one or more cytotoxins are referred to as "immunotoxins." A cytotoxin or cytotoxic agent includes any agent that is detrimental to (e.g., kills) cells. Examples include taxon, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, t. colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents also include, for example, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), ablating agents (e.g., mechlorethamine, thioepa chlorambucil, mephalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin, anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine). (See e.g., Seattle Genetics US20090304721).

[0242] Other examples of therapeutic cytotoxins that can be conjugated to an antibody or fragment thereof of the invention include duocarmycins, calicheamicins, maytansines and auristatins, and derivatives thereof. An example of a calicheamicin antibody conjugate is commercially available (MylotargTM; Wyeth-Ayerst).

[0243] Cytotoxins can be conjugated to antibodies or fragments thereof of the invention using linker technology available in the art. Examples of linker types that have been used to conjugate a cytotoxin to an antibody include, but are not limited to, hydrazones, thioethers, esters, disulfides and peptide-containing linkers. A linker can be chosen that is, for example, susceptible to cleavage by low pH within the lysosomal compartment or susceptible to cleavage by proteases, such as proteases preferentially expressed in tumor tissue such as cathepsins (e.g., cathepsins B, C, D).

[0244] For further discussion of types of cytotoxins, linkers and methods for conjugating therapeutic agents to antibodies, see also Saito et al., (2003) *Adv. Drug Deliv. Rev.* 55:199-215; Trail et al., (2003) *Cancer Immunol. Immunother.* 52:328-337; Payne, (2003) *Cancer Cell* 3:207-212; Allen, (2002) *Nat. Rev. Cancer* 2:750-763; Pastan and Kreitman, (2002) *Curr.*

Opin. Investig. Drugs 3:1089-1091; Senter and Springer, (2001) Adv. Drug Deliv. Rev. 53:247-264.

[0245] Antibodies or fragments thereof of the present invention also can be conjugated to a radioactive isotope to generate cytotoxic radiopharmaceuticals, also referred to as radioimmunoconjugates. Examples of radioactive isotopes that can be conjugated to antibodies for use diagnostically or therapeutically include, but are not limited to, iodine¹¹¹, indium¹¹¹, yttrium⁹⁰, and lutetium¹⁷⁷. Method for preparing radioimmunoconjugates are established in the art. Examples of radioimmunoconjugates are commercially available, including ZevalinTM (DEC Pharmaceuticals) and BexxarTM (Corixa Pharmaceuticals), and similar methods can be used to prepare radioimmunoconjugates using the antibodies of the invention. In certain embodiments, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) which can be attached to the antibody via a linker molecule. Such linker molecules are commonly known in the art and described in Denardo et al., (1998) Clin Cancer Res. 4(10):2483-90; Peterson et al., (1999) Bioconjug. Chem. 10(4):553-7; and Zimmerman et al., (1999) Nucl. Med. Biol. 26(8):943-50, each incorporated by reference in their entirety.

[0246] Techniques for conjugating therapeutic moieties to antibodies are well known, see, e.g., Amon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies 84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., (1982) Immunol. Rev. 62:119-58.

[0247] Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Antibody Combinations

[0248] An another aspect, the invention pertains to HER3 antibodies, or fragments thereof of the invention used with other therapeutic agents such as another antibodies, small molecule inhibitors, mTOR inhibitors or PI3Kinase inhibitors. Examples include, but are not limited to, the following:

[0249] HER1 inhibitors: The HER3 antibodies or fragments thereof can be used with HER1 inhibitors which include, but are not limited to, Matuzumab (EMD72000), Erbitux[®]/Cetuximab (Imclone), Vectibix[®]/Panitumumab (Amgen), mAb 806, and Nimotuzumab (TheraCIM), Iressa[®]/Gefitinib (Astrazeneca); CI-1033 (PD183805) (Pfizer), Lapatinib (GW-572016) (GlaxoSmithKline), Tykerb[®]/Lapatinib Ditosylate (SmithKlineBeecham), Tarceva[®]/Erlotinib HCL (OSI-774) (OSI Pharma), and PKI-166 (Novartis), and N-[4-[(3-Chloro-4-fluorophenyl)amino]-7-[[3 "S"]-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4(dimethylamino)-2-butenamide, sold under the tradename Tovok[®] by Boehringer Ingelheim).

[0250] HER2 inhibitors: The HER3 antibodies or fragments thereof can be used with HER2 inhibitors which include, but are not limited to, Pertuzumab (sold under the trademark Omnitarg[®], by Genentech), Trastuzumab (sold under the trademark Herceptin[®] by Genentech/Roche), MM-111, neratinib (also known as HKI-272, (2E)-N-[4-[[3-chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-3-cyano-7-ethoxyquinolin-6-yl]-4-(dimethylamino)but-2-enamide, and described PCT Publication No. WO 05/028443), lapatinib or lapatinib ditosylate (sold under the trademark Tykerb[®] by GlaxoSmithKline).

[0251] HER3 inhibitors: The HER3 antibodies or fragments thereof can be used with HER3 inhibitors which include, but are not limited to, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203 (Aveo), MEHD7945A (Genentech), and small molecules that inhibit HER3.

[0252] HER4 inhibitors: The HER3 antibodies or fragments thereof can be used with HER4 inhibitors.

[0253] PI3K inhibitors: The HER3 antibodies or fragments thereof can be used with PI3 kinase inhibitors which include, but are not limited to, 4-[2-(1H-Indazol-4-yl)-6-[[4-(methylsulfonyl)piperazin-1-yl]methyl]thieno[3,2-d]pyrimidin-4-yl]morpholine (also known as GDC 0941 and described in PCT Publication Nos. WO 09/036,082 and WO 09/055,730), 2-Methyl-2-[4-[3-methyl-2-oxo-8-(quinolin-3-yl)-2,3-dihydroimidazo[4,5-c]quinolin-1-yl]phenyl]propionitrile (also known as BEZ 235 or NVP-BEZ 235, and described in PCT Publication No. WO 06/122806), BKM120 and BYL719.

[0254] mTOR inhibitors: The HER3 antibodies or fragments thereof can be used with mTOR inhibitors which include, but are not limited to, Temsirolimus (sold under the tradename Torisel[®] by Pfizer), ridaforolimus (formally known as deferolimus, (1R,2R,4S)-4-[(2R)-2-[(1R,9S,12S,15R,16E,18R,19R,21R,23S,24E,26E,28Z,30S,32S,35R)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23,29,35-hexamethyl-2,3,10,14,20-penta-oxo-11,36-dioxo-4-azatricyclo[30.3.1.04,9]hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as Deforolimus, AP23573 and MK8669 (Ariad Pharm.), and described in PCT Publication No. WO 03/064383), everolimus (RAD001) (sold under the tradename Afinitor[®] by Novartis), One or more therapeutic agents may be administered either simultaneously or before or after administration of a HER3 antibody or fragment thereof of the present invention.

Methods of Producing Antibodies of the Invention

(i) Nucleic Acids Encoding the Antibodies

[0255] The invention provides substantially purified nucleic acid molecules which encode polypeptides comprising segments or domains of the HER3 antibody chains described above.

[0256] Some of the nucleic acids of the invention comprise the nucleotide sequence encoding the HER3 antibody heavy chain variable region, and/or the nucleotide sequence encoding the light chain variable region. In a specific embodiment, the nucleic acid molecules are those identified in Table 1 or Table 2. Some other nucleic acid molecules of the invention comprise nucleotide sequences that are substantially identical (e.g., at least 80%, 90%, 95%, 96%, 97%, 98%, or 99%) to the nucleotide sequences of those identified in Table 1 or Table 2. When expressed from appropriate expression vectors,

polypeptides encoded by these polynucleotides are capable of exhibiting HER3 antigen binding capacity.

[0257] Also provided in the invention are polynucleotides which encode at least one CDR region and usually all three CDR regions from the heavy or light chain of the antibody or fragment thereof set forth above. Some other polynucleotides encode all or substantially all of the variable region sequence of the heavy chain and/or the light chain of the antibody or fragment thereof set forth above. Because of the degeneracy of the code, a variety of nucleic acid sequences will encode each of the immunoglobulin amino acid sequences.

[0258] The nucleic acid molecules of the invention can encode both a variable region and a constant region of the antibody. Some of nucleic acid sequences of the invention comprise nucleotides encoding a mature heavy chain variable region sequence that is substantially identical (e.g., at least 80%, 90%, 95%, 96%, 97%, 98%, or 99%) to the mature heavy chain variable region sequence of a HER3 antibody set forth in Table 1 or Table 2. Some other nucleic acid sequences comprising nucleotide encoding a mature light chain variable region sequence that is substantially identical (e.g., at least 80%, 90%, 95%, 96%, 97%, 98%, or 99%) to the mature light chain variable region sequence of a HER3 antibody set forth in Table 1 or Table 2.

[0259] The polynucleotide sequences can be produced by de novo solid-phase DNA synthesis or by PCR mutagenesis of an existing sequence encoding the antibody or fragment thereof. Direct chemical synthesis of nucleic acids can be accomplished by methods known in the art, such as the phosphotriester method of Narang et al., (1979) Meth. Enzymol. 68:90; the phosphodiester method of Brown et al., (1979) Meth. Enzymol. 68:109; the diethylphosphoramidite method of Beaucage et al., (1981) Tetra. Lett., 22:1859; and the solid support method of U.S. Pat. No. 4,458,066. Introducing mutations to a polynucleotide sequence by PCR can be performed as described in, e.g., PCR Technology: Principles and Applications for DNA Amplification, H. A. Erlich (Ed.), Freeman Press, NY, N.Y., 1992; PCR Protocols: A Guide to Methods and Applications, Innis et al. (Ed.), Academic Press, San Diego, Calif., 1990; Mattila et al., (1991) Nucleic Acids Res. 19:967; and Eckert et al., (1991) PCR Methods and Applications 1:17.

[0260] Also provided in the invention are expression vectors and host cells for producing the antibodies or fragments thereof. Various expression vectors can be employed to express the polynucleotides encoding the HER3 antibody chains or fragments thereof. Both viral-based and nonviral expression vectors can be used to produce the antibodies in a mammalian host cell. Nonviral vectors and systems include plasmids, episomal vectors, typically with an expression cassette for expressing a protein or RNA, and human artificial chromosomes (see, e.g., Harrington et al., (1997) Nat Genet. 15:345). For example, nonviral vectors useful for expression of the HER3 polynucleotides and polypeptides in mammalian (e.g., human) cells include pThioHis A, B & C, pcDNA3.1/His, pEBVHis A, B & C, (Invitrogen, San Diego, Calif.), MPSV vectors, and numerous other vectors known in the art for expressing other proteins. Useful viral vectors include vectors based on retroviruses, adenoviruses, adenoassociated viruses, herpes viruses, vectors based on SV40, papilloma virus, HBP Epstein Barr virus, vaccinia virus vectors and Semliki Forest virus (SFV). See, Brent et al., (1995) supra; Smith, Annu. Rev. Microbiol. 49:807; and Rosenfeld et al., (1992) Cell 68:143.

[0261] The choice of expression vector depends on the intended host cells in which the vector is to be expressed. Typically, the expression vectors contain a promoter and other regulatory sequences (e.g., enhancers) that are operably linked to the polynucleotides encoding an antibody chain or fragment thereof. In some embodiments, an inducible promoter is employed to prevent expression of inserted sequences except under inducing conditions. Inducible promoters include, e.g., arabinose, lacZ, metallothionein promoter or a heat shock promoter. Cultures of transformed organisms can be expanded under noninducing conditions without biasing the population for coding sequences whose expression products are better tolerated by the host cells. In addition to promoters, other regulatory elements may also be required or desired for efficient expression of antibody chain or fragment thereof. These elements typically include an ATG initiation codon and adjacent ribosome binding site or other sequences. In addition, the efficiency of expression may be enhanced by the inclusion of enhancers appropriate to the cell system in use (see, e.g., Scharf et al., (1994) Results Probl. Cell Differ. 20:125; and Bittner et al., (1987) Meth. Enzymol., 153:516). For example, the SV40 enhancer or CMV enhancer may be used to increase expression in mammalian host cells.

[0262] The expression vectors may also provide a secretion signal sequence position to form a fusion protein with polypeptides encoded by inserted antibody or fragment sequences. More often, the inserted antibody or fragment sequences are linked to a signal sequences before inclusion in the vector. Vectors to be used to receive sequences encoding the antibody or fragment light and heavy chain variable domains sometimes also encode constant regions or parts thereof. Such vectors allow expression of the variable regions as fusion proteins with the constant regions thereby leading to production of intact antibodies or fragments thereof. Typically, such constant regions are human.

[0263] The host cells for harboring and expressing the antibody or fragment chains can be either prokaryotic or eukaryotic. *E. coli* is one prokaryotic host useful for cloning and expressing the polynucleotides of the present invention. Other microbial hosts suitable for use include bacilli, such as *Bacillus subtilis*, and other enterobacteriaceae, such as *Salmonella*, *Serratia*, and various *Pseudomonas* species. In these prokaryotic hosts, one can also make expression vectors, which typically contain expression control sequences compatible with the host cell (e.g., an origin of replication). In addition, any number of a variety of well-known promoters will be present, such as the lactose promoter system, a tryptophan (trp) promoter system, a beta-lactamase promoter system, or a promoter system from phage lambda. The promoters typically control expression, optionally with an operator sequence, and have ribosome binding site sequences and the like, for initiating and completing transcription and translation. Other microbes, such as yeast, can also be employed to express antibodies or fragments thereof. Insect cells in combination with baculovirus vectors can also be used.

[0264] In some preferred embodiments, mammalian host cells are used to express and produce the antibodies or fragments thereof. For example, they can be either a hybridoma cell line expressing endogenous immunoglobulin genes or a mammalian cell line harboring an exogenous expression vector. These include any normal mortal or normal or abnormal immortal animal or human cell. For example, a number of suitable host cell lines capable of secreting intact immunoglobulins have been developed including the CHO cell lines,

various Cos cell lines, HeLa cells, myeloma cell lines, transformed B-cells and hybridomas. The use of mammalian tissue cell culture to express polypeptides is discussed generally in, e.g., Winnacker, *FROM GENES TO CLONES*, VCH Publishers, N.Y., N.Y., 1987. Expression vectors for mammalian host cells can include expression control sequences, such as an origin of replication, a promoter, and an enhancer (see, e.g., Queen et al., (1986) *Immunol. Rev.* 89:49-68), and necessary processing information sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites, and transcriptional terminator sequences. These expression vectors usually contain promoters derived from mammalian genes or from mammalian viruses. Suitable promoters may be constitutive, cell type-specific, stage-specific, and/or modulatable or regulatable. Useful promoters include, but are not limited to, the metallothionein promoter, the constitutive adenovirus major late promoter, the dexamethasone-inducible MMTV promoter, the SV40 promoter, the MRP polIII promoter, the constitutive MPSV promoter, the tetracycline-inducible CMV promoter (such as the human immediate-early CMV promoter), the constitutive CMV promoter, and promoter-enhancer combinations known in the art.

[0265] Methods for introducing expression vectors containing the polynucleotide sequences of interest vary depending on the type of cellular host. For example, calcium chloride transfection is commonly utilized for prokaryotic cells, whereas calcium phosphate treatment or electroporation may be used for other cellular hosts. (See generally Sambrook, et al., *supra*). Other methods include, e.g., electroporation, calcium phosphate treatment, liposome-mediated transformation, injection and microinjection, ballistic methods, virosomes, immunoliposomes, polycation:nucleic acid conjugates, naked DNA, artificial virions, fusion to the herpes virus structural protein VP22 (Elliot and O'Hare, (1997) *Cell* 88:223), agent-enhanced uptake of DNA, and *ex vivo* transduction. For long-term, high-yield production of recombinant proteins, stable expression will often be desired. For example, cell lines which stably express antibody chains or fragments can be prepared using expression vectors of the invention which contain viral origins of replication or endogenous expression elements and a selectable marker gene. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth of cells which successfully express the introduced sequences in selective media. Resistant, stably transfected cells can be proliferated using tissue culture techniques appropriate to the cell type.

(ii) Generation of Monoclonal Antibodies of the Invention

[0266] Monoclonal antibodies (mAbs) can be produced by a variety of techniques, including conventional monoclonal antibody methodology e.g., the standard somatic cell hybridization technique of Kohler and Milstein, (1975) *Nature* 256: 495. Many techniques for producing monoclonal antibody can be employed e.g., viral or oncogenic transformation of B lymphocytes.

[0267] An animal system for preparing hybridomas is the murine system. Hybridoma production in the mouse is a well established procedure. Immunization protocols and techniques for isolation of immunized splenocytes for fusion are known in the art. Fusion partners (e.g., murine myeloma cells) and fusion procedures are also known.

[0268] Chimeric or humanized antibodies of the present invention can be prepared based on the sequence of a murine monoclonal antibody prepared as described above. DNA encoding the heavy and light chain immunoglobulins can be obtained from the murine hybridoma of interest and engineered to contain non-murine (e.g., human) immunoglobulin sequences using standard molecular biology techniques. For example, to create a chimeric antibody, the murine variable regions can be linked to human constant regions using methods known in the art (see e.g., U.S. Pat. No. 4,816,567 to Cabilly et al.). To create a humanized antibody, the murine CDR regions can be inserted into a human framework using methods known in the art. See e.g., U.S. Pat. No. 5,225,539 to Winter, and U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al.

[0269] In a certain embodiment, the antibodies of the invention are human monoclonal antibodies. Such human monoclonal antibodies directed against HER3 can be generated using transgenic or transchromosomal mice carrying parts of the human immune system rather than the mouse system. These transgenic and transchromosomal mice include mice referred to herein as HuMAb mice and KM mice, respectively, and are collectively referred to herein as "human Ig mice."

[0270] The HuMAb Mouse® (Medarex, Inc.) contains human immunoglobulin gene miniloci that encode un-rearranged human heavy (μ and γ) and κ light chain immunoglobulin sequences, together with targeted mutations that inactivate the endogenous μ and κ chain loci (see e.g., Lonberg et al., (1994) *Nature* 368(6474): 856-859). Accordingly, the mice exhibit reduced expression of mouse IgM or κ , and in response to immunization, the introduced human heavy and light chain transgenes undergo class switching and somatic mutation to generate high affinity human IgGk monoclonal (Lonberg et al., (1994) *supra*; reviewed in Lonberg, (1994) *Handbook of Experimental Pharmacology* 113:49-101; Lonberg and Huszar, (1995) *Intern. Rev. Immunol.* 13:65-93, and Harding and Lonberg, (1995) *Ann. N.Y. Acad. Sci.* 764:536-546). The preparation and use of HuMAb mice, and the genomic modifications carried by such mice, is further described in Taylor et al., (1992) *Nucleic Acids Research* 20:6287-6295; Chen et al., (1993) *International Immunology* 5:647-656; Tuailon et al., (1993) *Proc. Natl. Acad. Sci. USA* 94:3720-3724; Choi et al., (1993) *Nature Genetics* 4:117-123; Chen et al., (1993) *EMBO J.* 12:821-830; Tuailon et al., (1994) *J. Immunol.* 152:2912-2920; Taylor et al., (1994) *International Immunology* 579-591; and Fishwild et al., (1996) *Nature Biotechnology* 14:845-851, the contents of all of which are hereby specifically incorporated by reference in their entirety. See further, U.S. Pat. Nos. 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,789,650; 5,877,397; 5,661,016; 5,814,318; 5,874,299; and 5,770,429; all to Lonberg and Kay; U.S. Pat. No. 5,545,807 to Surani et al.; PCT Publication Nos. WO 92103918, WO 93/12227, WO 94/25585, WO 97113852, WO 98/24884 and WO 99/45962, all to Lonberg and Kay; and PCT Publication No. WO 01/14424 to Korman et al.

[0271] In another embodiment, human antibodies of the invention can be raised using a mouse that carries human immunoglobulin sequences on transgenes and transchromosomes such as a mouse that carries a human heavy chain transgene and a human light chain transchromosome. Such mice, referred to herein as "KM mice", are described in detail in PCT Publication WO 02/43478 to Ishida et al.

[0272] Still further, alternative transgenic animal systems expressing human immunoglobulin genes are available in the art and can be used to raise HER3 antibodies of the invention. For example, an alternative transgenic system referred to as the Xenomouse (Abgenix, Inc.) can be used. Such mice are described in, e.g., U.S. Pat. Nos. 5,939,598; 6,075,181; 6,114,598; 6,150,584 and 6,162,963 to Kucherlapati et al.

[0273] Moreover, alternative transchromosomal animal systems expressing human immunoglobulin genes are available in the art and can be used to raise HER3 antibodies of the invention. For example, mice carrying both a human heavy chain transchromosome and a human light chain transchromosome, referred to as "TC mice" can be used; such mice are described in Tomizuka et al., (2000) Proc. Natl. Acad. Sci. USA 97:722-727. Furthermore, cows carrying human heavy and light chain transchromosomes have been described in the art (Kuroiwa et al., (2002) Nature Biotechnology 20:889-894) and can be used to raise HER3 antibodies of the invention.

[0274] Human monoclonal antibodies of the invention can also be prepared using phage display methods for screening libraries of human immunoglobulin genes. Such phage display methods for isolating human antibodies are established in the art or described in the examples below. See for example: U.S. Pat. Nos. 5,223,409; 5,403,484; and 5,571,698 to Ladner et al.; U.S. Pat. Nos. 5,427,908 and 5,580,717 to Dower et al.; U.S. Pat. Nos. 5,969,108 and 6,172,197 to McCafferty et al.; and U.S. Pat. Nos. 5,885,793; 6,521,404; 6,544,731; 6,555,313; 6,582,915 and 6,593,081 to Griffiths et al.

[0275] Human monoclonal antibodies of the invention can also be prepared using SCID mice into which human immune cells have been reconstituted such that a human antibody response can be generated upon immunization. Such mice are described in, for example, U.S. Pat. Nos. 5,476,996 and 5,698,767 to Wilson et al.

(Iii) Framework or Fc Engineering

[0276] Engineered antibodies of the invention include those in which modifications have been made to framework residues within VH and/or VL, e.g. to improve the properties of the antibody. Typically such framework modifications are made to decrease the immunogenicity of the antibody. For example, one approach is to "backmutate" one or more framework residues to the corresponding germline sequence. More specifically, an antibody that has undergone somatic mutation may contain framework residues that differ from the germline sequence from which the antibody is derived. Such residues can be identified by comparing the antibody framework sequences to the germline sequences from which the antibody is derived. To return the framework region sequences to their germline configuration, the somatic mutations can be "backmutated" to the germline sequence by, for example, site-directed mutagenesis. Such "backmutated" antibodies are also intended to be encompassed by the invention.

[0277] Another type of framework modification involves mutating one or more residues within the framework region, or even within one or more CDR regions, to remove T cell epitopes to thereby reduce the potential immunogenicity of the antibody. This approach is also referred to as "deimmunization" and is described in further detail in U.S. Patent Publication No. 20030153043 by Carr et al.

[0278] In addition or alternative to modifications made within the framework or CDR regions, antibodies of the

invention may be engineered to include modifications within the Fc region, typically to alter one or more functional properties of the antibody, such as serum half-life, complement fixation, Fc receptor binding, and/or antigen-dependent cellular cytotoxicity.

[0279] Furthermore, an antibody of the invention may be chemically modified (e.g., one or more chemical moieties can be attached to the antibody) or be modified to alter its glycosylation, again to alter one or more functional properties of the antibody. Each of these embodiments is described in further detail below. The numbering of residues in the Fc region is that of the EU index of Kabat.

[0280] In one embodiment, the hinge region of CH1 is modified such that the number of cysteine residues in the hinge region is altered, e.g., increased or decreased. This approach is described further in U.S. Pat. No. 5,677,425 by Bodmer et al. The number of cysteine residues in the hinge region of CH1 is altered to, for example, facilitate assembly of the light and heavy chains or to increase or decrease the stability of the antibody.

[0281] In another embodiment, the Fc hinge region of an antibody is mutated to decrease the biological half-life of the antibody. More specifically, one or more amino acid mutations are introduced into the CH2-CH3 domain interface region of the Fc-hinge fragment such that the antibody has impaired Staphylococcal protein A (SpA) binding relative to native Fc-hinge domain SpA binding. This approach is described in further detail in U.S. Pat. No. 6,165,745 by Ward et al.

[0282] In yet other embodiments, the Fc region is altered by replacing at least one amino acid residue with a different amino acid residue to alter the effector functions of the antibody. For example, one or more amino acids can be replaced with a different amino acid residue such that the antibody has an altered affinity for an effector ligand but retains the antigen-binding ability of the parent antibody. The effector ligand to which affinity is altered can be, for example, an Fc receptor or the C1 component of complement. This approach is described in further detail in U.S. Pat. Nos. 5,624,821 and 5,648,260, both by Winter et al.

[0283] In another embodiment, one or more amino acids selected from amino acid residues can be replaced with a different amino acid residue such that the antibody has altered C1q binding and/or reduced or abolished complement dependent cytotoxicity (CDC). This approach is described in further detail in U.S. Pat. No. 6,194,551 by Idusogie et al.

[0284] In another embodiment, one or more amino acid residues are altered to thereby alter the ability of the antibody to fix complement. This approach is described further in PCT Publication WO 94/29351 by Bodmer et al.

[0285] In yet another embodiment, the Fc region is modified to increase the ability of the antibody to mediate antibody dependent cellular cytotoxicity (ADCC) and/or to increase the affinity of the antibody for an Fc receptor by modifying one or more amino acids. This approach is described further in PCT Publication WO 00/42072 by Presta. Moreover, the binding sites on human IgG1 for FcγR1, FcγR2, FcγR3 and FcRn have been mapped and variants with improved binding have been described (see Shields et al., (2001) J. Biol. Chem. 276:6591-6604).

[0286] In still another embodiment, the glycosylation of an antibody is modified. For example, an aglycosylated antibody can be made (i.e., the antibody lacks glycosylation). Glycosylation can be altered to, for example, increase the affinity of

the antibody for “antigen”. Such carbohydrate modifications can be accomplished by, for example, altering one or more sites of glycosylation within the antibody sequence. For example, one or more amino acid substitutions can be made that result in elimination of one or more variable region framework glycosylation sites to thereby eliminate glycosylation at that site. Such aglycosylation may increase the affinity of the antibody for antigen. Such an approach is described in further detail in U.S. Pat. Nos. 5,714,350 and 6,350,861 by Co et al.

[0287] Additionally or alternatively, an antibody can be made that has an altered type of glycosylation, such as a hypofucosylated antibody having reduced amounts of fucosyl residues or an antibody having increased bisecting GlcNAc structures. Such altered glycosylation patterns have been demonstrated to increase the ADCC ability of antibodies. Such carbohydrate modifications can be accomplished by, for example, expressing the antibody in a host cell with altered glycosylation machinery. Cells with altered glycosylation machinery have been described in the art and can be used as host cells in which to express recombinant antibodies of the invention to thereby produce an antibody with altered glycosylation. For example, EP 1,176,195 by Hang et al. describes a cell line with a functionally disrupted FUT8 gene, which encodes a fucosyl transferase, such that antibodies expressed in such a cell line exhibit hypofucosylation. PCT Publication WO 03/035835 by Presta describes a variant CHO cell line, Lec13 cells, with reduced ability to attach fucose to Asn(297)-linked carbohydrates, also resulting in hypofucosylation of antibodies expressed in that host cell (see also Shields et al., (2002) *J. Biol. Chem.* 277:26733-26740). PCT Publication WO 99/54342 by Umana et al. describes cell lines engineered to express glycoprotein-modifying glycosyl transferases (e.g., beta(1,4)—N acetylglucosaminyltransferase III (GnTIII)) such that antibodies expressed in the engineered cell lines exhibit increased bisecting GlcNAc structures which results in increased ADCC activity of the antibodies (see also Umana et al., (1999) *Nat. Biotech.* 17:176-180).

[0288] In another embodiment, the antibody is modified to increase its biological half-life. Various approaches are possible. For example, one or more of the following mutations can be introduced: T252L, T254S, T256F, as described in U.S. Pat. No. 6,277,375 to Ward. Alternatively, to increase the biological half life, the antibody can be altered within the CH1 or CL region to contain a salvage receptor binding epitope taken from two loops of a CH2 domain of an Fc region of an IgG, as described in U.S. Pat. Nos. 5,869,046 and 6,121,022 by Presta et al.

(iv) Methods of Engineering Altered Antibodies

[0289] The HER3 antibodies or fragments thereof of the invention having VH and VL sequences or full length heavy and light chain sequences shown herein can be used to create new HER3 antibodies by modifying full length heavy chain and/or light chain sequences, VH and/or VL sequences, or the constant region(s) attached thereto. Thus, in another aspect of the invention, the structural features of a HER3 antibody or fragment thereof are used to create structurally related HER3 antibodies that retain at least one functional property of the antibodies of the invention, such as binding to human HER3 and also inhibiting one or more functional properties of HER3. For example, one or more CDR regions of the antibodies of the present invention, or mutations thereof, can be

combined recombinantly with known framework regions and/or other CDRs to create additional, recombinantly-engineered, HER3 antibodies as discussed above. Other types of modifications include those described in the previous section. The starting material for the engineering method is one or more of the VH and/or VL sequences provided herein, or one or more CDR regions thereof. To create the engineered antibody, it is not necessary to actually prepare (i.e., express as a protein) an antibody having one or more of the VH and/or VL sequences provided herein, or one or more CDR regions thereof. Rather, the information contained in the sequence(s) is used as the starting material to create a “second generation” sequence(s) derived from the original sequence(s) and then the “second generation” sequence(s) is prepared and expressed as a protein.

[0290] Accordingly, in another embodiment, the invention provides a method for preparing a antibody that binds to domain 3 of HER3 consisting of: a heavy chain variable region antibody sequence having a CDR1 sequence selected from the group consisting of SEQ ID NOs: 2, 22, 42, 62, 82, 102, 122, 142, and 162; a CDR2 sequence selected from the group consisting of SEQ ID NOs: 3, 23, 43, 63, 83, 103, 123, 143, and 163; and/or a CDR3 sequence selected from the group consisting of SEQ ID NOs: 4, 24, 44, 64, 84, 104, 124, 144, and 164; and a light chain variable region antibody sequence having a CDR1 sequence selected from the group consisting of SEQ ID NOs: 8, 28, 48, 68, 88, 108, 128, 148, and 168; a CDR2 sequence selected from the group consisting of SEQ ID NOs: 9, 29, 49, 69, 89, 109, 129, 149, and 169; and/or a CDR3 sequence selected from the group consisting of SEQ ID NOs: 10, 30, 50, 70, 90, 110, 130, 150, and 170; altering at least one amino acid residue within the heavy chain variable region antibody sequence and/or the light chain variable region antibody sequence to create at least one altered antibody sequence; and expressing the altered antibody sequence as a protein. The altered antibody sequence can also be prepared by screening antibody libraries having fixed CDR3 sequences or minimal essential binding determinants as described in US20050255552 and diversity on CDR1 and CDR2 sequences. The screening can be performed according to any screening technology appropriate for screening antibodies from antibody libraries, such as phage display technology.

[0291] Accordingly, in another embodiment, the invention provides a method for preparing a antibody that binds to domains 3-4 of HER3 consisting of: a heavy chain variable region antibody sequence having a CDR1 sequence selected from the group consisting of SEQ ID NOs: 182, 202, 222, 242, 262, 282, 302, 322, 342, 362, 382, 402, 422, 442, 462, 482, 502, 522, 542, 562, 582, 602, 622, 642, 662, and 682; a CDR2 sequence selected from the group consisting of SEQ ID NOs: 183, 203, 223, 243, 263, 283, 303, 323, 343, 363, 383, 403, 423, 443, 463, 483, 503, 523, 543, 563, 583, 603, 623, 643, 663, and 683; and/or a CDR3 sequence selected from the group consisting of SEQ ID NOs: 184, 204, 224, 244, 264, 284, 304, 324, 344, 364, 384, 404, 424, 444, 464, 484, 504, 524, 544, 564, 584, 604, 624, 644, 664, and 684; and a light chain variable region antibody sequence having a CDR1 sequence selected from the group consisting of SEQ ID NOs: 188, 208, 228, 248, 268, 288, 308, 328, 348, 368, 388, 408, 428, 448, 468, 488, 508, 528, 548, 568, 588, 608, 628, 648, 668, and 688; a CDR2 sequence selected from the group consisting of SEQ ID NOs: 189, 209, 229, 249, 269, 289, 309, 329, 349, 369, 389, 409, 429, 449, 469, 489, 509,

529, 549, 569, 589, 609, 629, 649, 669, and 689; and/or a CDR3 sequence selected from the group consisting of SEQ ID NOs: 190, 210, 230, 250, 270, 290, 310, 330, 350, 370, 390, 410, 430, 450, 470, 490, 510, 530, 550, 570, 590, 610, 630, 650, 670, and 690; altering at least one amino acid residue within the heavy chain variable region antibody sequence and/or the light chain variable region antibody sequence to create at least one altered antibody sequence; and expressing the altered antibody sequence as a protein. The altered antibody sequence can also be prepared by screening antibody libraries having fixed CDR3 sequences or minimal essential binding determinants as described in US20050255552 and diversity on CDR1 and CDR2 sequences. The screening can be performed according to any screening technology appropriate for screening antibodies from antibody libraries, such as phage display technology.

[0292] Standard molecular biology techniques can be used to prepare and express the altered antibody sequence. The antibody encoded by the altered antibody sequence(s) is one that retains one, some or all of the functional properties of the antibodies or fragments thereof described herein, which functional properties include, but are not limited to, specifically binding to human and/or cynomolgus HER3; the antibody binds to HER3 and inhibits HER3 biological activity by inhibiting the HER signaling activity in a phospho-HER assay.

[0293] The functional properties of the altered antibodies can be assessed using standard assays available in the art and/or described herein, such as those set forth in the Examples (e.g., ELISAs).

[0294] In certain embodiments of the methods of engineering antibodies of the invention, mutations can be introduced randomly or selectively along all or part of an antibody or fragment coding sequence and the resulting modified HER3 antibodies can be screened for binding activity and/or other functional properties as described herein. Mutational methods have been described in the art. For example, PCT Publication WO 02/092780 by Short describes methods for creating and screening antibody mutations using saturation mutagenesis, synthetic ligation assembly, or a combination thereof. Alternatively, PCT Publication WO 03/074679 by Lazar et al. describes methods of using computational screening methods to optimize physiochemical properties of antibodies.

Characterization of the Antibodies of the Invention

[0295] The antibodies of the invention can be characterized by various functional assays. For example, they can be characterized by their ability to inhibit biological activity by inhibiting HER signaling in a phospho-HER assay as described herein, their affinity to a HER3 protein (e.g., human and/or cynomolgus HER3), the epitope binning, their resistance to proteolysis, and their ability to block HER3 downstream signaling. Various methods can be used to measure HER3-mediated signaling. For example, the HER signaling pathway can be monitored by (i) measurement of phospho-HER3; (ii) measurement of phosphorylation of HER3 or other downstream signaling proteins (e.g. Akt), (iii) ligand blocking assays as described herein, (iv) heterodimer formation, (v) HER3 dependent gene expression signature, (vi) receptor internalization, and (vii) HER3 driven cell phenotypes (e.g. proliferation).

[0296] The ability of an antibody to bind to HER3 can be detected by labelling the antibody of interest directly, or the

antibody may be unlabelled and binding detected indirectly using various sandwich assay formats known in the art.

[0297] In some embodiments, the HER3 antibodies block or compete with binding of a reference HER3 antibody to a HER3. These can be fully human HER3 antibodies described above. They can also be other mouse, chimeric or humanized HER3 antibodies which bind to the same epitope as the reference antibody. The capacity to block or compete with the reference antibody binding indicates that a HER3 antibody under test binds to the same or similar epitope as that defined by the reference antibody, or to an epitope which is sufficiently proximal to the epitope bound by the reference HER3 antibody. Such antibodies are especially likely to share the advantageous properties identified for the reference antibody. The capacity to block or compete with the reference antibody may be determined by, e.g., a competition binding assay. With a competition binding assay, the antibody under test is examined for ability to inhibit specific binding of the reference antibody to a common antigen, such as a HER3 polypeptide or protein. A test antibody competes with the reference antibody for specific binding to the antigen if an excess of the test antibody substantially inhibits binding of the reference antibody. Substantial inhibition means that the test antibody reduces specific binding of the reference antibody usually by at least 10%, 25%, 50%, 75%, or 90%.

[0298] There are a number of known competition binding assays that can be used to assess competition of a HER3 antibody with the reference HER3 antibody for binding to a HER3. These include, e.g., solid phase direct or indirect radioimmunoassay (RIA), solid phase direct or indirect enzyme immunoassay (EIA), sandwich competition assay (see Stahl et al., (1983) *Methods in Enzymology* 9:242-253); solid phase direct biotin-avidin EIA (see Kirkland et al., (1986) *J. Immunol.* 137:3614-3619); solid phase direct labeled assay, solid phase direct labeled sandwich assay (see Harlow & Lane, *supra*); solid phase direct label RIA using 1-125 label (see Morel et al., (1988) *Molec. Immunol.* 25:7-15); solid phase direct biotin-avidin EIA (Cheung et al., (1990) *Virology* 176:546-552); and direct labeled RIA (Moldenhauer et al., (1990) *Scand. J. Immunol.* 32:77-82). Typically, such an assay involves the use of purified antigen bound to a solid surface or cells bearing either of these, an unlabelled test HER3-binding antibody and a labelled reference antibody. Competitive inhibition is measured by determining the amount of label bound to the solid surface or cells in the presence of the test antibody. Usually the test antibody is present in excess. Antibodies identified by competition assay (competing antibodies) include antibodies binding to the same epitope as the reference antibody and antibodies binding to an adjacent epitope sufficiently proximal to the epitope bound by the reference antibody for steric hindrance to occur.

[0299] To determine if the selected HER3 monoclonal antibodies bind to unique epitopes, each antibody can be biotinylated using commercially available reagents (e.g., reagents from Pierce, Rockford, Ill.). Competition studies using unlabeled monoclonal antibodies and biotinylated monoclonal antibodies can be performed using a HER3 polypeptide coated-ELISA plates. Biotinylated MAb binding can be detected with a strep-avidin-alkaline phosphatase probe. To determine the isotype of a purified HER3-binding antibody, isotype ELISAs can be performed. For example, wells of microtiter plates can be coated with 1 µg/ml of anti-human IgG overnight at 4° C. After blocking with 1% BSA, the plates

are reacted with 1 µg/ml or less of the monoclonal HER3 antibody or purified isotype controls, at ambient temperature for one to two hours. The wells can then be reacted with either human IgG1 or human IgM-specific alkaline phosphatase-conjugated probes. Plates are then developed and analyzed so that the isotype of the purified antibody can be determined.

[0300] To demonstrate binding of monoclonal HER3 antibodies to live cells expressing a HER3 polypeptide, flow cytometry can be used. Briefly, cell lines expressing HER3 (grown under standard growth conditions) can be mixed with various concentrations of a HER3-binding antibody in PBS containing 0.1% BSA and 10% fetal calf serum, and incubated at 4° C. for 1 hour. After washing, the cells are reacted with Fluorescein-labeled anti-human IgG antibody under the same conditions as the primary antibody staining. The samples can be analyzed by FACScan instrument using light and side scatter properties to gate on single cells. An alternative assay using fluorescence microscopy may be used (in addition to or instead of) the flow cytometry assay. Cells can be stained exactly as described above and examined by fluorescence microscopy. This method allows visualization of individual cells, but may have diminished sensitivity depending on the density of the antigen.

[0301] The antibodies or fragments thereof of the invention can be further tested for reactivity with a HER3 polypeptide or antigenic fragment by Western blotting. Briefly, purified HER3 polypeptides or fusion proteins, or cell extracts from cells expressing HER3 can be prepared and subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis. After electrophoresis, the separated antigens are transferred to nitrocellulose membranes, blocked with 10% fetal calf serum, and probed with the monoclonal antibodies to be tested. Human IgG binding can be detected using anti-human IgG alkaline phosphatase and developed with BCIP/NBT substrate tablets (Sigma Chem. Co., St. Louis, Mo.).

[0302] A number of readouts can be used to assess the efficacy, and specificity, of HER3 antibodies in cell-based assays of ligand-induced heterodimer formation. Activity can be assessed by one or more of the following:

[0303] (i) Inhibition of ligand-induced heterodimerisation of HER2 with other EGF family members in a target cell line, for example MCF-7 breast cancer cells. Immunoprecipitation of HER2 complexes from cell lysates can be performed with a receptor-specific antibody, and the absence/presence of other EGF receptors and their biologically relevant ligands within the complex can be analysed following electrophoresis/Western transfer by probing with antibodies to other EGF receptors.

[0304] (ii) Inhibition of the activation of signaling pathways by ligand-activated heterodimers.

[0305] Association with HER3 appears key for other members of the EGF family of receptors to elicit maximal cellular response following ligand binding. In the case of the kinase-defective HER3, HER2 provides a functional tyrosine kinase domain to enable signaling to occur following binding of growth factor ligands. Thus, cells co-expressing HER2 and HER3 can be treated with ligand, for example heregulin, in the absence and presence of inhibitor and the effect on HER3 tyrosine phosphorylation monitored by a number of ways including immunoprecipitation of HER3 from treated cell lysates and subsequent Western blotting using anti-phosphotyrosine antibodies (see Agus op. cit. for details). Alternatively, a high-throughput assay can be developed by trapping HER3 from solubilized lysates onto the wells of a 96-well

plate coated with an anti-HER3 receptor antibody, and the level of tyrosine phosphorylation measured using, for example, europium-labelled anti-phosphotyrosine antibodies, as embodied by Waddleton et al., (2002) *Anal. Biochem.* 309:150-157.

[0306] In a broader extension of this approach, effector molecules known to be activated downstream of activated receptor heterodimers, such as mitogen-activated protein kinases (MAPK) and Akt, may be analysed directly, by immunoprecipitation from treated lysates and blotting with antibodies that detect the activated forms of these proteins, or by analysing the ability of these proteins to modify/activate specific substrates.

[0307] (iii) Inhibition of ligand-induced cellular proliferation. A variety of cell lines are known to co-express combinations of ErbB receptors, for example many breast and prostate cancer cell lines. Assays may be performed in 24/48/96-well formats with the readout based around DNA synthesis (tritiated thymidine incorporation), increase in cell number (crystal violet staining) etc.

[0308] A number of readouts can be used to assess the efficacy, and specificity, of HER3 antibodies in cell-based assays of ligand-independent homo- and heterodimer formation. For example, HER2 overexpression triggers ligand-independent activation of the kinase domain as a result of spontaneous dimer formation. Over expressed HER2 generates either homo- or heterodimers with other HER molecules such as HER1, HER3 and HER4.

[0309] Ability of antibodies or fragments thereof to block in vivo growth of tumour xenografts of human tumour cell lines whose tumorigenic phenotype is known to be at least partly dependent on ligand activation of HER3 heterodimer cell signaling e.g. BxPC3 pancreatic cancer cells etc. This can be assessed in immunocompromised mice either alone or in combination with an appropriate cytotoxic agent for the cell line in question. Examples of functional assays are also described in the Example section below.

Prophylactic and Therapeutic Uses

[0310] The present invention provides methods of treating a disease or disorder associated with the HER3 signaling pathway by administering to a subject in need thereof an effective amount of the antibody or fragment thereof of the invention. In a specific embodiment, the present invention provides a method of treating or preventing cancers (e.g., breast cancer, colorectal cancer, lung cancer, multiple myeloma, ovarian cancer, liver cancer, gastric cancer, pancreatic cancer, acute myeloid leukemia, chronic myeloid leukemia, osteosarcoma, squamous cell carcinoma, peripheral nerve sheath tumors, schwannoma, head and neck cancer, bladder cancer, esophageal cancer, Barretts esophageal cancer, glioblastoma, clear cell sarcoma of soft tissue, malignant mesothelioma, neurofibromatosis, renal cancer, melanoma, prostate cancer, benign prostatic hyperplasia (BPH), gynaecomastia, and endometriosis) by administering to a subject in need thereof an effective amount of the antibodies or fragments thereof of the invention. In some embodiments, the present invention provides methods of treating or preventing cancers associated with a HER3 signaling pathway by administering to a subject in need thereof an effective amount of the antibodies of the invention.

[0311] In a specific embodiment, the present invention provides methods of treating cancers associated with a HER3 signaling pathway that include, but are not limited to breast

cancer, colorectal cancer, lung cancer, multiple myeloma, ovarian cancer, liver cancer, gastric cancer, pancreatic cancer, acute myeloid leukemia, chronic myeloid leukemia, osteosarcoma, squamous cell carcinoma, peripheral nerve sheath tumors schwannoma, head and neck cancer, bladder cancer, esophageal cancer, Barretts esophageal cancer, glioblastoma, clear cell sarcoma of soft tissue, malignant mesothelioma, neurofibromatosis, renal cancer, melanoma, prostate cancer, benign prostatic hyperplasia (BPH), gynacomastica, and endometriosis.

[0312] The antibodies or fragments thereof of the invention can also be used to treat or prevent other disorders associated with aberrant or defective HER3 signaling, including but are not limited to respiratory diseases, osteoporosis, osteoarthritis, polycystic kidney disease, diabetes, schizophrenia, vascular disease, cardiac disease, non-oncogenic proliferative diseases, fibrosis, and neurodegenerative diseases such as Alzheimer's disease.

[0313] Suitable agents for combination treatment with HER3 antibodies include standard of care agents known in the art that are able to modulate the ErbB signaling pathway. Suitable examples of standard of care agents for HER2 include, but are not limited to Herceptin and Tykerb. Suitable examples of standard of care agents for EGFR include, but are not limited to Iressa, Tarceva, Erbitux and Vectibix as described above. Other agents that may be suitable for combination treatment with HER3 antibodies include, but are not limited to those that modulate receptor tyrosine kinases, G-protein coupled receptors, growth/survival signal transduction pathways, nuclear hormone receptors, apoptotic pathways, cell cycle and angiogenesis.

Diagnostic Uses

[0314] In one aspect, the invention encompasses diagnostic assays for determining HER3 and/or nucleic acid expression as well as HER3 protein function, in the context of a biological sample (e.g., blood, serum, cells, tissue) or from individual afflicted with cancer, or is at risk of developing cancer.

[0315] Diagnostic assays, such as competitive assays rely on the ability of a labelled analogue (the "tracer") to compete with the test sample analyte for a limited number of binding sites on a common binding partner. The binding partner generally is insolubilized before or after the competition and then the tracer and analyte bound to the binding partner are separated from the unbound tracer and analyte. This separation is accomplished by decanting (where the binding partner was preinsolubilized) or by centrifuging (where the binding partner was precipitated after the competitive reaction). The amount of test sample analyte is inversely proportional to the amount of bound tracer as measured by the amount of marker substance. Dose-response curves with known amounts of analyte are prepared and compared with the test results in order to quantitatively determine the amount of analyte present in the test sample. These assays are called ELISA systems when enzymes are used as the detectable markers. In an assay of this form, competitive binding between antibodies and HER3 antibodies results in the bound HER3, preferably the HER3 epitopes of the invention, being a measure of antibodies in the serum sample, most particularly, inhibiting antibodies in the serum sample.

[0316] A significant advantage of the assay is that measurement is made of inhibiting antibodies directly (i.e., those which interfere with binding of HER3, specifically, epitopes).

Such an assay, particularly in the form of an ELISA test has considerable applications in the clinical environment and in routine blood screening.

[0317] Another aspect of the invention provides methods for determining HER3 nucleic acid expression or HER3 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

[0318] Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs) on the expression or activity of HER3 in clinical trials.

Pharmaceutical Compositions

[0319] To prepare pharmaceutical or sterile compositions including antibodies or fragments thereof, the antibodies or fragments thereof are mixed with a pharmaceutically acceptable carrier or excipient. The compositions can additionally contain one or more other therapeutic agents that are suitable for treating or preventing cancer (breast cancer, colorectal cancer, lung cancer, multiple myeloma, ovarian cancer, liver cancer, gastric cancer, pancreatic cancer, acute myeloid leukemia, chronic myeloid leukemia, osteosarcoma, squamous cell carcinoma, peripheral nerve sheath tumors schwannoma, head and neck cancer, bladder cancer, esophageal cancer, glioblastoma, clear cell sarcoma of soft tissue, malignant mesothelioma, neurofibromatosis, renal cancer, and melanoma, Barretts esophageal cancer, prostate cancer, benign prostatic hyperplasia (BPH), gynacomastica, and endometriosis).

[0320] Formulations of therapeutic and diagnostic agents can be prepared by mixing with physiologically acceptable carriers, excipients, or stabilizers in the form of, e.g., lyophilized powders, slurries, aqueous solutions, lotions, or suspensions (see, e.g., Hardman et al., (2001) Goodman and Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, N.Y.; Gennaro (2000) Remington: The Science and Practice of Pharmacy, Lippincott, Williams, and Wilkins, New York, N.Y.; Avis, et al. (eds.) (1993) Pharmaceutical Dosage Forms: Parenteral Medications, Marcel Dekker, NY; Lieberman, et al. (eds.) (1990) Pharmaceutical Dosage Forms: Tablets, Marcel Dekker, NY; Lieberman, et al. (eds.) (1990) Pharmaceutical Dosage Forms: Disperse Systems, Marcel Dekker, NY; Weiner and Kotkoskie (2000) Excipient Toxicity and Safety, Marcel Dekker, Inc., New York, N.Y.).

[0321] Selecting an administration regimen for a therapeutic depends on several factors, including the serum or tissue turnover rate of the entity, the level of symptoms, the immunogenicity of the entity, and the accessibility of the target cells in the biological matrix. In certain embodiments, an administration regimen maximizes the amount of therapeutic delivered to the patient consistent with an acceptable level of side effects. Accordingly, the amount of biologic delivered depends in part on the particular entity and the severity of the condition being treated. Guidance in selecting appropriate doses of antibodies, cytokines, and small molecules are available (see, e.g., Wawrzynczak (1996) Antibody Therapy, Bios Scientific Pub. Ltd, Oxfordshire, UK; Kresina (ed.) (1991) Monoclonal Antibodies, Cytokines and Arthritis, Marcel

Dekker, New York, N.Y.; Bach (ed.) (1993) *Monoclonal Antibodies and Peptide Therapy in Autoimmune Diseases*, Marcel Dekker, New York, N.Y.; Baert et al., (2003) *New Engl. J. Med.* 348:601-608; Milgrom et al., (1999) *New Engl. J. Med.* 341:1966-1973; Slamon et al., (2001) *New Engl. J. Med.* 344:783-792; Beniaminovitz et al., (2000) *New Engl. J. Med.* 342:613-619; Ghosh et al., (2003) *New Engl. J. Med.* 348:24-32; Lipsky et al., (2000) *New Engl. J. Med.* 343:1594-1602).

[0322] Determination of the appropriate dose is made by the clinician, e.g., using parameters or factors known or suspected in the art to affect treatment or predicted to affect treatment. Generally, the dose begins with an amount somewhat less than the optimum dose and it is increased by small increments thereafter until the desired or optimum effect is achieved relative to any negative side effects. Important diagnostic measures include those of symptoms of, e.g., the inflammation or level of inflammatory cytokines produced.

[0323] Actual dosage levels of the active ingredients in the pharmaceutical compositions of the present invention may be varied so as to obtain an amount of the active ingredient which is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient. The selected dosage level will depend upon a variety of pharmacokinetic factors including the activity of the particular compositions of the present invention employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compositions employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors known in the medical arts.

[0324] Compositions comprising antibodies or fragments thereof of the invention can be provided by continuous infusion, or by doses at intervals of, e.g., one day, one week, or 1-7 times per week. Doses may be provided intravenously, subcutaneously, topically, orally, nasally, rectally, intramuscular, intracerebrally, or by inhalation. A specific dose protocol is one involving the maximal dose or dose frequency that avoids significant undesirable side effects.

[0325] A total weekly dose may be at least 0.05 µg/kg body weight, at least 0.2 µg/kg, at least 0.5 µg/kg, at least 1 µg/kg, at least 10 µg/kg, at least 100 µg/kg, at least 0.2 mg/kg, at least 1.0 mg/kg, at least 2.0 mg/kg, at least 10 mg/kg, at least 25 mg/kg, or at least 50 mg/kg (see, e.g., Yang et al., (2003) *New Engl. J. Med.* 349:427-434; Herold et al., (2002) *New Engl. J. Med.* 346:1692-1698; Liu et al., (1999) *J. Neurol. Neurosurg. Psych.* 67:451-456; Portielji et al., (2003) *Cancer Immunol. Immunother.* 52:133-144). The desired dose of antibodies or fragments thereof is about the same as for an antibody or polypeptide, on a moles/kg body weight basis. The desired plasma concentration of the antibodies or fragments thereof is about, on a moles/kg body weight basis. The dose may be at least 15 µg at least 20 µg, at least 25 µg, at least 30 µg, at least 35 µg, at least 40 µg, at least 45 µg, at least 50 µg, at least 55 µg, at least 60 µg, at least 65 µg, at least 70 µg, at least 75 µg, at least 80 µg, at least 85 µg, at least 90 µg, at least 95 µg, or at least 100 µg. The doses administered to a subject may number at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12, or more.

[0326] For antibodies or fragments thereof of the invention, the dosage administered to a patient may be 0.0001 mg/kg to 100 mg/kg of the patient's body weight. The dosage may be

between 0.0001 mg/kg and 20 mg/kg, 0.0001 mg/kg and 10 mg/kg, 0.0001 mg/kg and 5 mg/kg, 0.0001 and 2 mg/kg, 0.0001 and 1 mg/kg, 0.0001 mg/kg and 0.75 mg/kg, 0.0001 mg/kg and 0.5 mg/kg, 0.0001 mg/kg to 0.25 mg/kg, 0.0001 to 0.15 mg/kg, 0.0001 to 0.10 mg/kg, 0.001 to 0.5 mg/kg, 0.01 to 0.25 mg/kg or 0.01 to 0.10 mg/kg of the patient's body weight.

[0327] The dosage of the antibodies or fragments thereof of the invention may be calculated using the patient's weight in kilograms (kg) multiplied by the dose to be administered in mg/kg. The dosage of the antibodies or fragments thereof of the invention may be 150 µg/kg or less, 125 µg/kg or less, 100 µg/kg or less, 95 µg/kg or less, 90 µg/kg or less, 85 µg/kg or less, 80 µg/kg or less, 75 µg/kg or less, 70 µg/kg or less, 65 µg/kg or less, 60 µg/kg or less, 55 µg/kg or less, 50 µg/kg or less, 45 µg/kg or less, 40 µg/kg or less, 35 µg/kg or less, 30 µg/kg or less, 25 µg/kg or less, 20 µg/kg or less, 15 µg/kg or less, 10 µg/kg or less, 5 µg/kg or less, 2.5 µg/kg or less, 2 µg/kg or less, 1.5 µg/kg or less, 1 µg/kg or less, 0.5 µg/kg or less, or 0.5 µg/kg or less of a patient's body weight.

[0328] Unit dose of the antibodies or fragments thereof of the invention may be 0.1 mg to 20 mg, 0.1 mg to 15 mg, 0.1 mg to 12 mg, 0.1 mg to 10 mg, 0.1 mg to 8 mg, 0.1 mg to 7 mg, 0.1 mg to 5 mg, 0.1 to 2.5 mg, 0.25 mg to 20 mg, 0.25 to 15 mg, 0.25 to 12 mg, 0.25 to 10 mg, 0.25 to 8 mg, 0.25 mg to 7 mg, 0.25 mg to 5 mg, 0.5 mg to 2.5 mg, 1 mg to 20 mg, 1 mg to 15 mg, 1 mg to 12 mg, 1 mg to 10 mg, 1 mg to 8 mg, 1 mg to 7 mg, 1 mg to 5 mg, or 1 mg to 2.5 mg.

[0329] The dosage of the antibodies or fragments thereof of the invention may achieve a serum titer of at least 0.1 µg/ml, at least 0.5 µg/ml, at least 1 µg/ml, at least 2 µg/ml, at least 5 µg/ml, at least 6 µg/ml, at least 10 µg/ml, at least 15 µg/ml, at least 20 µg/ml, at least 25 µg/ml, at least 50 µg/ml, at least 100 µg/ml, at least 125 µg/ml, at least 150 µg/ml, at least 175 µg/ml, at least 200 µg/ml, at least 225 µg/ml, at least 250 µg/ml, at least 275 µg/ml, at least 300 µg/ml, at least 325 µg/ml, at least 350 µg/ml, at least 375 µg/ml, or at least 400 µg/ml in a subject.

[0330] Alternatively, the dosage of the antibodies or fragments thereof of the invention may achieve a serum titer of at least 0.1 µg/ml, at least 0.5 µg/ml, at least 1 µg/ml, at least 2 µg/ml, at least 5 µg/ml, at least 6 µg/ml, at least 10 µg/ml, at least 15 µg/ml, at least 20 µg/ml, at least 25 µg/ml, at least 50 µg/ml, at least 100 µg/ml, at least 125 µg/ml, at least 150 µg/ml, at least 175 µg/ml, at least 200 µg/ml, at least 225 µg/ml, at least 250 µg/ml, at least 275 µg/ml, at least 300 µg/ml, at least 325 µg/ml, at least 350 µg/ml, at least 375 µg/ml, or at least 400 µg/ml in the subject.

[0331] Doses of antibodies or fragments thereof of the invention may be repeated and the administrations may be separated by at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or at least 6 months.

[0332] An effective amount for a particular patient may vary depending on factors such as the condition being treated, the overall health of the patient, the method route and dose of administration and the severity of side effects (see, e.g., Maynard et al., (1996) *A Handbook of SOPs for Good Clinical Practice*, Interpharm Press, Boca Raton, Fla.; Dent (2001) *Good Laboratory and Good Clinical Practice*, Urch Publ., London, UK).

[0333] The route of administration may be by, e.g., topical or cutaneous application, injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocu-

lar, intraarterial, intracerebrospinal, intralesional, or by sustained release systems or an implant (see, e.g., Sidman et al., (1983) *Biopolymers* 22:547-556; Langer et al., (1981) *J. Biomed. Mater. Res.* 15:167-277; Langer (1982) *Chem. Tech.* 12:98-105; Epstein et al., (1985) *Proc. Natl. Acad. Sci. USA* 82:3688-3692; Hwang et al., (1980) *Proc. Natl. Acad. Sci. USA* 77:4030-4034; U.S. Pat. Nos. 6,350,466 and 6,316,024). Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. In addition, pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent. See, e.g., U.S. Pat. Nos. 6,019,968, 5,985,320, 5,985,309, 5,934,272, 5,874,064, 5,855,913, 5,290,540, and 4,880,078; and PCT Publication Nos. WO 92/19244, WO 97/32572, WO 97/44013, WO 98/31346, and WO 99/66903, each of which is incorporated herein by reference their entirety.

[0334] A composition of the present invention may also be administered via one or more routes of administration using one or more of a variety of methods known in the art. As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending upon the desired results. Selected routes of administration for antibodies or fragments thereof of the invention include intravenous, intramuscular, intradermal, intraperitoneal, subcutaneous, spinal or other parenteral routes of administration, for example by injection or infusion. Parenteral administration may represent modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal injection and infusion. Alternatively, a composition of the invention can be administered via a non-parenteral route, such as a topical, epidermal or mucosal route of administration, for example, intranasally, orally, vaginally, rectally, sublingually or topically. In one embodiment, the antibodies or fragments thereof of the invention is administered by infusion. In another embodiment, the multispecific epitope binding protein of the invention is administered subcutaneously.

[0335] If the antibodies or fragments thereof of the invention are administered in a controlled release or sustained release system, a pump may be used to achieve controlled or sustained release (see Langer, *supra*; Sefton, (1987) *CRC Crit. Ref Biomed. Eng.* 14:20; Buchwald et al., (1980), *Surgery* 88:507; Saudek et al., (1989) *N. Engl. J. Med.* 321:574). Polymeric materials can be used to achieve controlled or sustained release of the therapies of the invention (see e.g., *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, (1983) *J. Macromol. Sci. Rev. Macromol. Chem.* 23:61; see also Levy et al., (1985) *Science* 228:190; During et al., (1989) *Ann. Neurol.* 25:351; Howard et al., (1989) *J. Neurosurg.* 71:105; U.S. Pat. No. 5,679,377; U.S. Pat. No. 5,916,597; U.S. Pat. No. 5,912,015; U.S. Pat. No. 5,989,463; U.S. Pat. No. 5,128,326; PCT Publication No. WO 99/15154; and PCT Publication No. WO 99/20253. Examples of polymers used in sustained release formulations include, but are not limited to, poly(2-hydroxy ethyl methacrylate), poly(methyl methacrylate), poly(acrylic acid), poly(ethylene-co-vinyl acetate), poly(methacrylic acid), polyglycolides (PLG),

polyanhydrides, poly(N-vinyl pyrrolidone), poly(vinyl alcohol), polyacrylamide, poly(ethylene glycol), polylactides (PLA), poly(lactide-co-glycolides) (PLGA), and polyorthoesters. In one embodiment, the polymer used in a sustained release formulation is inert, free of leachable impurities, stable on storage, sterile, and biodegradable. A controlled or sustained release system can be placed in proximity of the prophylactic or therapeutic target, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

[0336] Controlled release systems are discussed in the review by Langer, (1990), *Science* 249:1527-1533). Any technique known to one of skill in the art can be used to produce sustained release formulations comprising one or more antibodies or fragments thereof of the invention. See, e.g., U.S. Pat. No. 4,526,938, PCT publication WO 91/05548, PCT publication WO 96/20698, Ning et al., (1996), *Radiotherapy & Oncology* 39:179-189, Song et al., (1995) *PDA Journal of Pharmaceutical Science & Technology* 50:372-397, Cleek et al., (1997) *Pro. Int'l. Symp. Control. Rel. Bioact. Mater.* 24:853-854, and Lam et al., (1997) *Proc. Int'l. Symp. Control Rel. Bioact. Mater.* 24:759-760, each of which is incorporated herein by reference in their entirety.

[0337] If the antibodies or fragments thereof of the invention are administered topically, they can be formulated in the form of an ointment, cream, transdermal patch, lotion, gel, shampoo, spray, aerosol, solution, emulsion, or other form well-known to one of skill in the art. See, e.g., Remington's *Pharmaceutical Sciences and Introduction to Pharmaceutical Dosage Forms*, 19th ed., Mack Pub. Co., Easton, Pa. (1995). For non-sprayable topical dosage forms, viscous to semi-solid or solid forms comprising a carrier or one or more excipients compatible with topical application and having a dynamic viscosity, in some instances, greater than water are typically employed. Suitable formulations include, without limitation, solutions, suspensions, emulsions, creams, ointments, powders, liniments, salves, and the like, which are, if desired, sterilized or mixed with auxiliary agents (e.g., preservatives, stabilizers, wetting agents, buffers, or salts) for influencing various properties, such as, for example, osmotic pressure. Other suitable topical dosage forms include sprayable aerosol preparations wherein the active ingredient, in some instances, in combination with a solid or liquid inert carrier, is packaged in a mixture with a pressurized volatile (e.g., a gaseous propellant, such as freon) or in a squeeze bottle. Moisturizers or humectants can also be added to pharmaceutical compositions and dosage forms if desired. Examples of such additional ingredients are well-known in the art.

[0338] If the compositions comprising antibodies or fragments thereof are administered intranasally, it can be formulated in an aerosol form, spray, mist or in the form of drops. In particular, prophylactic or therapeutic agents for use according to the present invention can be conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant (e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas). In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges (composed of, e.g., gelatin) for use in

an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

[0339] Methods for co-administration or treatment with a second therapeutic agent, e.g., a cytokine, steroid, chemotherapeutic agent, antibiotic, or radiation, are known in the art (see, e.g., Hardman et al., (eds.) (2001) Goodman and Gilman's The Pharmacological Basis of Therapeutics, 10^{sup}.th ed., McGraw-Hill, New York, N.Y.; Poole and Peterson (eds.) (2001) Pharmacotherapeutics for Advanced Practice: A Practical Approach, Lippincott, Williams & Wilkins, Phila., Pa.; Chabner and Longo (eds.) (2001) Cancer Chemotherapy and Biotherapy, Lippincott, Williams & Wilkins, Phila., Pa.). An effective amount of therapeutic may decrease the symptoms by at least 10%; by at least 20%; at least about 30%; at least 40%, or at least 50%.

[0340] Additional therapies (e.g., prophylactic or therapeutic agents), which can be administered in combination with the antibodies or fragments thereof the invention may be administered less than 5 minutes apart, less than 30 minutes apart, 1 hour apart, at about 1 hour apart, at about 1 to about 2 hours apart, at about 2 hours to about 3 hours apart, at about 3 hours to about 4 hours apart, at about 4 hours to about 5 hours apart, at about 5 hours to about 6 hours apart, at about 6 hours to about 7 hours apart, at about 7 hours to about 8 hours apart, at about 8 hours to about 9 hours apart, at about 9 hours to about 10 hours apart, at about 10 hours to about 11 hours apart, at about 11 hours to about 12 hours apart, at about 12 hours to 18 hours apart, 18 hours to 24 hours apart, 24 hours to 36 hours apart, 36 hours to 48 hours apart, 48 hours to 52 hours apart, 52 hours to 60 hours apart, 60 hours to 72 hours apart, 72 hours to 84 hours apart, 84 hours to 96 hours apart, or 96 hours to 120 hours apart from the antibodies or fragments thereof the invention. The two or more therapies may be administered within one same patient visit.

[0341] The antibodies or fragments thereof the invention and the other therapies may be cyclically administered. Cycling therapy involves the administration of a first therapy (e.g., a first prophylactic or therapeutic agent) for a period of time, followed by the administration of a second therapy (e.g., a second prophylactic or therapeutic agent) for a period of time, optionally, followed by the administration of a third therapy (e.g., prophylactic or therapeutic agent) for a period of time and so forth, and repeating this sequential administration, i.e., the cycle in order to reduce the development of resistance to one of the therapies, to avoid or reduce the side effects of one of the therapies, and/or to improve the efficacy of the therapies.

[0342] In certain embodiments, the antibodies or fragments thereof the invention can be formulated to ensure proper distribution in vivo. For example, the blood-brain barrier (BBB) excludes many highly hydrophilic compounds. To ensure that the therapeutic compounds of the invention cross the BBB (if desired), they can be formulated, for example, in liposomes. For methods of manufacturing liposomes, see, e.g., U.S. Pat. Nos. 4,522,811; 5,374,548; and 5,399,331. The liposomes may comprise one or more moieties which are selectively transported into specific cells or organs, thus enhance targeted drug delivery (see, e.g., Ranade, (1989) J. Clin. Pharmacol. 29:685). Exemplary targeting moieties include folate or biotin (see, e.g., U.S. Pat. No. 5,416,016 to Low et al); mannosides (Umezawa et al., (1988) Biochem. Biophys. Res. Commun. 153:1038); antibodies (Bloeman et al., (1995) FEBS Lett. 357:140; Owais et al., (1995) Antimi-

crob. Agents Chemother. 39:180); surfactant protein A receptor (Briscoe et al., (1995) Am. J. Physiol. 1233:134); p 120 (Schreier et al, (1994) J. Biol. Chem. 269:9090); see also K. Keinänen; M. L. Laukkanen (1994) FEBS Lett. 346:123; J. J. Killion; I. J. Fidler (1994) Immunomethods 4:273.

[0343] The invention provides protocols for the administration of pharmaceutical composition comprising antibodies or fragments thereof the invention alone or in combination with other therapies to a subject in need thereof. The therapies (e.g., prophylactic or therapeutic agents) of the combination therapies of the present invention can be administered concomitantly or sequentially to a subject. The therapy (e.g., prophylactic or therapeutic agents) of the combination therapies of the present invention can also be cyclically administered. Cycling therapy involves the administration of a first therapy (e.g., a first prophylactic or therapeutic agent) for a period of time, followed by the administration of a second therapy (e.g., a second prophylactic or therapeutic agent) for a period of time and repeating this sequential administration, i.e., the cycle, in order to reduce the development of resistance to one of the therapies (e.g., agents) to avoid or reduce the side effects of one of the therapies (e.g., agents), and/or to improve, the efficacy of the therapies.

[0344] The therapies (e.g., prophylactic or therapeutic agents) of the combination therapies of the invention can be administered to a subject concurrently. The term "concurrently" is not limited to the administration of therapies (e.g., prophylactic or therapeutic agents) at exactly the same time, but rather it is meant that a pharmaceutical composition comprising antibodies or fragments thereof the invention are administered to a subject in a sequence and within a time interval such that the antibodies of the invention can act together with the other therapy(ies) to provide an increased benefit than if they were administered otherwise. For example, each therapy may be administered to a subject at the same time or sequentially in any order at different points in time; however, if not administered at the same time, they should be administered sufficiently close in time so as to provide the desired therapeutic or prophylactic effect. Each therapy can be administered to a subject separately, in any appropriate form and by any suitable route. In various embodiments, the therapies (e.g., prophylactic or therapeutic agents) are administered to a subject less than 15 minutes, less than 30 minutes, less than 1 hour apart, at about 1 hour apart, at about 1 hour to about 2 hours apart, at about 2 hours to about 3 hours apart, at about 3 hours to about 4 hours apart, at about 4 hours to about 5 hours apart, at about 5 hours to about 6 hours apart, at about 6 hours to about 7 hours apart, at about 7 hours to about 8 hours apart, at about 8 hours to about 9 hours apart, at about 9 hours to about 10 hours apart, at about 10 hours to about 11 hours apart, at about 11 hours to about 12 hours apart, 24 hours apart, 48 hours apart, 72 hours apart, or 1 week apart. In other embodiments, two or more therapies (e.g., prophylactic or therapeutic agents) are administered to a within the same patient visit.

[0345] The prophylactic or therapeutic agents of the combination therapies can be administered to a subject in the same pharmaceutical composition. Alternatively, the prophylactic or therapeutic agents of the combination therapies can be administered concurrently to a subject in separate pharmaceutical compositions. The prophylactic or therapeutic agents may be administered to a subject by the same or different routes of administration.

[0346] The invention having been fully described, it is further illustrated by the following examples and claims, which are illustrative and are not meant to be further limiting.

EXAMPLES

Example 1

Methods, Materials and Screening for Antibodies

(i) Cell Lines

[0347] SK-BR-3, BT-474 and MCF-7 cell lines were purchased from ATCC and routinely maintained in growth media supplemented with 10% fetal bovine serum (FBS).

(ii) Generation of Recombinant Human, Cyno, Mouse and Rat HER3 Vectors

[0348] Murine HER3 extracellular domain was PCR amplified from mouse brain cDNA (Clontech) and sequence verified by comparison with Refseq NM_010153. Rat HER3 ECD was reverse transcribed from Rat-2 cell mRNA and sequence verified by comparison with NM_017218. Cynomolgus HER3 cDNA template was generated using RNA from various cyno tissues (Zyagen Laboratories), and the RT-PCR product cloned into pCR®-TOPO-XL (Invitrogen) prior to sequencing of both strands. Human HER3 was derived from a human fetal brain cDNA library (Source) and sequence verified by comparison with NM_001982.

[0349] To generate tagged recombinant proteins, human, mouse, rat and cyno HER3 was PCR amplified using Pwo Taq polymerase (Roche Diagnostics). Amplified PCR products were gel purified and cloned into a pDonR201 (Invitrogen) gateway entry vector that had previously been modified to include an in-frame N-terminal CD33 leader sequence and a C-terminal TAG, e.g., FLAG TAG. The TAG allows purification of monomeric proteins via an anti-TAG monoclonal antibody. The target genes were flanked with AttB1 and AttB2 allowing recombination into Gateway adapted proprietary destination vectors (e.g., pcDNA3.1) using the Gateway® cloning technology (Invitrogen). Recombination reactions were performed using a Gateway LR reaction with proprietary destination vectors containing a CMV promoter to create the TAG expression vectors, although any commercially available vector can be used.

[0350] Further recombinant HER3 proteins were generated that fused the HER3 ECD upstream of a C-terminal Factor X cleavage site and the human IgG hinge and Fc domain to create an Fc-tagged protein. To achieve this, the various HER3 ECD's were PCR amplified and cloned into a vector (e.g., pcDNA3.1) modified to contain an in-frame C-terminal fusion of Factor X site-Hinge-hFc. The generated open reading frame was flanked with AttB and AttB2 sites for further cloning with the Gateway® recombinant cloning technology (Invitrogen). An LR Gateway reaction was used to transfer HER3-Fc into a destination expression construct containing a CMV promoter. HER3 point mutation expression constructs were generated using standard site directed mutagenesis protocols and the resultant vectors sequence verified.

TABLE 3

Generation of HER3 expression vectors. HER3 amino acid numbering is based on NP_001973 (human), NP_034283 (mouse) and NP_058914 (rat).	
Name	Description
Hu HER3	CD33-[Human HER3, residues 20-640]-TAG
Mu HER3	CD33-[Murine HER3, residues 20-643]-TAG
Rat HER3	CD33-[Rat HER3, residues 20-643]-TAG
Cyno HER3	CD33-[Cyno HER3, residues 20-643]-TAG
HER3 D1-2	CD33-[Human HER3, residues 20-329]-TAG
HER3 D2	CD33-[Human HER3, residues 185-329]-TAG
HER3 D3-4	CD33-[Human HER3, residues 330-643]-TAG
HER3 D3	CD33-[Human HER3, residues 330-495]-TAG
HER3 D4	CD33-[Human HER3, residues 496-643]-TAG
Hu HER3-Fc	[Human HER3, residues 1-643]-Fc
Mu HER3-Fc	[Murine HER3, residues 1-643]-Fc
Cyno HER3-Fc	[Cyno HER3, residues 1-643]-Fc
Rat HER3-Fc	[Rat HER3, residues 1-643]-Fc
HER3 D2-Fc	[Human HER3 residues 207-329]-Fc

(iii) Expression of Recombinant HER3 Proteins

[0351] The desired HER3 recombinant proteins were expressed in HEK293 derived cell lines previously adapted to suspension culture and grown in a Novartis proprietary serum-free medium. Small scale expression verification was undertaken in transient 6-well-plate transfection assays on the basis of lipofection. Large-scale protein production via transient transfection and was performed at the 10-20 L scale in the Wave™ bioreactor system (Wave Biotech). DNA Polyethylenimine (Polysciences) was used as a plasmid carrier at a ratio of 1:3 (w:w). The cell culture supernatants were harvested 7-10 days post transfection and concentrated by cross-flow filtration and diafiltration prior to purification.

(iv) Tagged Protein Purification

[0352] Recombinant tagged HER3 proteins (e.g., TAG-HER3) were purified by collecting the cell culture supernatant and concentrating 10-fold by cross-flow filtration with a 10 kDa cut off filter (Fresenius). An anti-TAG column was prepared by coupling an anti-TAG monoclonal antibody to CNBr activated Sepharose 4B at a final ratio of 10 mg antibody per mL of resin. Concentrated supernatant was applied to a 35 ml anti-Tag column at a flow rate of 1-2 mL/minute. After base-line washing with PBS, bound material was eluted with 100 mM glycine (pH 2.7), neutralized and sterile filtered. Protein concentrations were determined by measuring the absorbance at 280 nm and converting using a theoretical factor of 0.66 AU/mg. The purified protein was finally characterized by SDS-PAGE, N-terminal sequencing and LC-MS.

(v) Fc Tag Purification

[0353] Concentrated cell culture supernatant was applied to a 50 ml Protein A Sepharose Fast Flow column at a flow rate of 1 ml/min. After baseline washing with PBS, the column was washed with 10 column volumes of 10 mM NaH₂PO₄/30% (v/v) Isopropanol, pH 7.3 followed by 5 column volumes of PBS. Finally, bound material was eluted with 50 mM Citrate/140 mM NaCl (pH 2.7), neutralized and sterile filtered.

(vi) HuCAL GOLD® OR PLATINUM® Pannings

[0354] For the selection of antibodies recognizing human HER3 multiple panning strategies were employed. Therapeu-

tic antibodies against human HER3 protein were generated by selection of clones having high binding affinities, using as the source of antibody variant proteins a commercially available phage display library, the MorphoSys HuCAL GOLD® or Platinum® library. The phagemid library is based on the HuCAL® concept (Knappik et al., (2000) J Mol Biol 296:57-86) and employs the CysDisplay® technology for displaying the Fab on the phage surface (WO01/05950 to Lohning).

[0355] For the isolation of anti-HER3 antibodies, standard as well as RapMAT panning strategies were performed using solid phase, solution, whole cell and differential whole cell panning approaches.

(vii) Solid Phase Panning

[0356] To identify anti-HER3 antibodies a variety of solid phase panning strategies were performed using differing recombinant HER3 proteins. To perform each round of solid phase panning, Maxisorp plates (Nunc) were coated with HER3 protein. Tagged proteins were either captured using plates previously coated with anti-Fc (goat or mouse anti-human IgG, Jackson Immuno Research), anti-Tag antibody or via passive adsorption. The coated plates were washed with PBS and blocked. Coated plates were washed twice with PBS prior to the addition of HuCAL GOLD® or Platinum® phage-antibodies for 2 hours at room temperature on a shaker. Bound phages were eluted were added to *E. coli* TG-1 and incubated for phage infection. Subsequently infected bacteria were isolated and plated on agar plates. Colonies were scraped off the plates and phages were rescued and amplified. Each HER3 panning strategy comprised of individual rounds of panning and contained unique antigens, antigen concentrations and washing stringency.

(viii) Solution Phase Panning

[0357] Each round of solution phase panning was performed using various biotinylated recombinant HER3 proteins in the presence or absence of neuregulin 1-31 (R&D Systems). Proteins were biotinylated using the EZ-link sulfo-NHS-LC biotinylation kit (Pierce) according to the manufacturers instructions. 800 µl of Streptavidin linked magnetic beads (Dynabeads, Dynal) were washed once with PBS and blocked overnight with Chemiblocker (Chemicon). HuCAL GOLD® or Platinum® phage-antibodies and the appropriate biotinylated HER3 were incubated in a reaction tube. Streptavidin magnetic beads were added for 20 minutes and were collected with a magnetic particle separator (Dynal). Bound phages were eluted from the Dynabeads by adding DTT containing buffer to each tube and added to *E. coli* TG-1. Phage infection was performed in an identical manner to that described in solid phase panning. Each HER3 panning strategy comprised of individual rounds of panning and contained unique antigens, antigen concentrations and washing stringency. In order to isolate antibodies targeting a specific epitope, competition pannings were performed. In these panning strategies HER3 was incubated and pre-blocked with a reference antibody prior to addition of HuCAL GOLD® or Platinum® phage-antibodies. As an alternative strategy reference antibodies were used to specifically elute phage-antibodies complexed with HER3.

(ix) Cell Based Panning

[0358] For cell pannings, HuCAL GOLD® or Platinum® phage-antibodies were incubated with approximately 10⁷ cells on a rotator for 2 hours at room temperature, followed by centrifugation. The cell pellet was isolated phages were eluted from the cells The supernatant was collected and added

to *E. coli* TG-1 culture continued by the process described above. Two cell based strategies were employed to identify anti-HER3 antibodies:

[0359] a) Whole cell panning: In this strategy a variety of intact cell lines were used as the antigens.

[0360] b) Differential whole cell panning: In this strategy the antigens sequentially consisted of cells and recombinant HER3 proteins. The cell based pannings were performed as described above whilst solid phase panning protocols were employed when recombinant proteins were utilized as antigens. The washes were conducted using PBS (2-3×) and PBST (2-3×).

(x) RapMAT™ Library Generation and Pannings

[0361] In order to increase antibody binding affinity whilst maintaining library diversity the second round output of both solution and solid phase pannings were entered into the RapMAT™ process whilst the third round output of the whole cell and differential whole cell panning strategies were entered (Prassler et al., (2009) Immunotherapy; 1: 571-583). RapMAT™ libraries were generated by sub-cloning Fab-encoding inserts of phages selected via panning into the display vector pMORPH®25_bla_LHC and were further digested to either generate H-CDR2RapMAT™ libraries and L-CDR3RapMAT™ libraries by using specific restriction enzymes. The inserts were replaced with TRIM maturation cassettes (Virnekas et al., (1994) Nucleic Acids Research 22:5600-5607) for H-CDR2 or L-CDR3 according to pool composition. Library sizes were estimated to range between 8×10⁶-1×10⁸ clones. RapMAT antibody-phage were produced and subjected to two further rounds of solution, solid phase or cell based panning using the experimental methods described previously.

[0362] This extensive panning strategy, involving an iterative refinement of library design was specifically developed to bias screening away from pure ligand-competitive antibodies by including ligand-blocking antibodies directly in the pannings. Secondly, the FAB to IgG conversion process was adapted to maximize the recovery of candidate clones and ensure that all selective binders were profiled in functional assays. From 44 initial pannings, yielding around 28 families of specific Her3 binding antibodies, only three antibody families displayed the desired property of blocking both ligand-dependent and independent signal transduction. Family A that binds isolated domains 1-2 and 2 of Her3. Family B that binds isolated domains 3-4, but not 4 alone; and family C, which binds domain 3.

Example 2

Transient Expression of Anti-HER3 IgG's

[0363] Suspension adapted HEK293-6E cells were cultivated in a BioWave20. The cells were transiently transfected with the relevant sterile DNA: PEI-MIX and further cultivated. After transfection, cells were removed by crossflow filtration using Fresenius filters. The cell free material was concentrated with crossflow filtration using a cut off filter (Fresenius) and the concentrate was sterile filtered through a stericup filter. The sterile supernatant was stored at 4° C.

Example 3

Purification of anti-HER3 IgG

[0364] The purification of IgG was performed on a ÄKTA 100 explorer Air chromatography system in a cooling cabinet,

using a XK16/20 column with 25 mL of self-packed MabSelect SuRe resin (all GE Healthcare). All flow rates were 3.5 mL/min, except for loading, at a pressure limit of 5 bar. The column was equilibrated with 3 column volumes of PBS prior to loading the filtered fermentation supernatant. The column was washed with PBS. IgG was eluted with a pH gradient, starting at citrate/NaCl (pH 4.5), going linearly down to citrate/NaCl (pH 2.5), followed by a constant step of the same pH 2.5 buffer. The IgG containing fractions were pooled and immediately neutralized and sterile filtered (Millipore Steriflip, 0.22 µm). OD₂₈₀ was measured and the protein concentration calculated based on the sequence data. The pools were separately tested for aggregation (SEC-MALS) and purity (SDS-PAGE and MS).

Example 4

Expression and Purification of HuCAL®-Fab Antibodies in *E. coli*

[0365] Expression of Fab fragments encoded by pMORPH®X9_Fab_MH in TG-1 cells was carried out in shaker flask cultures using YT medium supplemented with chloramphenicol. Cultures were shaken until the OD₆₀₀ nm reached 0.5. Expression was induced by addition of IPTG (isopropyl-β-D-thiogalactopyranoside). Cells were disrupted using lysozyme. His₆-tagged Fab ('His₆' disclosed as SEQ ID NO: 702) fragments were isolated via IMAC (Bio-Rad). Buffer exchange to 1× Dulbecco's PBS (pH 7.2) was performed using PD10 columns. Samples were sterile filtered. Protein concentrations were determined by UV-spectrophotometry. The purity of the samples was analyzed in denaturing, reducing 15% SDS-PAGE. The homogeneity of Fab preparations was determined in native state by size exclusion chromatography (HP-SEC) with calibration standards.

Example 5

HER3 Antibody Affinity (K_D) Measurements by Solution Equilibrium Titration (SET)

[0366] Affinity determination in solution was essentially performed as previously described (Friguet et al., (1985) J Immunol Methods 77:305-19). In order to improve the sensitivity and accuracy of the SET method, it was transferred from classical ELISA to ECL based technology (Haenel et al., (2005) Anal biochem 339:182-84).

[0367] Unlabeled HER3-Tag (human, rat, mouse or cyno) described previously was used for affinity determination by SET.

[0368] The data was evaluated with XLfit software (ID Business Solutions) applying customized fitting models. For K_D determination of each IgG the following model was used (modified according to Piehler, et al (Piehler et al., (1997) J Immunol Methods 201:189-206).

$$y = \frac{2B_{max}}{[IgG]} \left(\frac{[IgG]}{2} - \frac{\left(\frac{x + [IgG] + K_D}{2} - \sqrt{\frac{(x + [IgG] + K_D)^2}{4} - x[IgG]} \right)^2}{2[IgG]} \right)$$

[IgG]: applied total IgG concentration

x: applied total soluble antigen concentration (binding sites)

B_{max}: maximal signal of IgG without antigen

K_D: affinity

Example 6

Antibody Cell Binding Determination by FACS

[0369] The binding of antibodies to endogenous human antigen expressed on human cancer cells was accessed by FACS. In order to determine antibody EC₅₀ values SK-Br-3 cells were harvested with accutase and diluted to 1×10⁶ cells/mL in FACS buffer (PBS/3% FBS/0.2% NaN₃). 1×10⁵ cells/well were added to each well of a 96-well plate (Nunc) and centrifuged at 210 g for 5 minutes at 4° C. before removing the supernatant. Serial dilutions of test antibodies (diluted in 1:4 dilution steps with FACS buffer) were added to the pelleted cells and incubated for 1 hour on ice. The cells were washed and pelleted three times with 100 L FACS buffer. PE conjugated goat anti-human IgG (Jackson ImmunoResearch) diluted 1/200 with FACS buffer were added to the cells and incubated on ice for 1 hour. Additional washing steps were performed three times with 100 µL FACS buffer followed by centrifugation steps at 210 g for 5 minutes at 4° C. Finally, cells were resuspended in 200 µL FACS buffer and fluorescence values were measured with a FACSArray (BD Biosciences). The amount of cell surface bound anti-HER3 antibody was assessed by measuring the mean channel fluorescence.

Example 7

HER3Domain Binding

[0370] 96-well Maxisorp plates (Nunc) were coated overnight with 200 ng of the appropriate recombinant human protein (HER3-Tag, D1-2-Tag, D2-Tag, D3-4-Tag, D4-Tag, and a tagged irrelevant control protein). All wells were then washed with PBS/0.1% Tween-20, blocked with PBS/1% BSA/0.1% Tween-20 and washed with PBS/0.1% Tween-20. Anti-HER3 antibodies were added to the relevant wells up to a final concentration of 10 µg/mL and incubated at room temperature. Plates were washed with PBS/0.1% Tween-20 prior to the addition of the appropriate peroxidase linked detection antibody diluted 1/10000 in PBS/1% BSA/0.1% Tween-20. The detection antibodies used were goat anti-mouse (Pierce, 31432), rabbit anti-goat (Pierce, 31402) and goat anti-human (Pierce, 31412). Plates were incubated at room temperature before washing with PBS/0.1% Tween-20. 100 µl TMB (3,3',5,5' tetramethyl benzidine) substrate solution (BioFfx) was added to all wells before stopping the reaction with 50 µl 12.5% H₂SO₄. The extent of HER3 antibody binding to each recombinant protein was determined by measuring the OD₄₅₀ using a SpectraMax plate reader (Molecular Devices). Where appropriate, dose response curves were analyzed using Graphpad Prism.

Example 8

X-Ray Crystallographic Structure Determination of the Human HER3/MOR12604 Fab Complex

[0371] The present example presents the crystal structure of HER3 bound to the Fab fragment of MOR12604 determined at 3.38 Å resolution. Tagged human HER3 extracellular domain was further purified on a HiLoad 26/60 Superdex 200 PrepGrade column (GE Healthcare) equilibrated in PBS (pH 7.3). MOR12604 Fab was expressed in *E. coli* and purified as previously described. HER3/MOR12604-Fab complex was prepared by mixing excess MOR12604 Fab with

tagged HER3 in a molar ratio of 2:1 (concentration estimated by LCUV methods) and purifying the complex on a Superdex 200 10/300 column (GE Healthcare) equilibrated in 25 mM Tris (pH 7.5), 150 mM NaCl. Peak fractions were analyzed by SDS-PAGE and LCMS. Fractions containing both HER3 and Fab in an approximate equimolar ratio were pooled and concentrated to 10 mg/ml. HER3/MOR12604 crystals were grown at 293K by sitting drop vapor diffusion from drops containing 150 nl HER3/MOR12604 complex and 150 nl of reservoir solution (200 mM di-potassium hydrogen phosphate and 20% PEG 3350). Crystals were transferred to 200 mM di-potassium hydrogen phosphate, 25% PEG 3350 and 15% glycerol and flash cooled in liquid nitrogen.

[0372] Data were collected at beamline 17-ID at the Advanced Photon Source (Argonne National Laboratory). HER3/MOR12604 Fab complex data were processed and scaled at 3.38 Å using autoPROC (Global Phasing, LTD) in space group $P2_12_1$ with cell dimensions $a=56.15$, $b=174.71$, $c=186.64$ Å, with good statistics. The HER3/MOR12604 Fab structure was solved by molecular replacement using Phaser (McCoy et al., (2007) *J. Appl. Cryst.* 40:658-674) with the published HER3 ECD structure lmb6 and a proprietary Fab as search models. The final model, which contains 1 molecule of the HER3/MOR12604 Fab complex per asymmetric unit, was built in COOT (Emsley & Cowtan (2004) *Acta Cryst.* 60:2126-2132) and refined to R and Rfree values of 19.9 and 23.3%, respectively, with an rmsd of 0.008 Å and 1.19° for bond lengths and bond angles, respectively, using BUSTER (Global Phasing, LTD). Residues of HER3 that contain atoms within 5 Å of any atom in MOR12604 Fab as identified in PyMOL (Schrödinger, LLC) are listed in Tables 5 and 6.

Example 9

Phospho-HER3 In Vitro Cell Assays

[0373] MCF-7 cells were routinely maintained in DMEM/F 12, 15 mM HEPES, L-glutamine, 10% FBS, BT474 in DMEM, 10% FBS and SK-Br-3 in McCoy's 5a, 10% FBS, 1.5 mM L-glutamine. Sub-confluent cells were trypsinized, washed with PBS and diluted to 5×10^5 cells/mL. 100 µL of cell suspension was then added to each well of a 96-well flat bottomed plate (Nunc) to give a final density of 5×10^4 cells/well. MCF7 cells were allowed to attach for approximately 3 hours before the media was exchanged for starvation media containing 0.5% FBS. All plates were then incubated overnight at 37° C. prior to treatment with the appropriate concentration of HER3 antibodies for 80 minutes at 37° C. MCF7 cells were treated with 50 ng/mL NRG1 for the final 20 minutes to stimulate HER3 and AKT phosphorylation whilst BT474/SK-Br-3 cells required no additional stimulation. All media was gently aspirated and the cells washed with ice-cold PBS containing 1 mM CaCl_2 and 0.5 mM MgCl_2 (Gibco). The cells were lysed by adding 50 µL ice-cold lysis buffer (20 mM Tris (pH8.0)/137 mM NaCl/10% Glycerol/2 mM EDTA/1% NP-40/1 mM sodium orthovanadate/1× Phospho-Stop/1× Complete mini protease inhibitors (Roche)/0.1 mM PMSF) and incubated on ice with shaking for 30 minutes. Lysates were then collected and spun at 1800 g for 15 minutes at 4° C. to remove cell debris.

[0374] HER3 capture plates were generated using a carbon plate (Mesoscale Discovery) coated overnight at 4° C. with 20 µL of 4 µg/mL MAB3481 capture antibody (R&D Systems) diluted in PBS and subsequently blocked with 3% bovine

serum albumin in 1× Tris buffer (Mesoscale Discovery)/0.1% Tween-20. HER3 was captured by adding the appropriate amount of lysate and incubating the plate at room temperature for one hour with shaking before the lysate was aspirated and the wells washed with 1× Tris buffer (Mesoscale Discovery)/0.1% Tween-20. Phosphorylated HER3 was detected using 1:8000 anti-pY1197 antibody (Cell Signaling) prepared in 3% milk/1× Tris/0.1% Tween-20 by incubating with shaking at room temperature for 1 hour. The wells were washed four times with 1× Tris/0.1% Tween-20 and phosphorylated proteins were detected by incubating with S-Tag labelled goat anti-rabbit Ab (#R32AB) diluted in 3% blocking buffer for one hour at room temperature. Each well was aspirated and washed four times with 1× Tris/0.1% Tween-20 before adding 20 µL of Read buffer T with surfactant (Mesoscale Discovery) and the signal quantified using a Mesoscale Sector Imager.

Example 10

Phospho-Akt (S473) In Vitro Cell Assays

[0375] Sub-confluent MCF7, SK-Br-3 and BT-474 cells were grown in complete media were harvested with accutase (PAA Laboratories) and resuspended in the appropriate growth media at a final concentration of 5×10^5 cells/mL. 100 µL of cell suspension was then added to each well of a 96-well flat bottomed plate (Nunc) to yield a final density of 5×10^4 cells/well. MCF7 cells were allowed to attach for approximately 3 hours before the media was exchanged for starvation media containing 0.5% FBS. All plates were then incubated overnight at 37° C. prior to treatment with the appropriate concentration of HER3 antibodies for 80 minutes at 37° C. MCF7 cells were treated with 50 ng/mL NRG1 for the final 20 minutes to stimulate HER3 and AKT phosphorylation whilst SK-Br-3 cells required no additional stimulation. All media was gently aspirated and the cells washed with ice-cold PBS containing 1 mM CaCl_2 and 0.5 mM MgCl_2 (Gibco). The cells were lysed by adding 50 µL ice-cold lysis buffer (20 mM Tris (pH8.0)/137 mM NaCl/10% Glycerol/2 mM EDTA/1% NP-40/1 mM sodium orthovanadate/Aprotinin (10 µg/mL)/Leupeptin (10 µg/mL)) and incubated on ice with shaking for 30 minutes. Lysates were then collected and spun at 1800 g for 15 minutes at 4° C. to remove cell debris. 20 µL of lysate was added to a multi-spot 384-well Phospho-Akt carbon plate (Mesoscale Discovery) that had previously been blocked with 3% BSA/1× Tris/0.1% Tween-20. The plate was incubated at room temperature for two hours with shaking before the lysate was aspirated and the wells washed four times with 1× Tris buffer (Mesoscale Discovery)/0.1% Tween-20. Phosphorylated Akt was detected using 20 µL of SULFO-TAG anti-phospho-Akt (S473) antibody (Mesoscale Discovery) diluted 50-fold in 1% BSA/1× Tris/0.1% Tween-20 by incubating with shaking at room temperature for 2 hours. The wells were washed four times with 1× Tris/0.1% Tween-20 before adding 20 µL of Read buffer T with surfactant (Mesoscale Discovery) and the signal quantified using a Mesoscale Sector Imager.

Example 11

Cell-Line Proliferation Assays

[0376] SK-Br-3 cells were routinely cultured in McCoy's 5A medium modified, supplemented with 10% fetal bovine serum and BT-474 cells were cultured in DMEM supple-

mented with 10% FBS. Sub-confluent cells were trypsinized, washed with PBS, diluted to 5×10^4 cells/mL with growth media and plated in 96-well clear bottom black plates (Costar 3904) at a density of 5000 cells/well. The cells were incubated overnight at 37° C. before adding the appropriate concentration of HER3 antibody (typical final concentrations of 10 or 1 μ g/mL). The plates were returned to the incubator for 6 days before assessing cell viability using CellTiter-Glo (Promega). 100 μ L of CellTiter-Glo solution was added to each well and incubated at room temperature with gentle shaking for 10 minutes. The amount of luminescence was determined using a SpectraMax plate reader (Molecular Devices). The extent of growth inhibition obtained with each antibody was calculated by comparing the luminescence values obtained with each HER3 antibody to a standard isotype control antibody.

[0377] For proliferation assays MCF-7 cells were routinely cultured in DMEM/F12 (1:1) containing 4 mM L-Glutamine/15 mM HEPES/10% FBS. Sub-confluent cells were trypsinized, washed with PBS and diluted to 1×10^5 cells/mL with DMEM/F12 (1:1) containing 4 mM L-Glutamine/15 mM HEPES/10 μ g/mL Human Transferrin/0.2% BSA. Cells were plated in 96-well clear bottom black plates (Costar) at a density of 5000 cells/well. The appropriate concentration of HER3 antibody (typical final concentrations of 10 or 1 μ g/mL) was then added. 10 ng/mL of NRG1- β 1 EGF domain (R&D Systems) was also added to the appropriate wells to stimulate cell growth. The plates were returned to the incubator for 6 days before assessing cell viability using CellTiter-Glo (Promega). The extent of growth inhibition obtained with each antibody was calculated by subtracting the background (no neuregulin) luminescence values and comparing the resulting values obtained with each anti-HER3 antibody to a standard isotype control antibody.

Example 12

In Vivo BxPC3 Efficacy Studies

[0378] BxPC3 cells were cultured in RPMI-1640 medium containing 10% heat-inactivated fetal bovine serum without antibiotics until the time of implantation.

[0379] Female athymic nu/nu Balb/C mice (Harlan Laboratories) were implanted subcutaneously with 10×10^6 cells in a mixture of 50% phosphate buffered saline with 50% matrigel. The total injection volume containing cells in suspension was 200 μ L. Once tumors had reached approximately 200 mm³ in size, animals were enrolled in the efficacy study. In general, a total of 10 animals per group were enrolled in studies. Animals were excluded from enrollment if they exhibited unusual tumor growth characteristics prior to enrollment.

[0380] Animals were dosed intravenously via lateral tail vein injection. Animals were on a 20 mg/kg, twice weekly schedule for the duration of the study. Tumor volume and T/C values were calculated as detailed for the BT-474 studies.

Example 13

In Vivo BT474 Efficacy Studies

[0381] BT-474 cells were cultured in DMEM containing 10% heat-inactivated fetal bovine serum without antibiotics until the time of implantation.

[0382] One day before cell inoculation, female athymic nu/nu Balb/C mice (Harlan Laboratories) were implanted subcutaneously with a sustained release 17 β -estradiol pellet

(Innovative Research of America) to maintain serum estrogen levels. One day after 17 β -estradiol pellet implantation, 5×10^6 cells were injected orthotopically into the 4th mammary fat-pad in a suspension containing 50% phenol red-free matrigel (BD Biosciences) in Hank's balanced salt solution. The total injection volume containing cells in suspension was 200 μ L. 20 days following cell implantation animals with a tumor volume of approximately 200 mm³ were enrolled in the efficacy study. In general, a total of 10 animals per group were enrolled in efficacy studies.

[0383] For single-agent studies, animals were dosed intravenously via lateral tail vein injection with control IgG or MOR12606 or MOR13655. Animals were on a 20 mg/kg, twice weekly dosing schedule for the duration of the study. For combination studies, animals were dosed twice weekly at 20 mg/kg for both MOR10703 and MOR12606. For the duration of the studies, tumor volume was measured by caliper twice per week. Percent treatment/control (T/C) values were calculated using the following formula:

$$\% T/C = 100 \times \Delta T / \Delta C \text{ if } \Delta T > 0$$

where:

T=mean tumor volume of the drug-treated group on the final day of the study;

ΔT =mean tumor volume of the drug-treated group on the final day of the study–mean tumor volume of the drug-treated group on initial day of dosing;

C=mean tumor volume of the control group on the final day of the study; and

ΔC =mean tumor volume of the control group on the final day of the study–mean tumor volume of the control group on initial day of dosing.

[0384] Body weight was measured twice per week and dose was body weight adjusted. The % change in body weight was calculated as $(BW_{\text{current}} - BW_{\text{initial}}) / (BW_{\text{initial}}) \times 100$. Data is presented as percent body weight change from the day of treatment initiation.

[0385] All data were expressed as mean $\pm$ standard error of the mean (SEM). Delta tumor volume and body weight were used for statistical analysis. Between groups comparisons were carried out using a one-way ANOVA followed by a post hoc Tukey. For all statistical evaluations the level of significance was set at $p < 0.05$. Significance compared to the vehicle control group is reported.

Results and Discussion

[0386] Collectively, these results show that a class of antibodies bind to amino acid residues within domain 3 or 4. Binding of these antibodies inhibits both ligand-dependent and ligand-independent signaling.

(i) Affinity Determination

[0387] Antibody affinity was determined by solution equilibrium titration (SET) as described above. The results are summarized in Table 3 and example titration curves for MOR12615 and MOR12604 are contained in FIG. 1. The data indicate that a number of antibodies were identified that tightly bound human HER3.

TABLE 3

K _D values of anti-HER3 IgGs as determined by solution equilibrium titration (SET).				
MOR#	SET K _D (pM)			
	hu HER3-Tag	cy HER3-Tag	mu HER3-Tag	ra HER3-Tag
MOR12514	970	1400	2400	nd
MOR12515	870	720	1500	nd
MOR12516	1800	3600	3900	nd
MOR12615	102	257	336	310
MOR12920	nd	nd	nd	nd
MOR12921	150	600	560	690
MOR12922	nd	nd	nd	nd
MOR13654	110	nd	nd	nd
MOR13655	66	nd	nd	nd
MOR13656	nd	nd	nd	Nd
MOR13657	87	nd	nd	nd
MOR13658	27	nd	nd	nd
MOR13659	nd	nd	nd	nd
MOR13660	nd	nd	nd	nd
MOR13661	nd	nd	nd	nd
MOR13662	nd	nd	nd	nd
MOR13663	nd	nd	nd	nd
MOR13664	nd	nd	nd	nd
MOR13665	nd	nd	nd	nd
MOR13666	150	nd	nd	nd
MOR13667	nd	nd	nd	nd
MOR13668	nd	nd	nd	nd
MOR13669	nd	nd	nd	nd
MOR13670	nd	nd	nd	nd
MOR14537	210	140	220	285
MOR14538	45	26	23	51
MOR12603	2000	6100	4100	11000
MOR12604	1100	2200	1900	5200
MOR12605	1800	2900	2300	9600
MOR12606	1500	2600	1400	8100
MOR14533	640	2950	2000	9650
MOR14534	2150	6350	4000	30000

Hu (human), Cy (cynomolgus monkey), Mu (murine) and ra (rat), nd (not determined).

(ii) SK-Br-3 Cell EC₅₀ Determination

[0388] The ability of the identified antibodies to bind HER3 expressing cells was determined by calculating EC₅₀ values for their binding to the HER2 amplified cell line SK-Br-3 (see FIG. 2, Table 4).

TABLE 4

FACS EC ₅₀ values of anti-HER3 IgG on cells.	
MOR#	SK-Br-3 FACS EC ₅₀ (pM)
14537	179
14538	279
14533	42
14534	28

(iii) HER3 Domain Binding

[0389] A subset of anti-HER3 antibodies were characterized for their ability to bind the various extracellular domains of human HER3 in an ELISA assay. To achieve this, the extracellular domain of HER3 was divided into its four constitutive domains and various combinations of these domains were cloned, expressed and purified as independent proteins as described above. Using this strategy the following domains were successfully generated as soluble proteins: domains 1 and 2 (D1-2), domain 2 (D2), domains 3 and 4 (D3-4) and domain 4 (D4). The integrity of each isolated domain was

previously confirmed using a panel of internally generated antibodies as positive controls.

[0390] As shown in FIG. 3, MOR12615 and MOR12604 were observed to successfully bind the HER3 extracellular domain and isolated D3-4 protein. No binding was observed with D1-2 or D2 protein. This binding data suggests that these antibodies recognize an epitope primarily contained within domains 3 or 4. Interestingly, MOR12604 could bind isolated D3 protein suggesting that its epitope could be further refined to residues within domain 3. Since MOR12615 and MOR12604 are representative members of two distinct families of anti-HER3 antibodies based upon their hCDR3 sequences antibodies MOR12514, MOR12515, MOR12516, MOR12615, MOR12920, MOR12921, MOR12922, MOR13654, MOR13655, MOR13656, MOR13657, MOR13658, MOR13659, MOR13660, MOR13661, MOR13662, MOR13663, MOR13664, MOR13665, MOR13666, MOR13667, MOR13668, MOR13669, MOR13670, MOR14537 and MOR14538 can be classed as D3-4 binder. Antibodies MOR12603, MOR12604, MOR12605, MOR12606, MOR14533 and MOR14534 can be classed as D3 binders.

(iv) HER3/MOR12604 Crystal Structure

[0391] The 3.38 Å resolution x-ray crystal structure of MOR12604 Fab fragment bound to the HER3 extracellular domain was solved to further define the HER3 epitope that is recognized by this family of related antibodies (see FIG. 4). Overlay of the MOR12604/HER3 crystal structure with published HER3 crystal structures suggested that HER3 bound by MOR12604 is in the tethered (inactive) conformation (see FIG. 4B). This conformation is characterized by a significant interaction interface between domains 2 and 4 mediated by a (3-hairpin dimerization loop in domain 2. The observed conformation of HER3 is similar to that previously described by Cho et al. (Cho & Leahy, (2002), Science 297:1330-1333) who published the crystal structure of the HER3 extra-cellular domain in the absence of neuregulin. Since neuregulin can activate HER3, the tethered conformation of HER3 is presumed to be inactive. Similar tethered conformations have also been observed when the related EGFR family members HER4 (Bouyain et al., (2005) Proc. Natl. Acad. Sci. USA, 102:15024-15029) and HER1 (Ferguson et al., (2003) Molec. Cell 11:507-517) have been crystallized.

[0392] The spatial relationships between domains 1 to 4 of HER3 in the inactive (tethered) state are significantly different from that of the extended (active) state. This finding is based upon the crystal structures of the related EGFR family members HER2 and ligand-bound HER1 (Cho et al., (2003) Nature 421:756-760; Ogiso et al., (2002) Cell 110:775-787; Garrett et al., (2002) Cell 110:763-773) both of which are in an extended (active) state. In the extended state, the domain 2β-hairpin dimerization loop is released from its inhibitory interaction with 4 and is thus free to interact with its dimerization partner proteins. Thus, the domain 2β-hairpin dimerization loop is functionally important both in maintaining the tethered (inactive) state and in mediating dimerization of EGF receptors in the extended state, leading to activation of the intracellular kinase domain.

[0393] In the crystal structure, electron density for MOR12604 Fab, HER3 domain 3, HER3 domain 4 and a portion of domain 2 (residues 261-278) including the β-hairpin dimerization loop were all well defined. Weak or no electron density was observed for HER3 residues 20-260 and

279-303 which are located in domain 1 and domain 2, suggesting that when HER3 is bound by MOR12604 it retains some degree of flexibility. This finding is consistent with a comparison of other crystal structures of HER3 alone and bound to various Fab fragments that showed slight differences in relative domain positioning within the tethered state.

[0394] The crystal structure also revealed that the HER3 epitope recognized by MOR12604 is a non-linear epitope that includes residues from domain 3 (see FIG. 4, Tables 5 and 6). The HER3 epitope recognized by this family of highly related antibodies can therefore be defined as:

[0395] Domain 3: residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455.

[0396] The MOR12604 binding surface can be further subdivided into two surfaces highlighted as solid and dashed circles in FIG. 4D:

[0397] Surface A: residues 362-376

[0398] Surface B: residues 335-342, 398, 400, 424-428, 431, 433-434 and 455

[0399] Surface A or Surface B contribute approximately the same surface area to the overall HER3/12604 interface (Surface A—640 Å², Surface B—546 Å²).

[0400] Interestingly, MOR12604 binding to domain 3 resulted in a significant conformational change in the loop defined by HER3 residues 371-377. This conformation of this loop is different from other published HER3 structures thus suggesting that it is induced by MOR12604 binding. The MOR12604 epitope determined from the crystal structure is consistent with our ELISA domain binding data where MOR12604 was determined to bind isolated D3 protein. Furthermore, comparison of the MOR12604 epitope with the EGFR residues contacted by TGFα highlighted a high degree of overlap (Garrett et al., (2002) Cell 110:763-773). Since neuregulin is thought to interact with HER3 in a similar manner to TGFα/EGFR it is highly likely that MOR12604 will prevent ligand binding thus blocking neuregulin induced HER3 activation.

[0401] Binding within domain 3 by MOR12604 would suggest that MOR12604 could function by any (or a combination) of the following mechanisms:

[0402] by blocking HER3 residues required for ligand binding

[0403] by preventing HER3 adopting the active conformation due to steric hindrance between the antibody and domains of HER3

[0404] by preventing HER3 adopting the active conformation by reducing the degree of flexibility in HER3 hinge regions (e.g. domain 3)

[0405] by inducing a conformational change in domain 3 loop 371-377 that prevents HER3 from transitioning to the open conformation

[0406] by destabilizing HER3 such that it is prone to degradation

[0407] by acting as a partial agonist to accelerate the down regulation of HER3

[0408] by inhibiting dimerization with a binding partner

[0409] by each arm of MOR12604 binding a molecule of HER3 such that the antibody generates an un-natural HER3 dimer that is either prone to proteolytic degradation or cannot dimerize with other receptor tyrosine kinases

TABLE 5

Interactions between MOR12604 Fab heavy chain and human HER3.
Fab VH residues are numbered based upon their linear amino acid sequence (SEQ ID NO: 1). HER3 residues are numbered based upon NP_001973. HER3 residues shown have at least one atom within 5 Å of an atom in the MOR12604 Fab.

MOR12604 Fab			Human HER3		
Residue	Number	Chain	Residue	Number	Domain
GLN	1	H	PRO	372	3
			TRP	373	3
			HIS	374	3
			LYS	375	3
VAL	2	H	PRO	372	3
			TRP	373	3
LEU	4	H	TRP	373	3
ALA	24	H	TRP	373	3
THR	28	H	TRP	373	3
PHE	29	H	TRP	373	3
TYR	32	H	GLY	370	3
			ASP	371	3
			PRO	372	3
			TRP	373	3
ILE	34	H	TRP	373	3
ARG	98	H	ASP	371	3
			TRP	373	3
TRP	100	H	ILE	365	3
			THR	366	3
			ASN	369	3
			GLY	370	3
PRO	101	H	ASP	371	3
			ILE	365	3
TYR	102	H	THR	366	3
			ILE	365	3
			GLN	400	3
			LYS	434	3
ASP	106	H	ASP	371	3
PHE	107	H	ASP	371	3
			TRP	373	3
			HIS	374	3

TABLE 6

Interactions between MOR12604 Fab light chain and human HER3.
Fab VL residues are numbered based upon their linear amino acid sequence (SEQ ID NO: 1). HER3 residues are numbered based upon NP_001973. HER3 residues shown have at least one atom within 5 Å of an atom in the MOR12604 Fab.

MOR12604 Fab			Human HER3		
Residue	Number	Chain	Residue	Number	Domain
VAL	30	L	MET	433	3
			TYR	455	3
PHE	31	L	ASN	425	3
			PHE	428	3
			LEU	431	3
			MET	433	3
TYR	49	L	TYR	455	3
			LEU	364	3
			ILE	365	3
			THR	366	3
ASP	50	L	GLN	400	3
			TYR	424	3
			LYS	434	3
			ASN	425	3
ALA	51	L	ASN	425	3
SER	52	L	TYR	424	3
			ASN	425	3
			ASP	362	3
ASN	53	L	LEU	364	3
			ASN	398	3

TABLE 6-continued

Interactions between MOR12604 Fab light chain and human HER3. Fab VL residues are numbered based upon their linear amino acid sequence (SEQ ID NO: 1). HER3 residues are numbered based upon NP_001973. HER3 residues shown have at least one atom within 5 Å of an atom in the MOR12604 Fab.					
MOR12604 Fab			Human HER3		
Residue	Number	Chain	Residue	Number	Domain
ARG	54	L	GLN	400	3
			TYR	424	3
			GLY	335	3
			SER	336	3
			GLY	337	3
			SER	338	3
			PHE	340	3
ALA	55	L	GLN	341	3
			LEU	364	3
			THR	366	3
			GLN	341	3
THR	56	L	GLN	341	3
THR	56	L	THR	366	3
			HIS	374	3
			ILE	376	3
GLY	57	L	GLN	341	3
VAL	58	L	GLN	341	3
ALA	60	L	GLY	337	3
GLY	64	L	SER	338	3
			ASN	425	3
SER	65	L	ASN	425	3
GLY	66	L	ARG	426	3
			ASN	425	3
			ARG	426	3
SER	67	L	ASN	425	3
LYS	91	L	ARG	426	3
			LYS	434	3

(v) Inhibition of Cell Signaling

[0410] To ascertain the effect of anti-HER3 antibodies upon ligand dependent HER3 activity MCF7 cells were incubated with IgG prior to stimulation with neuregulin. Example inhibition curves are illustrated in FIG. 5 and summarized in Table 7. The effect of anti-HER3 antibodies upon HER2-mediated HER3 activation was also studied using the HER2 amplified cell lines SK-Br-3 and BT474 (FIG. 6, FIG. 7, and Table 7).

TABLE 7

pHER3 IC ₅₀ and extent of inhibition values of anti-HER3 IgG in MCF7, BT474 and SK-Br-3 cells.						
MOR#	MCF7 pHER3		SK-Br-3 pHER3		BT474 pHER3	
	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition
MOR12514	435	67	223	77	707	70
MOR12515	674	71	278	76	365	71
MOR12516	590	62	1873	74	nd	63
MOR12615	447	75	179	71	421	56
MOR12920	3066	66	851	57	2021	57
MOR12921	1230	79	252	68	418	65
MOR12922	788	62	81	64	702	58
MOR13654	331	77	182	69	195	61
MOR13655	149	80	90	69	19	61
MOR13656	504	73	86	60	nd	nd
MOR13657	283	75	142	71	372	63
MOR13658	459	83	347	74	571	67
MOR13659	505	66	277	51	nd	nd

TABLE 7-continued

pHER3 IC ₅₀ and extent of inhibition values of anti-HER3 IgG in MCF7, BT474 and SK-Br-3 cells.						
MOR#	MCF7 pHER3		SK-Br-3 pHER3		BT474 pHER3	
	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition
MOR13660	533	49	188	54	nd	nd
MOR13661	649	55	421	55	nd	nd
MOR13662	550	52	331	56	nd	nd
MOR13663	449	58	290	56	nd	nd
MOR13664	480	55	388	57	nd	nd
MOR13665	795	62	546	59	nd	nd
MOR13666	168	73	166	69	420	65
MOR13667	603	72	267	59	nd	nd
MOR13668	1640	77	657	58	nd	nd
MOR13669	nd	66	743	58	nd	nd
MOR13670	643	69	730	60	nd	nd
MOR14537	200	73	97	69	nd	nd
MOR14538	615	83	263	71	nd	nd
MOR12603	11	77	18	74	79	70
MOR12604	57	79	29	71	142	62
MOR12605	318	89	7	73	1486	64
MOR12606	34	87	25	75	108	73
MOR14533	50	67	20	68	nd	nd
MOR14534	16	71	10	63	nd	nd

[0411] To determine whether inhibition of HER3 activity impacted downstream cell signaling, Akt, phosphorylation was measured in NRG stimulated MCF7 cells and HER2 amplified SK-Br-3/BT474 cells following treatment with anti-HER3 antibodies (see FIG. 5, FIG. 6, and Table 8)

TABLE 8

pAkt (S ⁴⁷³) IC ₅₀ and extent of inhibition values of anti-HER3 IgG in SK-Br-3, BT-474 and MCF7 cells						
MOR#	SK-Br-3 pAkt		BT-474 pAkt		MCF7 pAkt	
	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition
MOR12514	nd	nd	nd	nd	nd	nd
MOR12515	nd	nd	nd	nd	nd	nd
MOR12516	nd	nd	nd	nd	nd	nd
MOR12615	101	86	466	63	815	78
MOR12920	nd	nd	nd	nd	nd	nd
MOR12921	nd	nd	nd	nd	nd	nd
MOR12922	nd	nd	nd	nd	nd	nd
MOR13654	89	92	142	58	244	72
MOR13655	62	86	nd	50	251	79
MOR13656	nd	nd	nd	nd	nd	nd
MOR13657	33	91	586	53	385	75
MOR13658	172	92	461	56	341	81
MOR13659	nd	nd	nd	nd	nd	nd
MOR13660	nd	nd	nd	nd	nd	nd
MOR13661	nd	nd	nd	nd	nd	nd
MOR13662	nd	nd	nd	nd	nd	nd
MOR13663	nd	nd	nd	nd	nd	nd
MOR13664	nd	nd	nd	nd	nd	nd
MOR13665	nd	nd	nd	nd	nd	nd
MOR13666	78	90	275	50	49	72
MOR13667	nd	nd	nd	nd	nd	nd
MOR13668	nd	nd	nd	nd	nd	nd
MOR13669	nd	nd	nd	nd	nd	nd
MOR13670	nd	nd	nd	nd	nd	nd
MOR14537	nd	nd	nd	nd	nd	nd
MOR14538	nd	nd	nd	nd	nd	nd
MOR12603	17	84	137	77	nd	nd
MOR12604	17	85	225	70	235	74
MOR12605	140	84	173	67	533	76
MOR12606	8	85	91	77	nd	nd

TABLE 8-continued

pAkt (S ⁴⁷³) IC ₅₀ and extent of inhibition values of anti-HER3 IgG in SK-Br-3, BT-474 and MCF7 cells						
MOR#	SK-Br-3 pAkt		BT-474 pAkt		MCF7 pAkt	
	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition
MOR14533	nd	nd	nd	nd	nd	nd
MOR14534	nd	nd	nd	nd	nd	nd

[0412] In summary MOR12514, MOR12515, MOR12516, MOR12615, MOR12920, MOR12921, MOR12922, MOR13654, MOR13655, MOR13656, MOR13657, MOR13658, MOR13659, MOR13660, MOR13661, MOR13662, MOR13663, MOR13664, MOR13665, MOR13666, MOR13667, MOR13668, MOR13669, MOR13670, MOR14537, MOR14538, MOR12603, MOR12604, MOR12605, MOR12606, MOR14533 and MOR14534 are each capable of inhibiting cellular HER3 activity and downstream signaling in both a ligand-dependent and ligand-independent manner.

(vi) Inhibition of Proliferation

[0413] Since MOR12514, MOR12515, MOR12516, MOR12615, MOR12920, MOR12921, MOR12922, MOR13654, MOR13655, MOR13656, MOR13657, MOR13658, MOR13659, MOR13660, MOR13661, MOR13662, MOR13663, MOR13664, MOR13665, MOR13666, MOR13667, MOR13668, MOR13669, MOR13670, MOR14537, MOR14538, MOR12603, MOR12604, MOR12605, MOR12606, MOR14533 and MOR14534 are capable of inhibiting HER3 activity a sub-set were tested for their ability to block ligand dependent and independent in vitro cell growth (example data is shown in FIG. 8, FIG. 9, FIG. 10 and summarized in Table 9). The anti-HER3 antibodies tested were all effective inhibitors of cell proliferation thus confirming that antibodies that bind D3 or D3-4 are capable of inhibiting HER3 driven phenotypes.

TABLE 9

Inhibition of proliferation following treatment with anti-HER3 IgG in SK-Br-3, BT-474 and MCF7 cells.						
MOR#	SK-Br-3		BT-474		MCF7	
	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% in- hibition
MOR12514	44	36	nd	nd	317	29
MOR12515	278	36	nd	nd	1091	26
MOR12516	2082	34	nd	nd	492	34
MOR12615	121	40	459	35	2537	42
MOR12920	2910	32	nd	nd	1921	22
MOR12921	432	42	nd	nd	2310	31
MOR12922	709	36	nd	nd	467	27
MOR13654	136	34	632	27	nd	nd
MOR13655	74	39	141	31	86	46
MOR13656	nd	nd	nd	nd	nd	nd
MOR13657	179	39	473	30	nd	nd
MOR13658	191	42	423	34	174	49
MOR13659	nd	nd	nd	nd	nd	nd
MOR13660	nd	nd	nd	nd	nd	nd
MOR13661	nd	nd	nd	nd	nd	nd
MOR13662	nd	nd	nd	nd	nd	nd
MOR13663	nd	nd	nd	nd	nd	nd
MOR13664	nd	nd	nd	nd	nd	nd

TABLE 9-continued

Inhibition of proliferation following treatment with anti-HER3 IgG in SK-Br-3, BT-474 and MCF7 cells.						
MOR#	SK-Br-3		BT-474		MCF7	
	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% inhibition	IC ₅₀ (pM)	% in- hibition
MOR13665	nd	nd	nd	nd	nd	nd
MOR13666	870	39	1120	31	nd	nd
MOR13667	nd	nd	nd	nd	nd	nd
MOR13668	nd	nd	nd	nd	nd	nd
MOR13669	nd	nd	nd	nd	nd	nd
MOR13670	nd	nd	nd	nd	nd	nd
MOR14537	47	48	nd	nd	nd	nd
MOR14538	81	53	nd	nd	nd	nd
MOR12603	34	36	136	37	58	44
MOR12604	15	42	nd	nd	73	39
MOR12605	0.01	29	nd	nd	28	45
MOR12606	nd	36	127	40	52	39
MOR14533	26	46	nd	nd	nd	nd
MOR14534	27	40	nd	nd	nd	nd

(vii) In Vivo Inhibition of Tumor Growth

[0414] To determine the in vivo activity of the described anti-HER3 antibodies, MOR12606 and MOR13655 were tested for anti-tumor activity in both BxPC3 and BT-474 tumor models. Repeated dosing of the BxPC3 model using MOR12606 or MOR13655 yielded 25% regression and 5% T/C, respectively (FIG. 11A).

[0415] Single agent treatment of the HER2-driven BT474 model with either MOR12606 or MOR13655 resulted in 53% or 46% T/C, respectively (FIG. 11B).

[0416] We also investigated the effect of combining two HER3-targeted antibodies that bind two distinct, non-overlapping epitopes. Repeated dosing of the BT474 model with a combination of MOR10703 and MOR12606 yielded 7% T/C (FIG. 12).

INCORPORATION BY REFERENCE

[0417] All references cited herein, including patents, patent applications, papers, text books, and the like, and the references cited therein, to the extent that they are not already, are hereby incorporated herein by reference in their entirety.

EQUIVALENTS

[0418] The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The foregoing description and examples detail certain preferred embodiments of the invention and describe the best mode contemplated by the inventors. It will be appreciated, however, that no matter how detailed the foregoing may appear in text, the invention may be practiced in many ways and the invention should be construed in accordance with the appended claims and any equivalents thereof.

 SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 702

<210> SEQ ID NO 1

<211> LENGTH: 1342

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

Met Arg Ala Asn Asp Ala Leu Gln Val Leu Gly Leu Leu Phe Ser Leu
 1 5 10 15
 Ala Arg Gly Ser Glu Val Gly Asn Ser Gln Ala Val Cys Pro Gly Thr
 20 25 30
 Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Glu Asn Gln Tyr Gln Thr
 35 40 45
 Leu Tyr Lys Leu Tyr Glu Arg Cys Glu Val Val Met Gly Asn Leu Glu
 50 55 60
 Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
 65 70 75 80
 Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Thr
 85 90 95
 Leu Pro Leu Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp
 100 105 110
 Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser
 115 120 125
 His Ala Leu Arg Gln Leu Arg Leu Thr Gln Leu Thr Glu Ile Leu Ser
 130 135 140
 Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr
 145 150 155 160
 Ile Asp Trp Arg Asp Ile Val Arg Asp Arg Asp Ala Glu Ile Val Val
 165 170 175
 Lys Asp Asn Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly
 180 185 190
 Arg Cys Trp Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr
 195 200 205
 Ile Cys Ala Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn
 210 215 220
 Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
 225 230 235 240
 Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
 245 250 255
 Pro Arg Cys Pro Gln Pro Leu Val Tyr Asn Lys Leu Thr Phe Gln Leu
 260 265 270
 Glu Pro Asn Pro His Thr Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala
 275 280 285
 Ser Cys Pro His Asn Phe Val Val Asp Gln Thr Ser Cys Val Arg Ala
 290 295 300
 Cys Pro Pro Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys
 305 310 315 320
 Glu Pro Cys Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser
 325 330 335
 Gly Ser Arg Phe Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val
 340 345 350

-continued

Asn	Cys	Thr	Lys	Ile	Leu	Gly	Asn	Leu	Asp	Phe	Leu	Ile	Thr	Gly	Leu	
	355						360					365				
Asn	Gly	Asp	Pro	Trp	His	Lys	Ile	Pro	Ala	Leu	Asp	Pro	Glu	Lys	Leu	
	370					375					380					
Asn	Val	Phe	Arg	Thr	Val	Arg	Glu	Ile	Thr	Gly	Tyr	Leu	Asn	Ile	Gln	
385					390					395					400	
Ser	Trp	Pro	Pro	His	Met	His	Asn	Phe	Ser	Val	Phe	Ser	Asn	Leu	Thr	
				405					410					415		
Thr	Ile	Gly	Gly	Arg	Ser	Leu	Tyr	Asn	Arg	Gly	Phe	Ser	Leu	Leu	Ile	
		420						425					430			
Met	Lys	Asn	Leu	Asn	Val	Thr	Ser	Leu	Gly	Phe	Arg	Ser	Leu	Lys	Glu	
	435						440					445				
Ile	Ser	Ala	Gly	Arg	Ile	Tyr	Ile	Ser	Ala	Asn	Arg	Gln	Leu	Cys	Tyr	
	450					455				460						
His	His	Ser	Leu	Asn	Trp	Thr	Lys	Val	Leu	Arg	Gly	Pro	Thr	Glu	Glu	
465					470					475					480	
Arg	Leu	Asp	Ile	Lys	His	Asn	Arg	Pro	Arg	Arg	Asp	Cys	Val	Ala	Glu	
				485					490					495		
Gly	Lys	Val	Cys	Asp	Pro	Leu	Cys	Ser	Ser	Gly	Gly	Cys	Trp	Gly	Pro	
			500					505					510			
Gly	Pro	Gly	Gln	Cys	Leu	Ser	Cys	Arg	Asn	Tyr	Ser	Arg	Gly	Gly	Val	
		515					520					525				
Cys	Val	Thr	His	Cys	Asn	Phe	Leu	Asn	Gly	Glu	Pro	Arg	Glu	Phe	Ala	
	530					535					540					
His	Glu	Ala	Glu	Cys	Phe	Ser	Cys	His	Pro	Glu	Cys	Gln	Pro	Met	Glu	
545					550					555					560	
Gly	Thr	Ala	Thr	Cys	Asn	Gly	Ser	Gly	Ser	Asp	Thr	Cys	Ala	Gln	Cys	
				565					570					575		
Ala	His	Phe	Arg	Asp	Gly	Pro	His	Cys	Val	Ser	Ser	Cys	Pro	His	Gly	
			580					585					590			
Val	Leu	Gly	Ala	Lys	Gly	Pro	Ile	Tyr	Lys	Tyr	Pro	Asp	Val	Gln	Asn	
		595					600					605				
Glu	Cys	Arg	Pro	Cys	His	Glu	Asn	Cys	Thr	Gln	Gly	Cys	Lys	Gly	Pro	
	610					615					620					
Glu	Leu	Gln	Asp	Cys	Leu	Gly	Gln	Thr	Leu	Val	Leu	Ile	Gly	Lys	Thr	
625					630					635					640	
His	Leu	Thr	Met	Ala	Leu	Thr	Val	Ile	Ala	Gly	Leu	Val	Val	Ile	Phe	
				645					650					655		
Met	Met	Leu	Gly	Gly	Thr	Phe	Leu	Tyr	Trp	Arg	Gly	Arg	Arg	Ile	Gln	
		660						665					670			
Asn	Lys	Arg	Ala	Met	Arg	Arg	Tyr	Leu	Glu	Arg	Gly	Glu	Ser	Ile	Glu	
	675						680					685				
Pro	Leu	Asp	Pro	Ser	Glu	Lys	Ala	Asn	Lys	Val	Leu	Ala	Arg	Ile	Phe	
	690					695					700					
Lys	Glu	Thr	Glu	Leu	Arg	Lys	Leu	Lys	Val	Leu	Gly	Ser	Gly	Val	Phe	
705					710					715					720	
Gly	Thr	Val	His	Lys	Gly	Val	Trp	Ile	Pro	Glu	Gly	Glu	Ser	Ile	Lys	
				725					730					735		
Ile	Pro	Val	Cys	Ile	Lys	Val	Ile	Glu	Asp	Lys	Ser	Gly	Arg	Gln	Ser	
		740						745					750			
Phe	Gln	Ala	Val	Thr	Asp	His	Met	Leu	Ala	Ile	Gly	Ser	Leu	Asp	His	

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755	760	765
Ala His Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln 770 775 780		
Leu Val Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg 785 790 795 800		
Gln His Arg Gly Ala Leu Gly Pro Gln Leu Leu Asn Trp Gly Val 805 810 815		
Gln Ile Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Gly Met Val His 820 825 830		
Arg Asn Leu Ala Ala Arg Asn Val Leu Leu Lys Ser Pro Ser Gln Val 835 840 845		
Gln Val Ala Asp Phe Gly Val Ala Asp Leu Leu Pro Pro Asp Asp Lys 850 855 860		
Gln Leu Leu Tyr Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu 865 870 875 880		
Glu Ser Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser 885 890 895		
Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr 900 905 910		
Ala Gly Leu Arg Leu Ala Glu Val Pro Asp Leu Leu Glu Lys Gly Glu 915 920 925		
Arg Leu Ala Gln Pro Gln Ile Cys Thr Ile Asp Val Tyr Met Val Met 930 935 940		
Val Lys Cys Trp Met Ile Asp Glu Asn Ile Arg Pro Thr Phe Lys Glu 945 950 955 960		
Leu Ala Asn Glu Phe Thr Arg Met Ala Arg Asp Pro Pro Arg Tyr Leu 965 970 975		
Val Ile Lys Arg Glu Ser Gly Pro Gly Ile Ala Pro Gly Pro Glu Pro 980 985 990		
His Gly Leu Thr Asn Lys Lys Leu Glu Glu Val Glu Leu Glu Pro Glu 995 1000 1005		
Leu Asp Leu Asp Leu Asp Leu Glu Ala Glu Glu Asp Asn Leu Ala 1010 1015 1020		
Thr Thr Thr Leu Gly Ser Ala Leu Ser Leu Pro Val Gly Thr Leu 1025 1030 1035		
Asn Arg Pro Arg Gly Ser Gln Ser Leu Leu Ser Pro Ser Ser Gly 1040 1045 1050		
Tyr Met Pro Met Asn Gln Gly Asn Leu Gly Glu Ser Cys Gln Glu 1055 1060 1065		
Ser Ala Val Ser Gly Ser Ser Glu Arg Cys Pro Arg Pro Val Ser 1070 1075 1080		
Leu His Pro Met Pro Arg Gly Cys Leu Ala Ser Glu Ser Ser Glu 1085 1090 1095		
Gly His Val Thr Gly Ser Glu Ala Glu Leu Gln Glu Lys Val Ser 1100 1105 1110		
Met Cys Arg Ser Arg Ser Arg Ser Arg Ser Pro Arg Pro Arg Gly 1115 1120 1125		
Asp Ser Ala Tyr His Ser Gln Arg His Ser Leu Leu Thr Pro Val 1130 1135 1140		
Thr Pro Leu Ser Pro Pro Gly Leu Glu Glu Glu Asp Val Asn Gly 1145 1150 1155		

-continued

Tyr Val	Met Pro Asp Thr	His	Leu Lys Gly Thr	Pro	Ser Ser Arg
1160		1165		1170	
Glu Gly	Thr Leu Ser Ser	Val	Gly Leu Ser Ser	Val	Leu Gly Thr
1175		1180		1185	
Glu Glu	Glu Asp Glu Asp	Glu	Glu Tyr Glu Tyr	Met	Asn Arg Arg
1190		1195		1200	
Arg Arg	His Ser Pro Pro	His	Pro Pro Arg Pro	Ser	Ser Leu Glu
1205		1210		1215	
Glu Leu	Gly Tyr Glu Tyr	Met	Asp Val Gly Ser	Asp	Leu Ser Ala
1220		1225		1230	
Ser Leu	Gly Ser Thr Gln	Ser	Cys Pro Leu His	Pro	Val Pro Ile
1235		1240		1245	
Met Pro	Thr Ala Gly Thr	Thr	Pro Asp Glu Asp	Tyr	Glu Tyr Met
1250		1255		1260	
Asn Arg	Gln Arg Asp Gly	Gly	Gly Pro Gly Gly	Asp	Tyr Ala Ala
1265		1270		1275	
Met Gly	Ala Cys Pro Ala	Ser	Glu Gln Gly Tyr	Glu	Glu Met Arg
1280		1285		1290	
Ala Phe	Gln Gly Pro Gly	His	Gln Ala Pro His	Val	His Tyr Ala
1295		1300		1305	
Arg Leu	Lys Thr Leu Arg	Ser	Leu Glu Ala Thr	Asp	Ser Ala Phe
1310		1315		1320	
Asp Asn	Pro Asp Tyr Trp	His	Ser Arg Leu Phe	Pro	Lys Ala Asn
1325		1330		1335	
Ala Gln	Arg Thr				
1340					

<210> SEQ ID NO 2
 <211> LENGTH: 5
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 2

Ser Tyr Ala Ile Ser
 1 5

<210> SEQ ID NO 3
 <211> LENGTH: 17
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 3

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
 1 5 10 15

Gly

<210> SEQ ID NO 4
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

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<400> SEQUENCE: 4

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 5

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 5

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 6

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 6

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 7

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 7

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 8

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 8

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 9

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 9

Asp Ala Ser Asn Arg Ala Thr
1 5

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<210> SEQ ID NO 10
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 10

Gln Gln His Gly Ser Gly Pro Thr Thr
1 5

<210> SEQ ID NO 11
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 11

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 12
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 12

Asp Ala Ser
1

<210> SEQ ID NO 13
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 13

His Gly Ser Gly Pro Thr
1 5

<210> SEQ ID NO 14
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 14

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60

-continued

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser
 115

<210> SEQ ID NO 15
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polypeptide

<400> SEQUENCE: 15

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Gly Ser Gly Pro Thr
 85 90 95
 Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 16
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polynucleotide

<400> SEQUENCE: 16

cagggtgcaat tgggttcagtc tggcgcggaac gtgaaaaaac cgggcagcag cgtgaaagtg 60
 agctgc aaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc 120
 cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat 180
 gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat 240
 atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg 300
 ccttattatt atatggattt ttggggccaa ggcaccctgg tgacgggttag ctca 354

<210> SEQ ID NO 17
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polynucleotide

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<400> SEQUENCE: 17

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gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc      60
ctgagctgca gagcgagcca gaattattgtt tttaatctgg cttggtacca gcagaaacca      120
ggtaagcac cgcgtctatt aatttatgat gcttctaatac gtgcaactgg ggtcccggcg      180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct      240
gaagactttg cggtttatta ttgccagcag catggttctg gtctactac ctttgccag      300
ggtacgaaag ttgaaattaa a                                           321

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<210> SEQ ID NO 18

<211> LENGTH: 448

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 18

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1           5           10           15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20          25          30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50          55          60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100         105         110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115         120         125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130         135         140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145         150         155         160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165         170         175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180         185         190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195         200         205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
210         215         220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225         230         235         240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245         250         255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260         265         270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala

```

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275	280	285
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val		
290	295	300
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr		
305	310	315
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr		
	325	330
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu		
	340	345
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys		
	355	360
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser		
	370	375
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp		
385	390	395
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser		
	405	410
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala		
	420	425
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
	435	440
		445

<210> SEQ ID NO 19

<211> LENGTH: 214

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 19

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly		
1	5	10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn		
	20	25
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile		
	35	40
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly		
	50	55
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro		
65	70	75
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Gly Ser Gly Pro Thr		
	85	90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala		
	100	105
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
	115	120
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
	130	135
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
145	150	155
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
	165	170
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
		175

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180	185	190	
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser			
195	200	205	

Phe Asn Arg Gly Glu Cys
210

<210> SEQ ID NO 20
 <211> LENGTH: 1344
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 20

caggtgcaat tgggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg agctgcaaa cctccggagg cacttttagc agctatgca ttagctgggt gcgccaagcc cctgggcagg gtctcgatg gatgggctt attattctc gttatggtaa ggctcggtat gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat atggaactga gcagcctgct tagcgaagat acggccgtgt attattgcgc gcgtaattgg ccttattatt atatggtatt ttggggccaa ggcaccctgg tgacgggttag ctcagcctcc accaagggtc catcggtctt ccccttgga cctcctcca agagcacctc tgggggcaca gcggccctgg gctgcctggt caaggactac tccccgaac cggtgacggt gtcgtggaac tcaggcgccc tgaccagcgg cgtgcacacc tccccgctg tcctacagtc ctcaggactc tactccctca gcagcgtggt gaccgtgccc tcacagcagc tgggcaccca gacctacatc tgcaactga atcacaagcc cagcaacacc aaggtggaca agagagtga gcccaaatct tgtgacaaaa ctcacacatg cccacgtgc ccagcacctg aactcctggg gggaccgtca gtcttctct tcccccaaa acccaaggac accctcatga tctcccgac cctgaggtc acatgcgtgg tgggtgagct gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg taccgggtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac aagtgaagg tctccaacaa agccctccca gccccatcg agaaaacat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac accctgccc catcccgga ggagatgacc aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catgcctgtg gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac tccgacggt ctttcttct ctacagcaag ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggtctgc acaaccacta cagcagaag agcctctccc tgtctcggg taaa	60 120 180 240 300 360 420 480 540 600 660 720 780 840 900 960 1020 1080 1140 1200 1260 1320 1344

<210> SEQ ID NO 21
 <211> LENGTH: 642
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 21

gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcca acgtgcgacc	60

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ctgagctgca gagcgagcca gaatatgtt tttaatctgg cttggtacca gcagaaacca 120
ggtaagcac cgcgtctatt aatttatgat gcttctaate gtgcaactgg ggtcccgcg 180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct 240
gaagactttg cggtttatta ttgccagcag catggttctg gtctactac ctttggccag 300
ggtaagaaa ttgaaattaa acgtacgggtg gccgtccca gcgtgttcat cttcccccc 360
agcgacgagc agctgaagag cggcacgcc agcgtggtgt gcctgctgaa caactttctac 420
ccccgggagg ccaaggtgca gtggaagggtg gacaacgccc tgcagagcgg caacagccag 480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> SEQ ID NO 22
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 22

Ser Tyr Ala Ile Ser
1 5

<210> SEQ ID NO 23
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 23

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 24
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 24

Asn Trp Pro Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 25
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 25

Gly Gly Thr Phe Ser Ser Tyr

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1 5

<210> SEQ ID NO 26
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 26

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 27
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 27

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 28
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 28

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 29
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 29

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 30
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 30

Gln Gln Thr Lys Asn Arg Pro Pro Thr
1 5

<210> SEQ ID NO 31
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 31

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 32
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 32

Asp Ala Ser
1

<210> SEQ ID NO 33
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 33

Thr Lys Asn Arg Pro Pro
1 5

<210> SEQ ID NO 34
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 34

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 35
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 35

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys Asn Arg Pro Pro
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 36

<211> LENGTH: 354

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 36

cagggtcaat tggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg 60
agctgcaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaaagcc 120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat 180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat 240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg 300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggtttag ctca 354

<210> SEQ ID NO 37

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 37

gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc 60
ctgagctgca gagcgagcca gaatattgtt tttaatctgg cttggtacca gcagaaacca 120
ggteaagcac cgcgtctatt aatttatgat gcttctaacc gtgcaactgg ggtcccggcg 180
cgtttttagcg gctctggatc cggaacggat tttaccctga ccattagcag cctggaacct 240
gaagactttt cgggtgtatta ttgccagcag actaagaatc gtcctcctac ctttggccag 300
ggtacgaaag ttgaaattaa a 321

<210> SEQ ID NO 38

<211> LENGTH: 448

<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 38

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
 20 25 30
 Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
 115 120 125
 Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 130 135 140
 Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
 145 150 155 160
 Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 165 170 175
 Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 180 185 190
 Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
 195 200 205
 Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
 210 215 220
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 260 265 270
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

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370	375	380
Asn Gly Gln Pro Glu	Asn Asn Tyr Lys Thr	Thr Pro Pro Val Leu Asp
385	390	395 400
Ser Asp Gly Ser Phe	Phe Leu Tyr Ser Lys	Leu Thr Val Asp Lys Ser
	405	410 415
Arg Trp Gln Gln Gly	Asn Val Phe Ser Cys	Ser Val Met His Glu Ala
	420	425 430
Leu His Asn His Tyr	Thr Gln Lys Ser Leu	Ser Leu Ser Pro Gly Lys
	435	440 445

<210> SEQ ID NO 39
 <211> LENGTH: 214
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 39

Asp Ile Val Leu Thr	Gln Ser Pro Ala Thr	Leu Ser Leu Ser Pro Gly
1	5	10 15
Glu Arg Ala Thr	Leu Ser Cys Arg Ala	Ser Gln Asn Ile Val Phe Asn
	20	25 30
Leu Ala Trp Tyr	Gln Gln Lys Pro Gly	Gln Ala Pro Arg Leu Leu Ile
	35	40 45
Tyr Asp Ala Ser	Asn Arg Ala Thr Gly	Val Pro Ala Arg Phe Ser Gly
	50	55 60
Ser Gly Ser Gly Thr	Asp Phe Thr Leu Thr	Ile Ser Ser Leu Glu Pro
	65	70 75 80
Glu Asp Phe Ala	Val Tyr Tyr Cys Gln	Gln Thr Lys Asn Arg Pro Pro
	85	90 95
Thr Phe Gly Gln	Gly Thr Lys Val Glu	Ile Lys Arg Thr Val Ala Ala
	100	105 110
Pro Ser Val Phe	Ile Phe Pro Pro Ser	Asp Glu Gln Leu Lys Ser Gly
	115	120 125
Thr Ala Ser Val	Val Cys Leu Leu Asn	Asn Phe Tyr Pro Arg Glu Ala
	130	135 140
Lys Val Gln Trp	Lys Val Asp Asn Ala	Leu Gln Ser Gly Asn Ser Gln
	145	150 155 160
Glu Ser Val Thr	Glu Gln Asp Ser Lys	Asp Ser Thr Tyr Ser Leu Ser
	165	170 175
Ser Thr Leu Thr	Leu Ser Lys Ala Asp	Tyr Glu Lys His Lys Val Tyr
	180	185 190
Ala Cys Glu Val	Thr His Gln Gly	Leu Ser Ser Pro Val Thr Lys Ser
	195	200 205
Phe Asn Arg Gly	Glu Cys	
	210	

<210> SEQ ID NO 40
 <211> LENGTH: 1344
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 40

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cagggtgcaat tgggttcagtc tggcgcgga	gtgaaaaaac cgggcagcag cgtgaaagt	60
agctgcaaaag cctccggagg cacttttagc	agctatgcga ttagctgggt gcgccaagcc	120
cctgggcagg gtctcgagtg gatgggcctt	attattcttc gttatggtaa ggctcgttat	180
gctcagaagt ttcagggtcg ggtgaccatt	accgcggatg aaagcaccag caccgcgtat	240
atggaactga gcagcctgcg tagcgaagat	acggccgtgt attattgcgc gcgtaattgg	300
ccttattatt atatggattt ttggggccaa	ggcaccctgg tgacggttag ctcagcctcc	360
accaagggtc catcggtctt cccctggca	cctcctcca agagcacctc tgggggcaca	420
gcggccctgg gctgcctggg caaggactac	ttccccgaac cggtgacggg gtcgtggaac	480
tcaggcgccc tgaccagcgg cgtgcacacc	ttcccgctg tcctacagtc ctcaggactc	540
tactccctca gcagcgtggt gaccgtgccc	tccagcagct tgggcaccca gacctacatc	600
tgcaactga atcacaagcc cagcaacacc	aagggtggaca agagagtga gcccaaactc	660
tgtgacaaaa ctcacacatg cccaccgtgc	ccagcacctg aactcctggg gggaccgtca	720
gtcttctct tcccccaaa acccaaggac	accctcatga tctcccgac cctgagggtc	780
acatgcgtgg tgggtgagct gagccacgaa	gacctgagg tcaagttcaa ctggtacgtg	840
gacggcgtgg aggtgcataa tgccaagaca	aagccgcggg aggagcagta caacagcacg	900
taccgggtgg tcagcgtcct caccgtctg	caccaggact ggctgaatgg caaggagtac	960
aagtgaagg tctccaacaa agccctccca	gccccatcg agaaaacat ctccaaagcc	1020
aaagggcagc cccgagaacc acaggtgtac	accctgcccc catcccgga ggagatgacc	1080
aagaaccagg tcagcctgac ctgcctggtc	aaaggcttct atcccagcga catgcgcgtg	1140
gagtgaggaga gcaatgggca gccggagaa	aactacaaga ccacgcctcc cgtgctggac	1200
tccgacggct ccttcttct ctacagcaag	ctcaccgtgg acaagagcag gtggcagcag	1260
gggaacgtct tctcatgctc cgtgatgcat	gaggctctgc acaaccacta cagcagaag	1320
agcctctccc tgtctcggg taaa		1344

<210> SEQ ID NO 41

<211> LENGTH: 642

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 41

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ctgagctgca gagcagacca gaatattgtt	tttaactctg cttggtacca gcagaaacca	120
ggteaagcac cgcgtctatt aatttatgat	gcttctaata gtgcaactgg ggtcccgcg	180
cgttttagcg gctctggatc cggcacggat	tttaccctga ccattagcag cctggaacct	240
gaagactttt cgggtgtatta ttgccagcag	actaagaatc gtctctctac ctttgccag	300
ggtacgaaag ttgaaattaa acgtacggtg	gccgctccca gcgtgttcat cttccccccc	360
agcgacgagc agctgaagag cggcacccgc	agcgtggtgt gcctgctgaa caactttctac	420
ccccgggagg ccaagggtga gtggaagggt	gacaacgccc tgcagagcgg caacagccag	480
gaaagcgtca ccgagcagga cagcaaggac	tccacctaca gcctgagcag caccctgacc	540
ctgagcaagg ccgactacga gaagcacaag	gtgtacgcct gcgaggtgac ccaccagggc	600

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ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> SEQ ID NO 42
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 42

Ser Tyr Ala Ile Ser
1 5

<210> SEQ ID NO 43
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 43

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 44
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 44

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 45
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 45

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 46
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 46

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 47

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<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 47

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 48
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 48

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 49
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 49

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 50
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 50

Gln Gln Lys Lys Ser Met Pro Leu Thr
1 5

<210> SEQ ID NO 51
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 51

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 52
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

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<400> SEQUENCE: 52

Asp Ala Ser
1

<210> SEQ ID NO 53

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 53

Lys Lys Ser Met Pro Leu
1 5

<210> SEQ ID NO 54

<211> LENGTH: 118

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 54

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 55

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 55

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
20 25 30Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60

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Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Lys Lys Ser Met Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 56

<211> LENGTH: 354

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 56

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cagggtcaat tggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaa cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaaagcc    120
cctgggcagg gtctcgatg gatgggcctt attattcctc gttatggtaa ggctcgttat    180
gtcagaagt ttcagggtcg ggtgaccatt accgcgatg aaagcaccag caccgcgtat     240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg    300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggttag ctca          354
```

<210> SEQ ID NO 57

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 57

```
gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc      60
ctgagctgca gagcgagcca gaatattgtt tttaatctgg cttggtacca gcagaaacca    120
ggteaagcac cgcgtctatt aatttatgat gcttctaadc gtgcaactgg ggtcccggcg    180
cgtttttagcg gctctggatc cggaacggat tttaccctga ccattagcag cctggaacct    240
gaagactttt cgggtgtatta ttgccagcag aagaagtcta tgccctctac ctttgccag    300
ggtacgaaag ttgaaattaa a                                321
```

<210> SEQ ID NO 58

<211> LENGTH: 448

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 58

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60

-continued

Gln	Gly	Arg	Val	Thr	Ile	Thr	Ala	Asp	Glu	Ser	Thr	Ser	Thr	Ala	Tyr	65	70	75	80
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	85	90	95	
Ala	Arg	Asn	Trp	Pro	Tyr	Tyr	Tyr	Met	Asp	Phe	Trp	Gly	Gln	Gly	Thr	100	105	110	
Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	115	120	125	
Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	130	135	140	
Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	145	150	155	160
Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	165	170	175	
Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	180	185	190	
Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	195	200	205	
Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	210	215	220	
His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	225	230	235	240
Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	245	250	255	
Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	260	265	270	
Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	275	280	285	
Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	290	295	300	
Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	305	310	315	320
Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	325	330	335	
Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	340	345	350	
Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	355	360	365	
Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	370	375	380	
Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	385	390	395	400
Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	405	410	415	
Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	420	425	430	
Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	435	440	445	

<210> SEQ ID NO 59

<211> LENGTH: 214

<212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 59

```

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1           5           10           15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
20           25           30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35           40           45
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50           55           60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65           70           75           80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Lys Lys Ser Met Pro Leu
85           90           95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100          105          110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115          120          125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130          135          140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145          150          155          160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165          170          175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180          185          190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195          200          205
Phe Asn Arg Gly Glu Cys
210

```

<210> SEQ ID NO 60

<211> LENGTH: 1344

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 60

```

cagggtgcaat tgggttcagtc tggcgcgga gtaaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat      180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat      240
atggaactga gcagcctcgc tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggtag ctcagcctcc      360
accaagggtc catcggctct cccctggca ccctcctcca agagcacctc tgggggcaca      420
gcggccctgg gctgcctggt caaggactac ttccccgaac cggtgacggt gtcgtggaac      480
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tcctacagtc ctcaggactc      540

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tactccctca gcagcgtggt gaccgtgccc tccagcagct tgggcaccca gacctacatc 600
tgcaacgtga atcacaaaggc cagcaacacc aaggtggaca agagagtga gcccaaatct 660
tgtgacaaaa ctcacacatg cccaccgtgc ccagcacctg aactcctggg gggaccgtca 720
gtcttctctt tcccccaaaa acccaaggac accctcatga tctcccgac cctgaggtc 780
acatgcgtgg tgggtggcgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg 840
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg 900
taccgggtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac 960
aagtgaagg tctccaacaa agccctccca gcccctatcg agaaaacat ctccaaagcc 1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccggga ggagatgacc 1080
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catgcctgtg 1140
gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac 1200
tccgacggct ctttcttct ctacagcaag ctcaccgtgg acaagagcag gtggcagcag 1260
gggaacgtct tctcatgctc cgtgatgcat gaggtcttgc acaaccacta cagcagaag 1320
agcctctccc tgtctcggg taaa 1344

```

```

<210> SEQ ID NO 61
<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 61
gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc 60
ctgagctgca gagcgagcca gaatatgtt ttaaatctgg cttggtacca gcagaaacca 120
ggtaagcac cgcgtctatt aatttatgat gcttctaata gtgcaactgg ggtcccgcg 180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct 240
gaagactttg cgggtgatta ttgccagcag aagaagtcta tgctcttac ctttgccag 300
ggtacgaaag ttgaaattaa acgtacggty gccgctccca gcgtgttcat cttccccccc 360
agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caattctac 420
ccccgggagg ccaaggtgca gtggaaggty gacaacgccc tgcagagcgg caacagccag 480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

```

```

<210> SEQ ID NO 62
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 62

```

```

Ser Tyr Ala Ile Ser
1           5

```

-continued

<210> SEQ ID NO 63
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 63

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 64
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 64

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 65
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 65

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 66
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 66

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 67
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 67

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 68
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 68

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 69

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 69

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 70

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 70

Gln Gln Phe Arg Arg Lys Ser Asn Thr
1 5

<210> SEQ ID NO 71

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 71

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 72

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 72

Asp Ala Ser
1

<210> SEQ ID NO 73

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 73

Phe Arg Arg Lys Ser Asn
1 5

-continued

<210> SEQ ID NO 74
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 74

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 75
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 75

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Phe Arg Arg Lys Ser Asn
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 76
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

-continued

<400> SEQUENCE: 76

```

cagggtgcaat tggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaa cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagt gatgggcctt attattcctc gttatggtaa ggctcgttat      180
gtcagaagt ttcagggtcg ggtgaccatt accgcgatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggttag ctca          354

```

<210> SEQ ID NO 77

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 77

```

gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc      60
ctgagctgca gagcgagcca gaatattgtt ttaaatctgg cttggtacca gcagaaacca      120
ggtaagcac cgcgtctatt aatttatgat gcttetaatc gtgcaactgg ggtcccgcg      180
cgtttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct      240
gaagactttg cgggtgtatta ttgccagcag tttcgtcgta agtctaatac ctttgccag      300
ggtaacgaaag ttgaaattaa a          321

```

<210> SEQ ID NO 78

<211> LENGTH: 448

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 78

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1           5           10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
          20          25          30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
          35          40          45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
          50          55          60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
          65          70          75          80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
          85          90          95

Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
          100         105         110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
          115         120         125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
          130         135         140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
          145         150         155         160

```


-continued

```

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
      165                      170                      175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
      180                      185                      190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
      195                      200                      205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
      210                      215                      220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
      225                      230                      235                      240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
      245                      250                      255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
      260                      265                      270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
      275                      280                      285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
      290                      295                      300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
      305                      310                      315                      320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
      325                      330                      335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
      340                      345                      350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
      355                      360                      365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
      370                      375                      380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
      385                      390                      395                      400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
      405                      410                      415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
      420                      425                      430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
      435                      440                      445

```

<210> SEQ ID NO 79

<211> LENGTH: 214

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 79

```

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1           5           10           15

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35           40           45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50           55           60

```

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Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Phe Arg Arg Lys Ser Asn
 85 90 95
 Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
 100 105 110
 Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125
 Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140
 Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160
 Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175
 Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190
 Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205
 Phe Asn Arg Gly Glu Cys
 210

<210> SEQ ID NO 80

<211> LENGTH: 1344

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 80

```

cagggtgcaat tgggttcagtc tggcgcgga gtaaaaaaac cgggcagcag cgtgaaagtg      60
agctgc aaag cctccgaggg cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat      180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacgggttag ctcagcctcc      360
accaagggtc catcgggtctt cccctggca cctcctcca agagcacctc tgggggcaca      420
gcggccctgg gctgcctggt caaggactac ttccccgaac cggtgacggt gtcgtggaac      480
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tcctacagtc ctcaggactc      540
tactcctca gcagcgtggt gaccgtgccc tcacagcgt tgggcacca gacctacatc      600
tgcaacgtga atcacacatg cccacgtgc ccagcacctg aactcctggg gggaccgtca      720
gtcttctct tcccccaaa acccaaggac accctcatga tctcccgga cctgaggtc      780
acatgcgtgg tgggtgacgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg      840
gacggcgctg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg      900
taccgggtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac      960
aagtgaagg tctccaacaa agcctccca gcccctatcg agaaaaccat ctccaaagcc      1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgga ggagatgacc      1080

```

-continued

```

aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catcgccgtg 1140
gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac 1200
tccgacggct ctttcttctc ctacagcaag ctcaccgtgg acaagagcag gtggcagcag 1260
gggaacgtct tctcatgctc cgtgatgcat gaggtctctg acaaccacta cagcagaag 1320
agcctctccc tgtctccggg taaa 1344

```

```

<210> SEQ ID NO 81
<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
    polynucleotide

```

```

<400> SEQUENCE: 81
gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc 60
ctgagctgca gagcgagcca gaatattgtt ttaatatctgg cttggtacca gcagaaacca 120
ggtaagcac cgcgtctatt aatttatgat gcttetaatc gtgcaactgg ggtcccgcg 180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct 240
gaagactttg cgggtgatta ttgccagcag tttcgtcgta agtctaatac ctttgccag 300
ggtacgaaag ttgaaattaa acgtacggtg gccgctccca gcgtgttcat ctteccccc 360
agcgacgagc agctgaagag cggcacccgc agcgtggtgt gcctgctgaa caattctac 420
ccccgggagg ccaaggtgca gtggaagggt gacaacgccc tgcagagcgg caacagccag 480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

```

```

<210> SEQ ID NO 82
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
    peptide

```

```

<400> SEQUENCE: 82

```

```

Ser Tyr Ala Ile Ser
1           5

```

```

<210> SEQ ID NO 83
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
    peptide

```

```

<400> SEQUENCE: 83

```

```

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1           5           10           15

```

```

Gly

```

```

<210> SEQ ID NO 84
<211> LENGTH: 9

```

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 84

Asn Trp Pro Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 85
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 85

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 86
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 86

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 87
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 87

Asn Trp Pro Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 88
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 88

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 89
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 89

-continued

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 90
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 90

Gln Gln Thr Lys Ser Lys Pro Ser Pro Thr
1 5 10

<210> SEQ ID NO 91
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 91

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 92
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 92

Asp Ala Ser
1

<210> SEQ ID NO 93
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 93

Thr Lys Ser Lys Pro Ser Pro
1 5

<210> SEQ ID NO 94
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 94

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

-continued

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Leu Val Thr Val Ser Ser
 115

<210> SEQ ID NO 95
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 95

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys Ser Lys Pro Ser
 85 90 95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 96
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 96

cagggtgcaat tggttcagtc tggcgcggaa gtgaaaaaac cgggcagcag cgtgaaagtg 60

agctgcaaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc 120

cctgggcagg gtctcgatg gatgggcctt attattcctc gttatggtaa ggctcgttat 180

gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat 240

atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg 300

ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggttag ctca 354

<210> SEQ ID NO 97
 <211> LENGTH: 324
 <212> TYPE: DNA

-continued

```

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 97
gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc      60
ctgagctgca gagcgagcca gaattattgtt tttaatctgg cttggtacca gcagaaacca      120
ggtaagcac cgcgtctatt aatttatgat gcttctaate gtgcaactgg ggtcccggcg      180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct      240
gaagactttg cgggtgtatta ttgccagcag actaagtcta agccttctcc tacctttggc      300
cagggtacga aagttgaaat taaa                                     324

<210> SEQ ID NO 98
<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

<400> SEQUENCE: 98
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
          20          25          30
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
          35          40          45
Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
          50          55          60
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
          65          70          75          80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
          85          90          95
Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
          100          105          110
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
          115          120          125
Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
          130          135          140
Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
          145          150          155          160
Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
          165          170          175
Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
          180          185          190
Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
          195          200          205
Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
          210          215          220
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
          225          230          235          240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
          245          250          255

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-continued

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 260 265 270
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 405 410 415
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435 440 445

<210> SEQ ID NO 99

<211> LENGTH: 215

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 99

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys Ser Lys Pro Ser
 85 90 95
 Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
 100 105 110
 Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
 115 120 125
 Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
 130 135 140
 Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
 145 150 155 160

-continued

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 100

<211> LENGTH: 1344

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 100

```

caggtgcaat tggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat      180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttgggggcaa ggcaccctgg tgacgggttag ctcagcctcc      360
accaagggtc catcggctct ccccttgca ccctcctcca agagcacctc tgggggcaca      420
gcggccctgg gctgcctggt caaggactac ttccccgaac cggtgacggt gtcgtggaac      480
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tctacagtc ctcaggactc      540
tactcctca gcagcgtggt gaccgtgccc tccagcagct tgggcacca gacctacatc      600
tgcaacgtga atcacaagcc cagcaacacc aaggtggaca agagagtga gccc aaatct      660
tgtgacaaaa ctcacacatg cccacgtgc ccagcacctg aactcctggg gggaccgtca      720
gtcttctct tcccccaaa acccaaggac accctcatga tctccggac cctgaggtc      780
acatgcgtgg tgggtgacgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg      840
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg      900
taccgggtgg tcagcgtcct caccgtctcg caccaggact ggctgaatgg caaggagtac      960
aagtgaagg tctccaacaa agccctccca gcccctatcg agaaaacat ctccaaagcc      1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgga ggagatgacc      1080
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catgccgtg      1140
gagtgaggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac      1200
tccgacggct ccttcttct ctacagcaag ctcaccgtgg acaagagcag gtggcagcag      1260
gggaacgtct tctcatgctc cgtgatgcat gaggtctctg acaaccacta cagcagaag      1320
agcctctccc tgtctccggg taaa                                     1344

```

<210> SEQ ID NO 101

<211> LENGTH: 645

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

-continued

polynucleotide

<400> SEQUENCE: 101

```
gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc    60
ctgagctgca gagcgagcca gaatattgtt tttaatctgg cttggtacca gcagaaacca    120
ggtaagcac cgcgtctatt aatttatgat gcttctaata gtgcaactgg ggtcccgcg    180
cgttttagcg gctctggatc cggcacggat ttaccctga ccattagcag cctggaacct    240
gaagactttg cgggtgtatta ttgccagcag actaagtcta agccttctcc tacctttggc    300
cagggtacga aagttgaaat taaacgtacg gtggccgctc ccagcgtgtt catcttcccc    360
cccagcgacg agcagctgaa gagcggcacc gccagcgtgg tgtgcctgct gaacaacttc    420
taccgccggg aggccaaggt gcagtggaag gtggacaacg ccctgcagag cggcaacagc    480
caggaaagcg tcaccgagca ggacagcaag gactccacct acagcctgag cagcacctcg    540
accctgagca aggccgacta cgagaagcac aaggtgtacg cctgcgaggt gaccaccag    600
ggcctgtcca gcccctgac caagagcttc aaccggggcg agtgt                    645
```

<210> SEQ ID NO 102

<211> LENGTH: 5

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 102

```
Ser Tyr Ala Ile Ser
1             5
```

<210> SEQ ID NO 103

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 103

```
Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1             5             10             15
```

Gly

<210> SEQ ID NO 104

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 104

```
Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1             5
```

<210> SEQ ID NO 105

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

-continued

peptide

<400> SEQUENCE: 105

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 106

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 106

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 107

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 107

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 108

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 108

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 109

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 109

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 110

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 110

Gln Gln Val Lys Lys Arg Pro Phe Thr
1 5

-continued

<210> SEQ ID NO 111
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 111

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 112
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 112

Asp Ala Ser
1

<210> SEQ ID NO 113
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 113

Val Lys Lys Arg Pro Phe
1 5

<210> SEQ ID NO 114
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 114

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

-continued

<210> SEQ ID NO 115
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 115

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5					10					15	
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Asn	Ile	Val	Phe	Asn
			20				25					30			
Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
		35				40					45				
Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr	Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly
	50				55					60					
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro
65				70					75					80	
Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Val	Lys	Lys	Arg	Pro	Phe
			85					90						95	
Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys					
		100					105								

<210> SEQ ID NO 116
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 116

cagggtgcaat	tggttcagtc	tggcgcgga	gtgaaaaaac	cgggcagcag	cgtgaaagtg	60
agctgc aaaag	cctccggagg	cacttttagc	agctatgcga	ttagctgggt	gcgccaagcc	120
cctgggcagg	gtctcgatg	gatgggcctt	attattcctc	gttatggtaa	ggctcggtat	180
gctcagaagt	ttcagggtcg	ggtgaccatt	accgcggatg	aaagcaccag	caccgcgtat	240
atggaactga	gcagcctcgc	tagcgaagat	acggccgtgt	attattgcgc	gcgtaattgg	300
ccttattatt	atatggattt	ttggggccaa	ggcaccctgg	tgacggttag	ctca	354

<210> SEQ ID NO 117
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 117

gatatactgc	tgacccagag	cccggcgacc	ctgagcctgt	ctccgggcga	acgtgcgacc	60
ctgagctgca	gagcgagcca	gaatattgtt	tttaactctg	cttggtacca	gcagaaacca	120
ggtcaagcac	cgcgtctatt	aatttatgat	gcttctaata	gtgcaactgg	ggccccggcg	180
cgttttagcg	gctctggatc	cggcacggat	tttaccctga	ccattagcag	cctggaacct	240
gaagactttg	cgggtgtatta	ttgccagcag	gttaagaagc	gtccttttac	ctttggccag	300
ggtacgaaa	gtgaaattaa	a				321

-continued

<210> SEQ ID NO 118
<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 118

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125
Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140
Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160
Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175
Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190
Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205
Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225 230 235 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245 250 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260 265 270
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
290 295 300
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

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Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
  355                               360               365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
  370                               375               380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
  385                               390               395               400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                     405               410               415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
                     420               425               430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
      435               440               445

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<210> SEQ ID NO 119
<211> LENGTH: 214
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

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<400> SEQUENCE: 119

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Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
  1           5           10           15

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
      35           40           45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
      50           55           60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
      65           70           75           80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Val Lys Lys Arg Pro Phe
      85           90           95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
      100          105          110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
      115          120          125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
      130          135          140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
      145          150          155          160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
      165          170          175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
      180          185          190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
      195          200          205

Phe Asn Arg Gly Glu Cys
      210

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<210> SEQ ID NO 120
<211> LENGTH: 1344
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 120

```
cagggtgcaat tggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg    60
agctgcaaag cctccgaggg cacttttagc agctatgcga ttagctgggt gcgccaagcc    120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat    180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat    240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg    300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacgggttag ctcagcctcc    360
accaagggtc catcggctct ccccttgga cctcctcca agagcacctc tgggggcaca    420
gcggccctgg gctgcctggt caaggactac ttcccgaac cggtgacggg gtcgtggaac    480
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tctacagtc ctcaggactc    540
tactcctca gcagcgtggt gaccgtgccc tccagcagct tgggcaccca gacctacatc    600
tgcaacgtga atcacagcc cagcaacacc aaggtggaca agagagtga gccc aaatct    660
tgtgacaaaa ctcacacatg cccacgtgc ccagcacctg aactcctggg gggaccgtca    720
gtcttctct tcccccaaa acccaaggac accctcatga tctccggac cctgagggtc    780
acatgcgtgg tgggtgacgt gagccacgaa gacctgagg tcaagttcaa ctggtacgtg    840
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg    900
taccgggtgg tcagcgtcct caccgtctg caccaggact ggctgaatgg caaggagtac    960
aagtgaagg tctccaacaa agccctccca gcccctatcg agaaaacat ctccaaagcc    1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgga ggagatgacc    1080
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catgcgcgtg    1140
gagtgaggga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac    1200
tccgacggct ccttcttct ctacagcaag ctcaccgtgg acaagagcag gtggcagcag    1260
gggaacgtct tctcatgctc cgtgatgcat gaggtctgct acaaccacta cagcagaag    1320
agcctctccc tgtctccggg taaa                                     1344
```

<210> SEQ ID NO 121

<211> LENGTH: 642

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 121

```
gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc    60
ctgagctgca gagcgagcca gaattattgt tttaattctg cttggtacca gcagaaacca    120
ggtaagcac cgcgtctatt aatttatgat gcttctaac gtgcaactgg ggtcccgccg    180
cgtttttagc gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct    240
gaagactttg cgggtgatta ttgccagcag gttaagaagc gtccttttac ctttgccag    300
ggtacgaaa ttgaaattaa acgtacgggt gccgctccca gcgtgttcat ctccccccc    360
agcgacgagc agctgaagag cggcacccgc agcgtggtgt gcctgctgaa caacttctac    420
```

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ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> SEQ ID NO 122
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 122

Ser Tyr Ala Ile Ser
1 5

<210> SEQ ID NO 123
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 123

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 124
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 124

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 125
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 125

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 126
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 126

-continued

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 127
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 127

Asn Trp Pro Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 128
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 128

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 129
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 129

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 130
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 130

Gln Gln Ser Tyr Thr Arg Pro Thr Thr
1 5

<210> SEQ ID NO 131
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 131

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 132
<211> LENGTH: 3
<212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 132

Asp Ala Ser
1

<210> SEQ ID NO 133
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 133

Ser Tyr Thr Arg Pro Thr
1 5

<210> SEQ ID NO 134
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 134

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 135
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 135

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile

-continued

35	40	45	
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly			
50	55	60	
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro			
65	70	75	80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr Thr Arg Pro Thr			
	85	90	95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> SEQ ID NO 136
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 136

cagggtgcaat tgggttcagtc tggcgcgga gtaaaaaac cgggcagcag cgtgaaagtg	60
agctgc aaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc	120
cctgggcagg gtctcgagtg gatgggctt attattctc gttatggtaa ggctcgttat	180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat	240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg	300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggttag ctca	354

<210> SEQ ID NO 137
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 137

gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc	60
ctgagctgca gagcgagcca gaattattgtt tttaatctgg cttggtacca gcagaaacca	120
ggtaagcac cgcgtctatt aatttatgat gcttctaate gtgcaactgg ggtcccgcg	180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct	240
gaagactttg cgggtgatta ttgccagcag tcttatactc gtcctactac ctttggccag	300
ggtacgaaag ttgaaattaa a	321

<210> SEQ ID NO 138
 <211> LENGTH: 448
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 138

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser	
1	15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr	
20	30

-continued

Ala	Ile	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
	35						40					45			
Gly	Leu	Ile	Ile	Pro	Arg	Tyr	Gly	Lys	Ala	Arg	Tyr	Ala	Gln	Lys	Phe
	50					55					60				
Gln	Gly	Arg	Val	Thr	Ile	Thr	Ala	Asp	Glu	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85						90					95	
Ala	Arg	Asn	Trp	Pro	Tyr	Tyr	Tyr	Met	Asp	Phe	Trp	Gly	Gln	Gly	Thr
			100					105					110		
Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro
		115						120					125		
Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly
	130					135					140				
Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn
145					150					155					160
Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln
				165					170						175
Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser
			180					185					190		
Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser
		195					200					205			
Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr
	210					215					220				
His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser
225					230					235					240
Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg
				245					250					255	
Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro
			260					265					270		
Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala
		275					280					285			
Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val
	290					295					300				
Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr
305					310					315					320
Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr
				325					330					335	
Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu
			340					345					350		
Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys
		355					360						365		
Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser
		370				375					380				
Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp
385					390					395					400
Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser
				405					410					415	
Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala
			420					425					430		
Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys
		435					440					445			

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<210> SEQ ID NO 139
 <211> LENGTH: 214
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 139

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Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1           5           10           15

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
          35           40           45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
          50           55           60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65           70           75           80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr Thr Arg Pro Thr
          85           90           95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
          100          105          110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
          115          120          125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
          130          135          140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145          150          155          160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
          165          170          175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
          180          185          190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
          195          200          205

Phe Asn Arg Gly Glu Cys
          210
  
```

<210> SEQ ID NO 140
 <211> LENGTH: 1344
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 140

```

caggtgcaat tgggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgatgt gatgggcctt attattcttc gttatggtaa ggctcgttat      180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacgggttag ctcagcctcc      360
  
```

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accaagggtc catcggtctt ccccttgga cctcctcca agagcacctc tgggggcaca 420
gcggccctgg gctgcctggt caaggactac ttccccgaac cggtgacggt gtcgtggaac 480
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tctacagtc ctcaggactc 540
tactcctca gcagcgtggt gaccgtgccc tccagcagct tgggcaccca gacctacatc 600
tgcaacgtga atcacaagcc cagcaacacc aaggtggaca agagagtga gccc aaatct 660
tgtgacaaaa ctcacacatg cccaccgtgc ccagcacctg aactcctggg gggaccgtca 720
gtcttctct tcccccaaa acccaaggac accctcatga tctcccgac cctgagggtc 780
acatgcgtgg tgggtggcgt gagccacgaa gacctgagg tcaagttcaa ctggtacgtg 840
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg 900
taccgggtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac 960
aagtgaagg tctccaacaa agcctcctca gcccctatcg agaaaacat ctccaaagcc 1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgga ggagatgacc 1080
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catgccgtg 1140
gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac 1200
tccgacggct ccttcttct ctacagcaag ctcaccgtgg acaagagcag gtggcagcag 1260
gggaacgtct tctcatgctc cgtgatgcat gaggtctctg acaaccacta cagcagaag 1320
agcctctccc tgtctccggg taaa 1344

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<210> SEQ ID NO 141
<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

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<400> SEQUENCE: 141

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gatatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc 60
ctgagctgca gagcgagcca gaatatgtt tttaatctgg cttggtacca gcagaaacca 120
ggtaagcac cgcgtctatt aatttatgat gcttctaac gtgcaactgg ggtcccgcg 180
cgttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct 240
gaagactttg cgggtgtatta ttgccagcag tcttatactc gtctactac ctttgccag 300
ggtagcaaa ttgaaattaa acgtacggtg gccgctccca gcgtgttcat ctccccccc 360
agcgacgagc agctgaagag cggcacgcc agcgtggtgt gcctgctgaa caacttctac 420
ccccgggagg ccaaggtgca gtggaagggt gacaacgccc tgcagagcgg caacagccag 480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

```

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<210> SEQ ID NO 142
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

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<400> SEQUENCE: 142

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-continued

Ser Tyr Ala Ile Ser
1 5

<210> SEQ ID NO 143
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 143

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 144
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 144

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 145
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 145

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 146
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 146

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 147
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 147

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

-continued

<210> SEQ ID NO 148
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 148

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 149
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 149

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 150
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 150

Gln Gln Thr Lys Ser Lys Pro Ser Pro Thr
1 5 10

<210> SEQ ID NO 151
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 151

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 152
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 152

Asp Ala Ser
1

<210> SEQ ID NO 153
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 153

Thr Lys Ser Lys Pro Ser Pro
1 5

<210> SEQ ID NO 154

<211> LENGTH: 118

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 154

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50 55 60Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100 105 110Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 155

<211> LENGTH: 108

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 155

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn
20 25 30Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys Ser Lys Pro Ser
85 90 95Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 156

<211> LENGTH: 354

<212> TYPE: DNA

-continued

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 156
caggtgcaat tggttcagtc tggcgcgga gtaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaa cctccggagg cacttttagc agctatgca ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagt gatgggcctt attattctc gttatggtaa ggctcgttat      180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggttag ctca          354

<210> SEQ ID NO 157
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 157
gagatcgtgc tgaccagag cccggcgacc ctgagcctgt ctccgggcca acgtgcgacc      60
ctgagctgca gagcgagcca gaattattgt ttaattctgg cttggtacca gcagaaacca      120
ggtaagcac cgcgtctatt aatttatgat gcttctaatac gtgcaactgg gatcccgcg      180
cgtttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct      240
gaagactttg cgggtgatta ttgccagcag actaagteta agcettctcc tacctttggc      300
cagggtacga aagttgaaat taaa          324

<210> SEQ ID NO 158
<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

<400> SEQUENCE: 158
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20         25         30
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35         40         45
Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50         55         60
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65         70         75         80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85         90         95
Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100        105        110
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115        120        125

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Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 130                      135                      140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                      150                      155                      160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                      165                      170                      175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                      180                      185                      190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
                      195                      200                      205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
                      210                      215                      220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                      230                      235                      240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                      245                      250                      255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
                      260                      265                      270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
                      275                      280                      285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
                      290                      295                      300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                      310                      315                      320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                      325                      330                      335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
                      340                      345                      350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
                      355                      360                      365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
                      370                      375                      380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                      390                      395                      400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                      405                      410                      415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
                      420                      425                      430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                      435                      440                      445

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<210> SEQ ID NO 159

<211> LENGTH: 215

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 159

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Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1                      5                      10                      15

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

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Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys Ser Lys Pro Ser
 85 90 95
 Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
 100 105 110
 Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
 115 120 125
 Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
 130 135 140
 Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
 145 150 155 160
 Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
 165 170 175
 Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
 180 185 190
 Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
 195 200 205
 Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> SEQ ID NO 160

<211> LENGTH: 1344

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 160

```

cagggtgcaat tgggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcgttat      180
gctcagaagt ttcagggtcg ggtgaccatt accgcgatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacgggttag ctacagcctcc      360
accaagggtc catcggtctt ccccttgga cctcctcca agagcacctc tgggggcaca      420
gcggccctgg gctgcctggt caaggactac ttcccgaac cggtgacggg gtcgtggaac      480
tcaggcgccc tgaccagcgg cgtgcacacc ttccggctg tctacagtc ctacaggactc      540
tactccctca gcagcgtggt gaccgtgccc tccagcagct tgggcaccca gacctacatc      600
tgcaacgtga atcacaagcc cagcaacacc aaggtggaca agagagtga gcccaaactc      660
tgtgacaaaa ctacacatg cccaccgtgc ccagcacctg aactcctggg gggaccgtca      720
gtcttcctct tcccccaaa acccaaggac accctcatga tctcccgga cctgaggtc      780
acatgcgtgg tgggtggacgt gagccacgaa gacctgagg tcaagttcaa ctggtacgtg      840
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg      900

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taccgggtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac 960
aagtgaagg tctccaacaa agccctccca gcccctatcg agaaaacat ctccaaagcc 1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgga ggagatgacc 1080
aagaaccagg tcagcctgac ctgcctgttc aaaggcttct atcccagcga catcgccgtg 1140
gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac 1200
tccgacggct ccttcttctc ctacagcaag ctcaccgtgg acaagagcag gtggcagcag 1260
gggaacgtct tctcatgctc cgtgatgcat gaggtctctg acaaccacta cagcagaag 1320
agcctctccc tgtctccggg taaa 1344

```

```

<210> SEQ ID NO 161
<211> LENGTH: 645
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 161

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gagatcgtgc tgacccagag cccggcgacc ctgagcctgt ctccgggcca acgtgcgacc 60
ctgagctgca gagcgagcca gaattattgt tttaatctgg cttggtacca gcagaaacca 120
ggtaagcac cgcgtctatt aatttatgat gcttctaac gtgcaactgg gatcccgcg 180
cgtttttagc gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct 240
gaagactttg cgggtgatta ttgccagcag actaagteta agccttctcc tacctttggc 300
cagggtacga aagttgaaat taaacgtacg gtggccgctc ccagcgtgtt catcttcccc 360
cccagcgacg agcagctgaa gagcggcacc gccagcgtgg tgtgcctgct gaacaacttc 420
tccccccggg aggccaaagt gcagtggaag gtggacaacg ccctgcagag cggcaacagc 480
caggaaagcg tcaccgagca ggacagcaag gactccacct acagcctgag cagcaccttg 540
accttgagca aggccgacta cgagaagcac aaggtgtacg cctgcgaggt gaccaccag 600
ggcctgtcca gcccgtgac caagagcttc aaccggggcg agtgt 645

```

```

<210> SEQ ID NO 162
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

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<400> SEQUENCE: 162

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Ser Tyr Ala Ile Ser
1           5

```

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<210> SEQ ID NO 163
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

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<400> SEQUENCE: 163

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```

Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe Gln
1           5           10           15

```

-continued

Gly

<210> SEQ ID NO 164
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 164

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 165
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 165

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> SEQ ID NO 166
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 166

Ile Pro Arg Tyr Gly Lys
1 5

<210> SEQ ID NO 167
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 167

Asn Trp Pro Tyr Tyr Tyr Met Asp Phe
1 5

<210> SEQ ID NO 168
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 168

Arg Ala Ser Gln Asn Ile Val Phe Asn Leu Ala
1 5 10

<210> SEQ ID NO 169
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 169

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> SEQ ID NO 170
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 170

Gln Gln Thr Lys Asn Arg Pro Pro Thr
1 5

<210> SEQ ID NO 171
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 171

Ser Gln Asn Ile Val Phe Asn
1 5

<210> SEQ ID NO 172
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 172

Asp Ala Ser
1

<210> SEQ ID NO 173
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 173

Thr Lys Asn Arg Pro Pro
1 5

<210> SEQ ID NO 174
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 174

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser

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1	5	10	15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr	20	25	30
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	35	40	45
Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe	50	55	60
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr	65	70	75
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	85	90	95
Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr	100	105	110
Leu Val Thr Val Ser Ser	115		

<210> SEQ ID NO 175
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 175

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly	1	5	10	15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Val Phe Asn	20	25	30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile	35	40	45	
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly	50	55	60	
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro	65	70	75	80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Lys Asn Arg Pro Pro	85	90	95	
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	100	105		

<210> SEQ ID NO 176
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 176

cagggtgcaat tgggttcagtc tggcgcgga gtaaaaaaac cgggcagcag cgtgaaagt	60
agctgcaaag cctccggagg cacttttagc agctatgcga ttagctgggt gcgccaaagcc	120
cctgggcagg gtctcgatgt gatgggcctt attattcctc gttatggtaa ggctcgttat	180
gctcagaagt ttcagggtcg ggtgaccatt accgcggatg aaagcaccag caccgcgtat	240
atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtaattgg	300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacggttag ctca	354

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<210> SEQ ID NO 177
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 177

gagatcgtgc tgacccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc      60
ctgagctgca gagcgagcca gaattattgtt tttaatctgg cttggtacca gcagaaacca      120
ggtaacgac cgcgtctatt aatttatgat gcttctaatac gtgcaactgg gatcccggcg      180
cgtttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct      240
gaagactttg cgggtgtatta ttgccagcag actaagaatac gtcctcctac ctttgccag      300
ggtacgaaaag ttgaaattaa a                                     321


<210> SEQ ID NO 178
<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

<400> SEQUENCE: 178

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20         25         30
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35         40         45
Gly Leu Ile Ile Pro Arg Tyr Gly Lys Ala Arg Tyr Ala Gln Lys Phe
50         55         60
Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65         70         75         80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85         90         95
Ala Arg Asn Trp Pro Tyr Tyr Tyr Met Asp Phe Trp Gly Gln Gly Thr
100        105        110
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115        120        125
Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130        135        140
Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145        150        155        160
Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165        170        175
Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180        185        190
Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195        200        205
Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
210        215        220

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His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	225	230	235	240
Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	245	250	255	
Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	260	265	270	
Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	275	280	285	
Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	290	295	300	
Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	305	310	315	320
Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	325	330	335	
Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	340	345	350	
Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	355	360	365	
Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	370	375	380	
Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	385	390	395	400
Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	405	410	415	
Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	420	425	430	
Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	435	440	445	

<210> SEQ ID NO 179

<211> LENGTH: 214

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 179

Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly	1	5	10	15
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Asn	Ile	Val	Phe	Asn	20	25	30	
Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	35	40	45	
Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	50	55	60	
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro	65	70	75	80
Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Thr	Lys	Asn	Arg	Pro	Pro	85	90	95	
Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	100	105	110	
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	115	120	125	

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Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> SEQ ID NO 180
 <211> LENGTH: 1344
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polynucleotide

<400> SEQUENCE: 180

```

cagggtcaat tggttcagtc tggcgcgga gtgaaaaaac cgggcagcag cgtgaaagtg      60
agctgcaaa cctccgaggt cacttttagc agctatgcga ttagctgggt gcgccaagcc      120
cctgggcagg gtctcgagtg gatgggcctt attattcctc gttatggtaa ggctcggtat      180
gtcagaagt ttcagggtcg ggtgaccatt accgcgatg aaagcaccag caccgcgtat      240
atggaactga gcagcctgag tagcgaagat acggccgtgt attattgcgc gcgtaattgg      300
ccttattatt atatggattt ttggggccaa ggcaccctgg tgacgggttag ctacagcctcc      360
accaagggtc catcggtctt ccccttgga cctcctcca agagcacctc tgggggcaca      420
gcggccctgg gctgcctggt caaggactac ttccccgaac cggtgacggt gtcgtggaac      480
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tctacagtc ctcaggactc      540
tactcctca gcagcgtggt gaccgtgccc tccagcagct tgggcacca gacctacatc      600
tgcaacgtga atcacaagcc cagcaacacc aaggtggaca agagagtga gccc aaatct      660
tgtgacaaaa ctacacatg cccaccgtgc ccagcacctg aactcctggg gggaccgtca      720
gtcttctct tcccccaaa acccaaggac accctcatga tctcccgga cctgaggtc      780
acatgcgtgg tgggtggacgt gagccacgaa gaccctgagg tcaagttaa ctggtacgtg      840
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg      900
taccgggtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac      960
aagtgaagg tctccaacaa agccctccca gccccatcg agaaaacat ctccaaagcc      1020
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgga ggagatgacc      1080
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catgcgctg      1140
gagtgggaga gcaatgggca gccggagaa aactacaaga ccacgcctcc cgtgctggac      1200
tccgacggct ccttcttct ctacagcaag ctaccctgg acaagagcag gtggcagcag      1260
gggaacgtct tctcatgctc cgtgatgcat gaggtctctg acaaccacta cacgcagaag      1320
agcctctccc tgtctccggg taaa                                     1344

```

<210> SEQ ID NO 181

-continued

<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 181

```
gagatcgtgc tgacccagag cccggcgacc ctgagcctgt ctccgggcga acgtgcgacc      60
ctgagctgca gagcgagcca gaattattgtt tttaatctgg cttggtacca gcagaaacca      120
ggteaagcac cgcgtctatt aatttatgat gcttctaate gtgcaactgg gatcccggcg      180
cgtttttagcg gctctggatc cggcacggat tttaccctga ccattagcag cctggaacct      240
gaagactttg cgggtgatta ttgccagcag actaagaatc gtctctctac ctttggccag      300
ggtagcgaag ttgaaattaa acgtacgggtg gccgctccca gcgtgttcat ctccccccc      360
agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caactttctac      420
ccccgggagg ccaaggtgca gtggaagggtg gacaacgccc tgcagagcgg caacagccag      480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc      540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc      600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt                                642
```

<210> SEQ ID NO 182
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 182

```
Ser Tyr Asp Ile His
1              5
```

<210> SEQ ID NO 183
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 183

```
Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1              5              10              15
```

Gly

<210> SEQ ID NO 184
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 184

```
Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1              5              10
```

<210> SEQ ID NO 185

-continued

<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 185

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 186
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 186

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 187
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 187

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 188
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 188

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 189
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 189

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 190
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 190

Gln Val Arg Asp Met Ser Leu Phe Asp Val
1 5 10

<210> SEQ ID NO 191

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 191

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 192

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 192

Gly Val Ser
1

<210> SEQ ID NO 193

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 193

Arg Asp Met Ser Leu Phe Asp
1 5

<210> SEQ ID NO 194

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 194

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly

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100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	
<210> SEQ ID NO 195 <211> LENGTH: 110 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide		
<400> SEQUENCE: 195		
Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln		
1	5	10 15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr		
	20	25 30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu		
	35	40 45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe		
	50	55 60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu		
65	70	75 80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Val Arg Asp Met Ser		
	85	90 95
Leu Phe Asp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu		
	100	105 110
<210> SEQ ID NO 196 <211> LENGTH: 363 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide		
<400> SEQUENCE: 196		
cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt		60
agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc		120
ccgggccagg gcctcgagt gatgggcgt atcgaccgt actctggcaa cacgaactac		180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat		240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct		300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc		360
tca		363
<210> SEQ ID NO 197 <211> LENGTH: 330 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide		
<400> SEQUENCE: 197		
gatatcgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt		60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag		120

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catccgggca aggcgcgcaa actgatgato tacggtgttt ctaaactgcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc caggttcgtg acatgtctct gttecgacgtg 300
tttgccggcg gcacgaagtt aaccgtccta 330

```

```

<210> SEQ ID NO 198
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

```

```

<400> SEQUENCE: 198

```

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195         200         205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210         215         220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245         250         255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260         265         270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275         280         285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290         295         300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly

```

```

<210> SEQ ID NO 199
<211> LENGTH: 216
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

<400> SEQUENCE: 199

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1          5          10          15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
          20          25          30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
          35          40          45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
          50          55          60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65          70          75          80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Val Arg Asp Met Ser
          85          90          95

Leu Phe Asp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
          100          105          110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
          115          120          125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
          130          135          140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145          150          155          160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
          165          170          175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
          180          185          190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys

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195	200	205
Thr Val Ala Pro Thr Glu Cys Ser		
210	215	

<210> SEQ ID NO 200
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 200

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgcccgata taccttact tcttacgaca tccattgggt gcgccaggcc	120
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa caggaactac	180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggg gactgttagc	360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctcaa gacacctct	420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg	480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtc	540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720
ggaccgtcag tcttctctt cccccaaaa cccaaggaca cctcatgat ctcccgacc	780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac	840
tggtagctgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag	900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc	1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg	1080
gagatgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac	1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200
gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggtctctgca caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 201
 <211> LENGTH: 648
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 201

gatatcgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120

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catccgggca aggcgcgcaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc caggttcgtg acatgtctct gttegacgtg 300
tttggcggcg gcacgaagtt aaccgtccta ggtcagccca aggctgcccc ctcggtcact 360
ctgttccccg cctcctctga ggagcttcaa gccacaagg ccacactggt gtgtctcata 420
agtgaacttct acccgggagc cgtgacagtg gctggaagg cagatagcag ccccgtaag 480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc 540
tatctgagcc tgacgcctga gcagtgaag tcccacagaa gctacagctg ccaggtaag 600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca 648

<210> SEQ ID NO 202
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 202

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 203
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 203

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 204
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 204

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 205
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 205

Gly Tyr Thr Phe Thr Ser Tyr
1 5

-continued

<210> SEQ ID NO 206
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 206

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 207
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 207

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 208
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 208

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 209
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 209

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 210
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 210

Tyr Ser Arg Asp Ser Pro Met Asp Gln Val
1 5 10

<210> SEQ ID NO 211
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 211

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 212

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 212

Gly Val Ser
1

<210> SEQ ID NO 213

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 213

Arg Asp Ser Pro Met Asp Gln
1 5

<210> SEQ ID NO 214

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 214

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 215

<211> LENGTH: 110

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

-continued

<400> SEQUENCE: 215

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Tyr Ser Arg Asp Ser Pro
85 90 95
Met Asp Gln Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 216

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 216

cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60
agctgcaaa cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc 120
ccggggccagg gcctcgatgt gatggggcgt atcgaccgt actctggcaa cacgaactac 180
gcgcagaaat ttcaggggcg ggtgaccatg acccgtgata ccagcattag caccgcgtat 240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct 300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctggt gactgttagc 360
tca 363

<210> SEQ ID NO 217

<211> LENGTH: 330

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 217

gatatcgcg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcggcgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tactctcgtg actctccgat ggaccaggtg 300
tttgccggcg gcacgaagtt aaccgtccta 330

<210> SEQ ID NO 218

<211> LENGTH: 451

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 218

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

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Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> SEQ ID NO 219

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 219

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Tyr Ser Arg Asp Ser Pro
85 90 95

Met Asp Gln Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
115 120 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 220

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

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<400> SEQUENCE: 220

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caggtgcaat tggcgagag cggcgagaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaaag cgtccggata taccttact tcttacgaca tccattgggt ggcgcaggcc    120
ccgggccagg gcctcgagt gatgggccc atcgacccgt actctggcaa cacgaactac    180
gcgcagaaat ttcagggccg ggtgacctg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcacctggt gactgttagc    360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctcaa gagcacctct    420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg    480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tccgggtgt cctacagtcc    540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccacg    600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag    660
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg    720
ggaccgtcag tcttctctt ccccccaaaa cccaaggaca ccctcatgat ctcccgacc    780
cctgagggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac    840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaca agccgcggga ggagcagtac    900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc    960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc   1020
tccaagcca aagggcagcc ccgagaacca caggtgtaca cctgcccc atcccgagg    1080
gagatgacca agaaccaggt cagcctgacc tgctgtgta aaggcttcta tccagcgac    1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc    1200
gtgtggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg    1260
tggcagcagg ggaacgtctt ctcattgtcc gtgatgcatg aggctctgca caaccactac    1320
acgcagaaga gcctctccct gtctccgggt aaa                                1353

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<210> SEQ ID NO 221

<211> LENGTH: 648

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 221

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gatatcgcg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca agggccgcaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg    180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc tactctcgtg actctccgat ggaccagggtg    300
tttggcggcg gcacgaagtt aaccgtccta ggtcagccca aggetgcccc ctgggtcact    360
ctgttccccg cctcctctga ggagcttcaa gccaaacagg ccacactggt gtgtctcata    420
agtgaattct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag    480
gcgggagtgg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc    540

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tatctgagcc tgacgcctga gcagtgggaag tcccacagaa gctacagctg ccagggtcacg 600

catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca 648

<210> SEQ ID NO 222

<211> LENGTH: 5

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 222

Ser Tyr Asp Ile His

1 5

<210> SEQ ID NO 223

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 223

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln

1 5 10 15

Gly

<210> SEQ ID NO 224

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 224

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val

1 5 10

<210> SEQ ID NO 225

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 225

Gly Tyr Thr Phe Thr Ser Tyr

1 5

<210> SEQ ID NO 226

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 226

Asp Pro Tyr Ser Gly Asn

1 5

-continued

<210> SEQ ID NO 227
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 227

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 228
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 228

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 229
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 229

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 230
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 230

Gln Ser Arg Asp Thr Tyr Arg Pro Val Lys Val
1 5 10

<210> SEQ ID NO 231
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 231

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 232
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

-continued

peptide

<400> SEQUENCE: 232

Gly Val Ser
1

<210> SEQ ID NO 233
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 233

Arg Asp Thr Tyr Arg Pro Val Lys
1 5

<210> SEQ ID NO 234
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 234

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 235
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 235

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe

-continued

50	55	60	
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu			
65	70	75	80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Arg Asp Thr Tyr			
	85	90	95
Arg Pro Val Lys Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu			
	100	105	110

<210> SEQ ID NO 236
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 236

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgtccggata taccttcact tcttacgaca tccattgggt gcgccaggcc	120
ccgggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa cacgaactac	180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc	360
tca	363

<210> SEQ ID NO 237
 <211> LENGTH: 333
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 237

gatatcgcgc tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg	180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg	240
caagcggaag acgaagcgga ttattactgc cagtctcgtg acacttacg tccggttaaa	300
gtgtttggcg gcggcacgaa gttaaccgtc cta	333

<210> SEQ ID NO 238
 <211> LENGTH: 451
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 238

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala	
1	15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr	
20	30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	

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35					40					45					
Gly	Arg	Ile	Asp	Pro	Tyr	Ser	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe
50						55					60				
Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Leu	Ser	Arg	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Gly	Ser	Phe	Tyr	Thr	Arg	Asp	Ser	Tyr	Phe	Asp	Val	Trp	Gly
		100						105					110		
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser
		115					120					125			
Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala
	130					135					140				
Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val
145					150					155					160
Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala
			165						170					175	
Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val
		180					185						190		
Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His
	195						200					205			
Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys
	210					215					220				
Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
225					230					235					240
Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
			245						250					255	
Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
		260						265					270		
Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
	275						280					285			
His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
	290					295					300				
Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
305					310					315					320
Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile
			325						330					335	
Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
		340						345					350		
Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
	355						360					365			
Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
	370					375					380				
Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
385					390					395					400
Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val
			405						410					415	
Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met
			420					425					430		
His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser
	435						440					445			

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Pro Gly Lys
450

<210> SEQ ID NO 239
 <211> LENGTH: 217
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 239

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Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20           25           30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35           40           45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50           55           60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65           70           75           80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Arg Asp Thr Tyr
85           90           95
Arg Pro Val Lys Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100          105          110
Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu
115          120          125
Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
130          135          140
Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
145          150          155          160
Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
165          170          175
Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
180          185          190
His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
195          200          205
Lys Thr Val Ala Pro Thr Glu Cys Ser
210          215

```

<210> SEQ ID NO 240
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 240

```

caggtgcaat tgggtcgagag cgggtcggaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaa gctccggata taccttact tcttacgaca tccattgggt gcgccaggcc    120
ccggggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac    180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300

```


-continued

ttctacactc gtgactotta cttcgatgtt tggggccaag gcacctgggt gactgttagc	360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctectccaa gaggacctct	420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg	480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc	540
tcaggactct actccctcag cagcgtggtg accgtgcct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttag	660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720
ggaccgtcag tcttctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc	780
cctgaggtca catgctggtt ggtggacgtg agccacgaag accctgaggt caagttcaac	840
tggtagctgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac	900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc	1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgggag	1080
gagatgacca agaaccaggt cagcctgacc tgctgtgtca aaggcttcta tcccagcgac	1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcatgtctc gtgatgcag aggtctctga caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 241

<211> LENGTH: 651

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 241

gatatcgccg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcgcgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg	180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg	240
caagcggaag acgaagcgga ttattactgc cagtctcgtg acacttacg tccggttaaa	300
gtgtttggcg gcggcacgaa gttaaccgtc ctaggtcagc ccaaggctgc cccctcggtc	360
actctgttcc cgccctctc tgaggagctt caagccaaca aggcacact ggtgtgtctc	420
ataagtactc tctaccggg agccgtgaca gtggcctgga aggcagatag cagccccgtc	480
aaggcgggag tggagaccac cacaccctcc aaacaaagca acaacaagta cgcggccagc	540
agctatctga gcctgacgcc tgagcagtg aagtcccaca gaagctacag ctgccaggtc	600
acgcataga ggagcaccgt ggagaagaca gtggccccta cagaatgttc a	651

<210> SEQ ID NO 242

<211> LENGTH: 5

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 242

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 243

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 243

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 244

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 244

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 245

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 245

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 246

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 246

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 247

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 247

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

-continued

<210> SEQ ID NO 248
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 248

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 249
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 249

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 250
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 250

Ser Ser Arg Asp Leu Ile Gly His Tyr Val
1 5 10

<210> SEQ ID NO 251
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 251

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 252
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 252

Gly Val Ser
1

<210> SEQ ID NO 253
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 253

Arg Asp Leu Ile Gly His Tyr
1 5

<210> SEQ ID NO 254

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 254

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 255

<211> LENGTH: 110

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 255

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Leu Ile
85 90 95

Gly His Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 256

-continued

<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 256

```
caggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagt      60
agctgcaaag cgccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagt gatgggcccgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tca                                                                                   363
```

<210> SEQ ID NO 257
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 257

```
gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc tttctcgtg acctgatcgg tcattacgtg      300
tttggcggcg gcacgaagtt aaccgtccta                                                                                   330
```

<210> SEQ ID NO 258
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 258

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
          20          25          30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
          35          40          45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
          50          55          60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
          85          90          95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
```

-continued

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445
 Pro Gly Lys
 450

<210> SEQ ID NO 259

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 259

-continued

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15
 Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Leu Ile
 85 90 95
 Gly His Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
 100 105 110
 Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
 115 120 125
 Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
 130 135 140
 Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
 145 150 155 160
 Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
 165 170 175
 Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
 180 185 190
 Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
 195 200 205
 Thr Val Ala Pro Thr Glu Cys Ser
 210 215

<210> SEQ ID NO 260

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 260

```

cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc    120
ccgggccagg gcctcgagt gatgggcccgt atcgaccctg actctggcaa cacgaactac    180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggg gactgttagc    360
tcagcctcca ccaagggttc atcggtcttc cccctggcac cctcctccaa gagcacctct    420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg    480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tccggctgt cctacagtcc    540
tcaggactct actcctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag    600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag    660
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg    720

```

-continued

```

ggaccgtcag ttttctctt cccccaaaa cccaaggaca ccctcatgat ctcccgacc 780
cctgaggtca catgctgtgt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcggtga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900
aacagcagct accgggtgtg cagcgtcttc accgtcctgc accaggactg gctgaatggc 960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgaa gaaaaccatc 1020
tccaaagcca aaggcgagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg 1080
gagatgacca agaaccaggt cagcctgacc tgcttggtca aaggttctta tccagcgac 1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc 1200
gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggtctctga caaccactac 1320
acgcagaaga gcctctccct gtctccgggt aaa 1353

```

```

<210> SEQ ID NO 261
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 261
gatatcgcgc tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tcttctcgtg acctgatcgg tcattacgtg 300
tttggcggcg gcacgaagtt aaccgtccta ggtagccca aggtgcccc ctgggtcact 360
ctgttcccg cctcctctga ggagcttcaa gccacaagg ccacactggt gtgtctcata 420
agtgaacttc acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag 480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc 540
tatctgagcc tgacgcctga gcagtggaag tcccacagaa gctacagctg ccaggtcacg 600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca 648

```

```

<210> SEQ ID NO 262
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 262

```

```

Gly Tyr Tyr Met His
1          5

```

```

<210> SEQ ID NO 263
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

```

-continued

peptide

<400> SEQUENCE: 263

Asp Ile Glu Pro Tyr His Gly Lys Pro Leu Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 264

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 264

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 265

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 265

Gly Tyr Thr Phe Thr Gly Tyr
1 5

<210> SEQ ID NO 266

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 266

Glu Pro Tyr His Gly Lys
1 5

<210> SEQ ID NO 267

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 267

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 268

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 268

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser

-continued

1	5	10

<210> SEQ ID NO 269
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 269

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 270
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 270

Ser Ser Arg Asp Leu Ile Gly His Tyr Val
1 5 10

<210> SEQ ID NO 271
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 271

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 272
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 272

Gly Val Ser
1

<210> SEQ ID NO 273
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 273

Arg Asp Leu Ile Gly His Tyr
1 5

<210> SEQ ID NO 274
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 274

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
          20           25           30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
          35           40           45
Gly Asp Ile Glu Pro Tyr His Gly Lys Pro Leu Tyr Ala Gln Lys Phe
          50           55           60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65           70           75           80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
          85           90           95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
          100          105          110
Gln Gly Thr Leu Val Thr Val Ser Ser
          115          120

```

<210> SEQ ID NO 275
 <211> LENGTH: 110
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 275

```

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
          20           25           30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Asn Ala Pro Lys Leu
          35           40           45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
          50           55           60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65           70           75           80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Leu Ile
          85           90           95
Gly His Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
          100          105          110

```

<210> SEQ ID NO 276
 <211> LENGTH: 378
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 276

```

cagggtgcaat tgggtgcagag cggtgcggaa gtgaaaaaac cgggcgaaag cctgaaaatt      60
agctgcaaag gctccggata tagcttcact aactcttggg ttgcttgggt gcgccagatg      120

```

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```

ccgggcaaag gtctcgagtg gatgggcato atctaccggt gtaacagcga caccatctat 180
agcccagagct ttcagggcca ggtgaccatt agcgcggata aaagcatcag caccgcgtat 240
ctgcaatgga gcagcctgaa agcgagcgat accgcgatgt attattgcgc gcgtgttcat 300
atcatccagc cgcgcgtctgc ttggtcttac aacgctatgg atgtttgggg ccaaggcacc 360
ctggtgactg ttagctca 378

```

```

<210> SEQ ID NO 277
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 277

```

```

gatatccaga tgacccagag cccgagcagc ctgagcgcca gcgtgggcga tcgctgacc 60
attacctgca gagccagcca gtctatttct acttacctga actggtacca gcagaaaccg 120
ggcaaagcgc cgaaactatt aatcttcggt gcttctaacc tgcaaagcgg cgtgccgagc 180
cgcttttagcg gcagcggatc cggcaccgat ttcaccctga ccattagctc tctgcaaccg 240
gaagactttg cgacctatta ttgccagcag tctatcactg aactgttcac ctttgccag 300
ggcacgaaag ttgaaattaa a 321

```

```

<210> SEQ ID NO 278
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

```

```

<400> SEQUENCE: 278

```

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20        25        30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35        40        45
Gly Asp Ile Glu Pro Tyr His Gly Lys Pro Leu Tyr Ala Gln Lys Phe
50        55        60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65        70        75        80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85        90        95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100       105       110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115       120       125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130       135       140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145       150       155       160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165       170       175

```

-continued

Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val
			180					185					190		
Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His
		195					200					205			
Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys
	210					215					220				
Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
225					230					235					240
Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
				245					250					255	
Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
			260					265					270		
Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
		275					280					285			
His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
	290					295					300				
Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
305					310					315					320
Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile
				325					330					335	
Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
			340					345					350		
Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
		355					360					365			
Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
		370				375					380				
Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
385					390					395					400
Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val
				405					410					415	
Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met
			420				425					430			
His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser
		435					440					445			
Pro	Gly	Lys													
		450													

<210> SEQ ID NO 279

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 279

Asp	Ile	Ala	Leu	Thr	Gln	Pro	Ala	Ser	Val	Ser	Gly	Ser	Pro	Gly	Gln
1				5					10				15		
Ser	Ile	Thr	Ile	Ser	Cys	Thr	Gly	Thr	Ser	Ser	Asp	Val	Gly	Thr	Tyr
			20				25					30			
Asn	Gln	Val	Ser	Trp	Tyr	Gln	Gln	His	Pro	Gly	Asn	Ala	Pro	Lys	Leu
		35				40					45				
Met	Ile	Tyr	Gly	Val	Ser	Lys	Arg	Pro	Ser	Gly	Val	Ser	Asn	Arg	Phe
		50				55				60					

-continued

Ser	Gly	Ser	Lys	Ser	Gly	Asn	Thr	Ala	Ser	Leu	Thr	Ile	Ser	Gly	Leu
65					70					75					80
Gln	Ala	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	Ser	Ser	Arg	Asp	Leu	Ile
			85						90					95	
Gly	His	Tyr	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu	Gly	Gln
			100					105					110		
Pro	Lys	Ala	Ala	Pro	Ser	Val	Thr	Leu	Phe	Pro	Pro	Ser	Ser	Glu	Glu
		115					120					125			
Leu	Gln	Ala	Asn	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ile	Ser	Asp	Phe	Tyr
	130					135					140				
Pro	Gly	Ala	Val	Thr	Val	Ala	Trp	Lys	Ala	Asp	Ser	Ser	Pro	Val	Lys
145					150					155					160
Ala	Gly	Val	Glu	Thr	Thr	Thr	Pro	Ser	Lys	Gln	Ser	Asn	Asn	Lys	Tyr
				165					170					175	
Ala	Ala	Ser	Ser	Tyr	Leu	Ser	Leu	Thr	Pro	Glu	Gln	Trp	Lys	Ser	His
			180					185					190		
Arg	Ser	Tyr	Ser	Cys	Gln	Val	Thr	His	Glu	Gly	Ser	Thr	Val	Glu	Lys
		195					200					205			
Thr	Val	Ala	Pro	Thr	Glu	Cys	Ser								
	210					215									

<210> SEQ ID NO 280

<211> LENGTH: 1368

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 280

cagggtcaat tgggtgcagag cggtgcggaa gtgaaaaaac cgggcgaaag cctgaaaatt	60
agctgcaaa gctccgata tagcttcaact aactcttggg ttgcttgggt gcgccagatg	120
ccgggcaaa gtcctcgatg gatgggcatc atctaccgg gtaacagcga caccatctat	180
agcccgagct ttcagggcca ggtgaccatt agcgcggata aaagcatcag caccgcgtat	240
ctgcaatgga gcagcctgaa agcgagcgat accgcgatgt attattgcgc gcgtgttcat	300
atcatccagc cgccgtctgc ttggtcttac aacgctatgg atgtttgggg ccaaggcacc	360
ctgggtgactg ttagctcagc ctccaccaag ggtccatcgg tcttccccct ggcaccctcc	420
tccaagagca cctctggggg cacagcggcc ctgggctgcc tggtaagga ctacttcccc	480
gaaccggtga cgggtgctgt gaactcaggc gccctgacca gcggcgtgca caccttcccg	540
gctgtcctac agtcctcagg actctactcc ctccagcagc tggtgaccgt gccctccagc	600
agcttgggca ccagaccta catctgcaac gtgaatcaca agcccagcaa caccaagggtg	660
gacaagagag ttgagcccaa atcttgtgac aaaactcaca catgccacc gtgccagca	720
cctgaactcc tggggggacc gtcagtcttc ctcttcccc caaaacccaa ggacaccctc	780
atgatctccc ggaccctga ggtcacatgc gtgggtgggtg acgtgagcca cgaagaccct	840
gagggtcaagt tcaactggta cgtggacggc gtggaggtgc ataagccaa gacaaagccg	900
cgggaggagc agtacaacag cacgtaccgg gtggtcagcg tctccaccgt cctgcaccag	960
gactggctga atggcaagga gtacaagtgc aaggtctcca acaaagccct ccagaccccc	1020
atcgagaaaa ccatctccaa agccaaaggg cagccccgag aaccacaggt gtacaccctg	1080

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cccccatccc gggaggagat gaccaagaac caggtcagcc tgacctgcct ggtaaaggc 1140
ttctatccca gcgacatcgc cgtggagtgg gagagcaatg ggcagccgga gaacaactac 1200
aagaccacgc ctcccggtgt ggactccgac ggctccttct tctctacag caagctcacc 1260
gtggacaaga gcagggtggca gcaggggaac gtcttctcat gctccgtgat gcatgaggct 1320
ctgcacaacc actacacgca gaagagcctc tccctgtctc cgggtaaa 1368

```

```

<210> SEQ ID NO 281
<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 281
gatatccaga tgacccagag cccgagcagc ctgagcgcca gcgtgggcca tcgctgacc 60
attacctgca gagccagcca gtctatttct acttacctga actggtacca gcagaaaccg 120
ggcaaagcgc cgaaactatt aatcttcggt gcttctaacc tgcaaagcgg cgtgccgagc 180
cgcttttagcg gcagcggatc cggcaccgat ttcaccctga ccattagctc tctgcaaccg 240
gaagactttg cgacctatta ttgccagcag tctatcactg aactgttcac ctttgccag 300
ggcacgaaag ttgaaattaa acgtacgggt gccgctccca gcgtgttcat cttccccccc 360
agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420
ccccgggagg ccaaggtgca gtggaagggt gacaacgccc tgcaagcgg caacagccag 480
gaaagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600
ctgtccagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

```

```

<210> SEQ ID NO 282
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 282

```

```

Gly Tyr Tyr Met His
1           5

```

```

<210> SEQ ID NO 283
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 283

```

```

Asp Ile Asp Pro His Ser Gly Asn Ala Val Tyr Ala Gln Lys Phe Gln
1           5           10           15

```

```

Gly

```

```

<210> SEQ ID NO 284
<211> LENGTH: 12
<212> TYPE: PRT

```

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 284

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 285
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 285

Gly Tyr Thr Phe Thr Gly Tyr
1 5

<210> SEQ ID NO 286
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 286

Asp Pro His Ser Gly Asn
1 5

<210> SEQ ID NO 287
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 287

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 288
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 288

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 289
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 289

-continued

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 290
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 290

Ser Ser Arg Asp Leu Ile Gly His Tyr Val
1 5 10

<210> SEQ ID NO 291
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 291

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 292
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 292

Gly Val Ser
1

<210> SEQ ID NO 293
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 293

Arg Asp Leu Ile Gly His Tyr
1 5

<210> SEQ ID NO 294
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 294

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

-continued

35	40	45
Gly Asp Ile Asp Pro His Ser Gly Asn Ala Val Tyr Ala Gln Lys Phe		
50	55	60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr		
65	70	75
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 295
 <211> LENGTH: 110
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 295

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln	
1	15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr	
20	30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu	
35	45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe	
50	60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu	
65	80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Leu Ile	
85	95
Gly His Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu	
100	110

<210> SEQ ID NO 296
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 296

cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaag cgctccgata taccttcacc ggctattaca tgcattgggt gcgccaggcc	120
ccgggccagg gcctcgagtg gatgggcgac atcgaccgcg attctggcaa cgctgtttac	180
gcgcagaaat ttcagggccg ggtgaccatg acccgatgata ccagcattag caccgcgtat	240
atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctggt gactgttagc	360
tca	363

<210> SEQ ID NO 297
 <211> LENGTH: 330

-continued

```

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 297

gatatcgcg c tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccggggc aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgacccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc tcttctcgtg acctgatcgg tcattacgtg      300
tttgcgggcg gcacgaagtt aaccgtccta                                     330

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```

<210> SEQ ID NO 298
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

```

```

<400> SEQUENCE: 298

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20          25          30

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

Gly Asp Ile Asp Pro His Ser Gly Asn Ala Val Tyr Ala Gln Lys Phe
50          55          60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195         200         205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210         215         220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met

```

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245					250					255					
Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
				260					265					270	
Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
				275					280					285	
His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
				290					295					300	
Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
				305					310					315	320
Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile
				325					330					335	
Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
				340					345					350	
Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
				355					360					365	
Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
				370					375					380	
Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
				385					390					395	400
Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val
				405					410					415	
Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met
				420					425					430	
His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser
				435					440					445	
Pro	Gly	Lys													
				450											

<210> SEQ ID NO 299

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 299

Asp	Ile	Ala	Leu	Thr	Gln	Pro	Ala	Ser	Val	Ser	Gly	Ser	Pro	Gly	Gln
1				5					10					15	
Ser	Ile	Thr	Ile	Ser	Cys	Thr	Gly	Thr	Ser	Ser	Asp	Val	Gly	Thr	Tyr
			20					25					30		
Asn	Gln	Val	Ser	Trp	Tyr	Gln	Gln	His	Pro	Gly	Lys	Ala	Pro	Lys	Leu
			35					40					45		
Met	Ile	Tyr	Gly	Val	Ser	Lys	Arg	Pro	Ser	Gly	Val	Ser	Asn	Arg	Phe
			50				55				60				
Ser	Gly	Ser	Lys	Ser	Gly	Asn	Thr	Ala	Ser	Leu	Thr	Ile	Ser	Gly	Leu
			65				70				75			80	
Gln	Ala	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	Ser	Ser	Arg	Asp	Leu	Ile
				85					90					95	
Gly	His	Tyr	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu	Gly	Gln
			100					105					110		
Pro	Lys	Ala	Ala	Pro	Ser	Val	Thr	Leu	Phe	Pro	Pro	Ser	Ser	Glu	Glu
			115				120						125		
Leu	Gln	Ala	Asn	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ile	Ser	Asp	Phe	Tyr

-continued

130	135	140	
Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys			
145	150	155	160
Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr			
	165	170	175
Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His			
	180	185	190
Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys			
	195	200	205
Thr Val Ala Pro Thr Glu Cys Ser			
	210	215	

<210> SEQ ID NO 300
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 300

cgagtgcaat tgggtgcagag cgggtcggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgtccggata taccttcacc ggctattaca tgcattgggt gcgccaggcc	120
ccgggccagg gcctcgatgt gatggggcag atcgaccgcg attctggcaa cgtgtttac	180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctgggt gactgttagc	360
tcagcctcca ccaagggtcc atcgtgtctc cccctggcac cctcctccaa gacacctct	420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg	480
tcgtggaact caggcgcctt gaccagcggc gtgcacacct tcccggtgt cctacagtcc	540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720
ggaccgtcag tcttctctct cccccaaaa cccaaggaca ccctcatgat ctcccgacc	780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac	840
tggtagctgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag	900
aacagcacgt accgggtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc	1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg	1080
gagatgacca agaaccagggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac	1140
atgcgcgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggetctgca caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 301
 <211> LENGTH: 648

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polynucleotide

<400> SEQUENCE: 301

```
gatatcgcgc tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccggggca aggcgccgaa actgatgac tacggtgttt ctaaactgcc gagcggcgtg      180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc tcttctcgtg acctgatcgg tcattacgtg      300
tttggcggcg gcacgaagt aaccgtccta ggtagccca aggtgcccc ctcggtcact      360
ctgttccccg cctcctctga ggagcttcaa gccacaagg ccacactggg gtgtctcata      420
agtgaattct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag      480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc      540
tatctgagcc tgacgcctga gcagtgaag tcccacagaa gctacagctg ccaggtcacg      600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca      648
```

<210> SEQ ID NO 302
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 302

```
Gly Tyr Tyr Met His
1           5
```

<210> SEQ ID NO 303
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 303

```
Val Ile Asp Pro Tyr Ser Gly Trp Thr Glu Tyr Ala Gln Lys Phe Gln
1           5           10          15
```

Gly

<210> SEQ ID NO 304
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 304

```
Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1           5           10
```

<210> SEQ ID NO 305
<211> LENGTH: 7

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 305

Gly Tyr Thr Phe Thr Gly Tyr
1 5

<210> SEQ ID NO 306
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 306

Asp Pro Tyr Ser Gly Trp
1 5

<210> SEQ ID NO 307
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 307

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 308
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 308

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 309
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 309

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 310
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 310

-continued

Ser Ser Arg Asp Leu Ile Gly His Tyr Val
1 5 10

<210> SEQ ID NO 311
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 311

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 312
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 312

Gly Val Ser
1

<210> SEQ ID NO 313
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 313

Arg Asp Leu Ile Gly His Tyr
1 5

<210> SEQ ID NO 314
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 314

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Val Ile Asp Pro Tyr Ser Gly Trp Thr Glu Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

-continued

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 315
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 315

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Leu Ile
85 90 95

Gly His Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 316
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polynucleotide

<400> SEQUENCE: 316

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60
agctgcaaaag cgtccggata taccttcacc ggctattaca tgcattgggt gcgccaggcc 120
ccggggccagg gcctcgatg gatgggcgtt attgacccgt actctggctg gactgaatac 180
gcgcagaaat ttcagggcgc ggtgaccatg acccgtgata ccagcattag caccgcgtat 240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct 300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc 360
tca 363

<210> SEQ ID NO 317
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polynucleotide

<400> SEQUENCE: 317

gatatcgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg 180

-continued

```

agcaaccgtt ttagcggtac caaaagcggc aacaccgcga gcctgacctat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc tcttctcgtg acctgatcgg tcattacgtg    300
ttggcgggcg gcacgaagtt aaccgtccta                                     330

```

```

<210> SEQ ID NO 318
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

```

```

<400> SEQUENCE: 318

```

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20          25          30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Val Ile Asp Pro Tyr Ser Gly Trp Thr Glu Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195         200         205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210         215         220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245         250         255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260         265         270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275         280         285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290         295         300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305         310         315         320

```

<400> SEQUENCE: 319

Asp 1	Ile	Ala	Leu	Thr 5	Gln	Pro	Ala	Ser	Val 10	Ser	Gly	Ser	Pro	Gly 15	Gln
Ser	Ile	Thr	Ile 20	Ser	Cys	Thr	Gly	Thr 25	Ser	Ser	Asp	Val	Gly 30	Thr	Tyr
Asn	Gln	Val 35	Ser	Trp	Tyr	Gln	Gln 40	His	Pro	Gly	Lys	Ala 45	Pro	Lys	Leu
Met 50	Ile	Tyr	Gly	Val	Ser	Lys 55	Arg	Pro	Ser	Gly	Val 60	Ser	Asn	Arg	Phe
Ser 65	Gly	Ser	Lys	Ser	Gly 70	Asn	Thr	Ala	Ser	Leu 75	Thr	Ile	Ser	Gly	Leu 80
Gln	Ala	Glu	Asp 85	Glu	Ala	Asp	Tyr	Tyr 90	Cys	Ser	Ser	Arg	Asp 95	Leu	Ile
Gly	His	Tyr	Val 100	Phe	Gly	Gly	Gly 105	Thr	Lys	Leu	Thr	Val	Leu 110	Gly	Gln
Pro	Lys	Ala 115	Ala	Pro	Ser	Val	Thr 120	Leu	Phe	Pro	Pro	Ser 125	Ser	Glu	Glu
Leu 130	Gln	Ala	Asn	Lys	Ala 135	Thr	Leu	Val	Cys	Leu	Ile 140	Ser	Asp	Phe	Tyr
Pro 145	Gly	Ala	Val	Thr 150	Val	Ala	Trp	Lys	Ala	Asp 155	Ser	Ser	Pro	Val	Lys 160
Ala	Gly	Val	Glu 165	Thr	Thr	Thr	Pro	Ser	Lys 170	Gln	Ser	Asn	Asn 175	Lys	Tyr
Ala	Ala	Ser 180	Ser	Tyr	Leu	Ser	Leu 185	Thr	Pro	Glu	Gln	Trp	Lys 190	Ser	His
Arg	Ser	Tyr 195	Ser	Cys	Gln	Val	Thr 200	His	Glu	Gly	Ser 205	Thr	Val	Glu	Lys

-continued

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 320
<211> LENGTH: 1353
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 320

```
cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaaag cgtccgdata taccttcacc ggctattaca tgcattgggt gcgccaggcc    120
ccgggccagg gcctcgagtg gatggcggtt attgaccctg actctggctg gactgaatac    180
gcgcagaaat ttcagggccg ggtgacctg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc    360
tcagcctcca ccaagggtcc atcgggtctc cccctggcac cctcctccaa gagcacctct    420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg    480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc    540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccacg    600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag    660
cccaaattctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg    720
ggaccgtcag tcttctcttt ccccccaaaa cccaaggaca ccctcatgat ctcccgacc    780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac    840
tggtacgtgg acggcggtga ggtgcataat gccaaagaaa agccgcggga ggagcagtac    900
aacagcacgt accgggtggt cagcgtcttc accgtctgc accaggactg gctgaatggc    960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc   1020
tccaagcca aaggcgagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg   1080
gagatgacca agaaccaggt cagcctgacc tgctgtgta aaggcttcta tccagcgac   1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc   1200
gtgtgggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg   1260
tggcagcagg ggaacgtctt ctcatgtccc gtgatgcatg aggtctgca caaccactac   1320
acgcagaaga gcctctccct gtctccgggt aaa                               1353
```

<210> SEQ ID NO 321
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 321

```
gatatcgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag   120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcgcgctg   180
```

-continued

agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgacct tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tcttctcgtg acctgatcgg tcattacgtg 300
tttggcggcg gcacgaagt aaccgtccta ggtagccca aggtgcccc ctcggtcact 360
ctgttcccg cctcctctga ggagcttcaa gccacaagg ccacactggg gtgtctcata 420
agtgaattct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag 480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc gccagcagc 540
tatctgagcc tgacgcctga gcagtggaag tccacagaa gctacagtg ccaggtcacg 600
catgaaggga gcaccgtgga gaagacagt gcccctacag aatgttca 648

<210> SEQ ID NO 322
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 322

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 323
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 323

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 324
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 324

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 325
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 325

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 326

-continued

<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 326

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 327
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 327

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 328
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 328

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 329
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 329

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 330
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 330

Gln Ser Arg Gly Glu Tyr Arg Pro Gly Trp Val
1 5 10

<210> SEQ ID NO 331
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 331

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 332

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 332

Gly Val Ser
1

<210> SEQ ID NO 333

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 333

Arg Gly Glu Tyr Arg Pro Gly Trp
1 5

<210> SEQ ID NO 334

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 334

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 335

<211> LENGTH: 111

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

-continued

<400> SEQUENCE: 335

```

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
           20           25           30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
           35           40           45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
           50           55           60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
           65           70           75           80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Arg Gly Glu Tyr
           85           90           95
Arg Pro Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
           100          105          110

```

<210> SEQ ID NO 336

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 336

```

caggtgcaat tgggtcgagag cgggtcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaaag cgctccgata taccttcact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tca                                              363

```

<210> SEQ ID NO 337

<211> LENGTH: 333

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 337

```

gatatcgcgc tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc cagtctcgtg gtgaataacc tccgggttgg      300
gtgtttggcg gcggcacgaa gttaaccgtc cta                                              333

```

<210> SEQ ID NO 338

<211> LENGTH: 451

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 338

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

-continued

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> SEQ ID NO 339

<211> LENGTH: 217

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 339

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Arg Gly Glu Tyr
85 90 95

Arg Pro Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu
115 120 125

Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
130 135 140

Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
145 150 155 160

Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
165 170 175

Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
180 185 190

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
195 200 205

Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 340

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

-continued

<400> SEQUENCE: 340

```

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc    120
ccgggccagg gcctcagatg gatgggccgt atcgaccgt actctggcaa cacgaactac    180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc    360
tcagcctcca ccaaggggtcc atcgggtcttc cccctggcac cctcctccaa gagcacctct    420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg    480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tccgggtgt cctacagtcc    540
tcaggactct actcctcag cagcgtggtg accgtgcct ccagcagctt gggcacccag    600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag    660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg    720
ggaccgtcag tcttctctt ccccccaaaa cccaaggaca cctcatgat ctcccggacc    780
cctgaggtca catgctggtt ggtggacgtg agccacgaag accctgaggt caagttcaac    840
tggtacgtgg acggcgtgga ggtgcataat gccaaagcaa agccgcggga ggagcagtac    900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc    960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc   1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca cctgcccc atcccgggag   1080
gagatgacca agaaccagggt cagcctgacc tgcttggtca aaggcttcta tcccagcgac   1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc   1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg   1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggetctgca caaccactac   1320
acgcagaaga gcctctccct gtctccgggt aaa                               1353

```

<210> SEQ ID NO 341

<211> LENGTH: 651

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 341

```

gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgccgaa actgatgatc tacgggtgtt ctaaacgtcc gagcggcgtg    180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc cagtctcgtg gtgaataccg tccgggttgg    300
gtgtttggcg gcggcacgaa gttaaccgtc ctaggtcagc ccaaggctgc cccctcggtc    360
actctgttcc cgcctctctc tgaggagctt caagccaaca aggccacact ggtgtgtctc    420
ataagtgact tctaccggg agccgtgaca gtggcctgga aggcagatag cagccccgtc    480
aaggcgggag tggagaccac cacaccctcc aaacaaagca acaacaagta cgcggccagc    540

```

-continued

agctatctga gcttgacgcc tgagcagtg aagtcaccaca gaagctacag ctgccaggtc 600

acgcatgaag ggagcacccgt ggagaagaca gtggccccta cagaatgttc a 651

<210> SEQ ID NO 342

<211> LENGTH: 5

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 342

Ser Tyr Asp Ile His

1 5

<210> SEQ ID NO 343

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 343

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln

1 5 10 15

Gly

<210> SEQ ID NO 344

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 344

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val

1 5 10

<210> SEQ ID NO 345

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 345

Gly Tyr Thr Phe Thr Ser Tyr

1 5

<210> SEQ ID NO 346

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 346

Asp Pro Tyr Ser Gly Asn

1 5

-continued

<210> SEQ ID NO 347
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 347

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 348
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 348

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 349
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 349

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 350
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 350

Ser Ser Ala Thr Gln Lys Pro Asp Val Thr Val
1 5 10

<210> SEQ ID NO 351
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 351

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 352
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 352

Gly Val Ser
1

<210> SEQ ID NO 353

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 353

Ala Thr Gln Lys Pro Asp Val Thr
1 5

<210> SEQ ID NO 354

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 354

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 355

<211> LENGTH: 111

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 355

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

-continued

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Ala Thr Gln Lys
85 90 95

Pro Asp Val Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 356

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 356

```
cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc    120
ccggggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa cacgaactac    180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc    360
tca                                                                    363
```

<210> SEQ ID NO 357

<211> LENGTH: 333

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 357

```
gatatcgcgc tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg    180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc tcttctgcta ctcagaaaacc ggacgttact    300
gtgtttggcg gcggcacgaa gttaaccgtc cta                                                                    333
```

<210> SEQ ID NO 358

<211> LENGTH: 451

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 358

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

[illegible]

-continued

450

<210> SEQ ID NO 359
 <211> LENGTH: 217
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 359

```

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
                20           25           30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
                35           40           45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
        50           55           60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65           70           75           80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Ala Thr Gln Lys
                85           90           95
Pro Asp Val Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
        100           105           110
Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu
        115           120           125
Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
        130           135           140
Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
145           150           155           160
Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
        165           170           175
Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
        180           185           190
His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
        195           200           205
Lys Thr Val Ala Pro Thr Glu Cys Ser
        210           215

```

<210> SEQ ID NO 360
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 360

```

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccggggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360

```

-continued

```

tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gageacctct 420
gggggcacag cgccctggg ctgctggtc aaggactact tccccgaacc ggtgacggtg 480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtec 540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccag 600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag 660
cccaaattct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg 720
ggaccgtcag tcttctctct cccccaaaa cccaaggaca cctcatgat ctcccgacc 780
cctgagggtca catgctggtt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac 900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc 960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc 1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg 1080
gagatgacca agaaccaggt cagcctgacc tgctgtgta aaggttcta tccagcgac 1140
atgcctgtg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc 1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggtctctga caaccactac 1320
acgcagaaga gcctctccct gtctcgggt aaa 1353

```

```

<210> SEQ ID NO 361
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 361
gatatcgcgc tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgcgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgca gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tcttctgcta ctcagaaaac ggacgttact 300
gtgtttggcg gcggcacgaa gttaaccgtc ctaggtcagc ccaaggctgc cccctcggtc 360
actctgttcc cgcctcctc tgaggagctt caagccaaca aggccacact ggtgtgtctc 420
ataagtgact tctaccggg agccgtgaca gtggcctgga aggcagatag cagccccgtc 480
aaggcgggag tggagaccac cacaccctcc aaacaaagca acaacaagta cgcggccagc 540
agctatctga gcctgacgcc tgagcagtg aagtcacaca gaagctacag ctgccaggtc 600
acgcatgaag ggagcacctg ggagaagaca gtggccccta cagaatgttc a 651

```

```

<210> SEQ ID NO 362
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

-continued

<400> SEQUENCE: 362

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 363

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 363

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 364

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 364

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 365

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 365

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 366

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 366

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 367

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 367

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

-continued

<210> SEQ ID NO 368
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 368

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 369
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 369

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 370
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 370

Ala Val Arg Asp Ser Val Trp His Val
1 5

<210> SEQ ID NO 371
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 371

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 372
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 372

Gly Val Ser
1

<210> SEQ ID NO 373
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

-continued

peptide

<400> SEQUENCE: 373

Arg Asp Ser Val Trp His
1 5

<210> SEQ ID NO 374

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 374

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 375

<211> LENGTH: 109

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 375

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Val Arg Asp Ser Val
85 90 95Trp His Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 376

<211> LENGTH: 363

-continued

```

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 376

caggtgcaat tggcgagag cggcgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaa cgtccggata taccttcact tcttacgaca tccattgggt gcgccaggcc      120
ccggggccagg gcctcgagt gatgggccgt atcgaccgt actctggcaa cacgaactac      180
gcgcagaaat ttcagggccg ggtgaccatg acccgatgata ccagcattag caccgcgtat      240
atggaactga gccgtctgag tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tca                                                                 363

<210> SEQ ID NO 377
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 377

gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc atttacaacc aggtgtcttg gtaccagcag      120
catccgggca agggccgcaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc gctgttcgtg actccgtttg gcattgtttt      300
ggcggcggca cgaagttaac cgtccta                                                                 327

<210> SEQ ID NO 378
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

<400> SEQUENCE: 378

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20         25         30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35         40         45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50         55         60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65         70         75         80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85         90         95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100        105        110

```

```
<210> SEQ ID NO 379
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

<400> SEQUENCE: 379
```

-continued

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15
 Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Val Arg Asp Ser Val
 85 90 95
 Trp His Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro
 100 105 110
 Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu
 115 120 125
 Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro
 130 135 140
 Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala
 145 150 155 160
 Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala
 165 170 175
 Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg
 180 185 190
 Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr
 195 200 205
 Val Ala Pro Thr Glu Cys Ser
 210 215

<210> SEQ ID NO 380

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 380

```

caggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaa cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgatgt gatgggccgt atcgaccctg actctggcaa caggaactac      180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tcagcctcca ccaaggggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct      420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc      540
tcaggactct actcctcag cagcgtggtg accgtgccct ccagcagctt gggcaccacg      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaattct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720

```


-continued

```

ggaccgtcag tcttctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780
cctgagggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcggtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac 900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc 960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgaa gaaaaccatc 1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg 1080
gagatgacca agaaccaggt cagcctgacc tgcttggtca aaggcttcta tcccagcgac 1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc 1200
gtgtgggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggtcttgca caaccactac 1320
acgcagaaga gcctctccct gtctccgggt aaa 1353

```

```

<210> SEQ ID NO 381
<211> LENGTH: 645
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 381

```

```

gatatcgcg tgacccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc atttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgcgcaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgacat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc gctgttcgtg actccgtttg gcatgtgttt 300
ggcgggcgca cgaagttaac cgtcctaggt cagcccaagg ctgccccctc ggtcactctg 360
tccccgccc cctctgagga gcttcaagcc aacaaggcca cactgggtgtg tctcataagt 420
gacttctacc cgggagccgt gacagtggcc tggaaggcag atagcagccc cgtcaaggcg 480
ggagtggaga ccaccacacc ctccaacaaa agcaacaaca agtacgcggc cagcagctat 540
ctgagcctga cgctgagca gtggaagtcc cacagaagct acagctgcca ggtcacgcat 600
gaagggagca ccgtggagaa gacagtggcc cctacagaat gttca 645

```

```

<210> SEQ ID NO 382
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 382

```

```

Ser Tyr Asp Ile His
1           5

```

```

<210> SEQ ID NO 383
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

-continued

<400> SEQUENCE: 383

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 384

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 384

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 385

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 385

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 386

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 386

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 387

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 387

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 388

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 388

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

-continued

<210> SEQ ID NO 389
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 389

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 390
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 390

Ser Ala Arg Asp Gly Trp Ser Glu Tyr Val
1 5 10

<210> SEQ ID NO 391
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 391

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 392
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 392

Gly Val Ser
1

<210> SEQ ID NO 393
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 393

Arg Asp Gly Trp Ser Glu Tyr
1 5

<210> SEQ ID NO 394
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 394

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
          20           25           30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
          35           40           45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
          50           55           60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
          65           70           75           80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
          85           90           95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
          100          105          110
Gln Gly Thr Leu Val Thr Val Ser Ser
          115          120

```

<210> SEQ ID NO 395

<211> LENGTH: 110

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 395

```

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
          20           25           30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
          35           40           45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
          50           55           60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
          65           70           75           80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ala Arg Asp Gly Trp
          85           90           95
Ser Glu Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
          100          105          110

```

<210> SEQ ID NO 396

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 396

```

cagggtgcaat tgggtgcagag cgggtcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa cacgaactac      180

```

-continued

```

gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttegatgtt tggggccaag gcaccctggt gactgttagc    360
tca                                                                    363

```

```

<210> SEQ ID NO 397
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 397
gatatcgcgc tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg    180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc tctgctcgtg acggttggtc tgaatacgtg    300
tttggcggcg gcacgaagtt aaccgtccta                                     330

```

```

<210> SEQ ID NO 398
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

```

```

<400> SEQUENCE: 398
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20         25         30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35         40         45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50         55         60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65         70         75         80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85         90         95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100        105        110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115        120        125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130        135        140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145        150        155        160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165        170        175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val

```

-continued

180	185	190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His		
195	200	205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys		
210	215	220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
225	230	235
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
245	250	255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
260	265	270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
275	280	285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
290	295	300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
305	310	315
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile		
325	330	335
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
340	345	350
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
355	360	365
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
370	375	380
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
385	390	395
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
405	410	415
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
420	425	430
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
435	440	445
Pro Gly Lys		
450		

<210> SEQ ID NO 399

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 399

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln		
1	5	10
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr		
20	25	30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu		
35	40	45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe		
50	55	60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu		

-continued

65	70	75	80
Gln Ala Glu Asp	Glu Ala Asp Tyr Tyr	Cys Ser Ala Arg Asp	Gly Trp
	85	90	95
Ser Glu Tyr Val Phe	Gly Gly Gly Thr Lys Leu Thr Val	Leu Gly Gln	
	100	105	110
Pro Lys Ala Ala Pro	Ser Val Thr Leu Phe Pro	Pro Ser Ser Glu Glu	
	115	120	125
Leu Gln Ala Asn Lys	Ala Thr Leu Val Cys Leu	Ile Ser Asp Phe Tyr	
	130	135	140
Pro Gly Ala Val Thr	Val Ala Trp Lys Ala Asp	Ser Ser Pro Val Lys	
	145	150	155
Ala Gly Val Glu Thr	Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr		
	165	170	175
Ala Ala Ser Ser Tyr	Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His		
	180	185	190
Arg Ser Tyr Ser Cys	Gln Val Thr His Glu Gly Ser Thr Val Glu Lys		
	195	200	205
Thr Val Ala Pro Thr	Glu Cys Ser		
	210	215	

<210> SEQ ID NO 400

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 400

```

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaaag cgctccgata taccttcaact tottacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gageacctct      420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgtg cctacagtcc      540
tcaggactct actccctcag cagcgtgggt accgtgccct ccagcagctt gggcaccag      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720
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cctgagggtc catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag      900
aacagcacgt accgggtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc      960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgaa gaaaaccatc     1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgaggag     1080
gagatgacca agaaccagggt cagcctgacc tgcttggtca aaggcttcta tccagcgac     1140

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atcgccgtgg agtgggagag caatgggcag cgggagaaca actacaagac cagcctccc 1200
gtgctggact cggacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggctctgca caaccactac 1320
acgcagaaga gcctctccct gtctccgggt aaa 1353

<210> SEQ ID NO 401
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polynucleotide

<400> SEQUENCE: 401

gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
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catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tctgctcgtg acggttggtc tgaatacgtg 300
tttgccggcg gcacgaagtt aaccgtecta ggtagccca aggctgcccc ctggtcact 360
ctgttcccc cctctctga ggagcttcaa gccacaagg ccacactggt gtgtctcata 420
agtgaattct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag 480
gcccggagtgg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc 540
tatctgagcc tgacgcctga gcagtgaag tcccacagaa gctacagctg ccaggtcacg 600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca 648

<210> SEQ ID NO 402
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 402

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 403
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 403

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 404
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 404

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 405
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 405

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 406
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 406

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 407
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 407

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 408
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 408

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 409
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 409

Gly Val Ser Lys Arg Pro Ser

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1 5

<210> SEQ ID NO 410
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 peptide

<400> SEQUENCE: 410

Ala Ser Ala Asp His Ser Tyr His Thr Val
1 5 10

<210> SEQ ID NO 411
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 peptide

<400> SEQUENCE: 411

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 412
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 peptide

<400> SEQUENCE: 412

Gly Val Ser
1

<210> SEQ ID NO 413
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 peptide

<400> SEQUENCE: 413

Ala Asp His Ser Tyr His Thr
1 5

<210> SEQ ID NO 414
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polypeptide

<400> SEQUENCE: 414

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

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Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 415

<211> LENGTH: 110

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 415

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Ala Asp His Ser
85 90 95

Tyr His Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 416

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 416

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agctgcaaa cgtccgata taccttcaact tcttacgaca tccattgggt gcgccaggcc 120

ccgggccagg gcctcgatgt gatgggcccgt atcgaccctg actctggcaa cacgaactac 180

gcgcagaaat ttcagggccc ggtgaccatg acccgtgata ccagcattag caccgcgtat 240

atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct 300

ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc 360

tca 363

<210> SEQ ID NO 417

<211> LENGTH: 330

<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 417
gatatcgcgcg tgaccagccc gccgagcggtg agcggtagccc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaactgcc gagcggcggtg      180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgacctat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc gcttctgctg accattctta ccatactgtg      300
tttggcggcg gcacgaagtt aaccgtccta                                     330

<210> SEQ ID NO 418
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

<400> SEQUENCE: 418
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195         200         205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210         215         220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245         250         255

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Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    260                      265                      270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    275                      280                      285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                      295                      300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
    305                      310                      315                      320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
    325                      330                      335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
    340                      345                      350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    355                      360                      365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                      375                      380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
    385                      390                      395                      400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
    405                      410                      415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
    420                      425                      430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    435                      440                      445

Pro Gly Lys
    450

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<210> SEQ ID NO 419

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 419

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Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
    20           25           30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
    35           40           45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
    50           55           60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
    65           70           75           80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Ala Asp His Ser
    85           90           95

Tyr His Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
    100          105          110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
    115          120          125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
    130          135          140

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Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 420

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 420

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caggtgcaat tggcgagag cggcgagaa gtgaaaaaac cgggtgccag cgtgaaagt 60
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ccgggccagg gcctcgagt gatgggagg atcgaccgt actctggcaa cacgaactac 180
gcgcagaaat ttcaggccg ggtgacctg acccgatgata ccagcattag caccgcgtat 240
atggaactga gccgtctgc tagcgaagat acggccgtgt attattgcgc gcgtggttct 300
ttctacactc gtgactctta cttcgatgt tggggccaag gcacctgggt gactgttagc 360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct 420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacgggtg 480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tccgggtgt cctacagtcc 540
tcaggactct actcctcag cagcgtgggt accgtgccct ccagcagctt gggcacccag 600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag 660
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg 720
ggaccgtcag tcttctctt cccccaaaa cccaaggaca cctcatgat ctcccgacc 780
cctgagggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcggtga ggtgcataat gccaaagaca agccgcggga ggagcagtag 900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc 960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc 1020
tccaaagcca aaggcgagcc ccgagaacca caggtgtaca cctgcccc atccgggag 1080
gagatgacca agaaccaggt cagcctgacc tgctgtgta aaggcttcta tccagcgac 1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc 1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggtctgca caaccactac 1320
acgcagaaga gcctctcct gtctccgggt aaa 1353

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<210> SEQ ID NO 421

<211> LENGTH: 648

<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 421

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gatatcgcgc tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaactgcc gagcggcgtg    180
agcaaccgtt ttagcggatc caaagcggc aacaccgcga gcctgacctat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc gcttctgctg accattctta ccatactgtg    300
tttggcggcg gcacgaagt aaccgtccta ggtagccca aggtgcctcc ctgggtcact    360
ctgttcccg cctcctctga ggagcttcaa gccacaagg ccacactggt gtgtctcata    420
agtgacttct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag    480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc gccagcagc    540
tatctgagcc tgacgcctga gcagtgaag tcccacagaa gctacagctg ccaggtcacg    600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca    648
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<210> SEQ ID NO 422
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 422

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 423
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 423

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 424
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 424

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 425
<211> LENGTH: 7
<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 425

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 426
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 426

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 427
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 427

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 428
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 428

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 429
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 429

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 430
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 430

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Gly Ser Arg Thr Ser His Asn Trp Val
1 5

<210> SEQ ID NO 431
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 431

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 432
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 432

Gly Val Ser
1

<210> SEQ ID NO 433
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 433

Arg Thr Ser His Asn Trp
1 5

<210> SEQ ID NO 434
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 434

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

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Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 435
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 435

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gly Ser Arg Thr Ser His
85 90 95

Asn Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 436
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 436

cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60

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ccgggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa caccgaactac 180

gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat 240

atggaactga gccgtctgcg tagcgaagat acggccctgt attattgcgc gcgtggttct 300

ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc 360

tca 363

<210> SEQ ID NO 437
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 437

gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60

agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120

catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg 180

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agcaaccgtt ttagcggtac caaaagcggc aacaccgcga gcttgacct tagcggcctg    240
caagcggaag acgaagcgga ttattactgc ggtctctgta cttctcataa ctgggtgttt    300
ggcggcggca cgaagttaac cgtccta                                     327

```

```

<210> SEQ ID NO 438
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

```

```

<400> SEQUENCE: 438

```

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195         200         205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210         215         220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245         250         255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260         265         270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275         280         285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290         295         300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305         310         315         320

```

<400> SEQUENCE: 439

Asp 1	Ile	Ala	Leu 5	Thr	Gln	Pro	Ala	Ser	Val 10	Ser	Gly	Ser	Pro	Gly 15	Gln
Ser	Ile	Thr	Ile 20	Ser	Cys	Thr	Gly	Thr 25	Ser	Ser	Asp	Val	Gly 30	Thr	Tyr
Asn	Gln	Val 35	Ser	Trp	Tyr	Gln	Gln 40	His	Pro	Gly	Lys	Ala 45	Pro	Lys	Leu
Met 50	Ile	Tyr	Gly	Val	Ser	Lys 55	Arg	Pro	Ser	Gly	Val 60	Ser	Asn	Arg	Phe
Ser 65	Gly	Ser	Lys	Ser	Gly 70	Asn	Thr	Ala	Ser	Leu 75	Thr	Ile	Ser	Gly	Leu 80
Gln	Ala	Glu	Asp 85	Glu	Ala	Asp	Tyr	Tyr	Cys 90	Gly	Ser	Arg	Thr	Ser 95	His
Asn	Trp	Val	Phe 100	Gly	Gly	Gly	Thr	Lys 105	Leu	Thr	Val	Leu	Gly 110	Gln	Pro
Lys	Ala	Ala 115	Pro	Ser	Val	Thr	Leu 120	Phe	Pro	Pro	Ser	Ser 125	Glu	Glu	Leu
Gln	Ala	Asn 130	Lys	Ala	Thr	Leu 135	Val	Cys	Leu	Ile	Ser 140	Asp	Phe	Tyr	Pro
Gly 145	Ala	Val	Thr	Val	Ala 150	Trp	Lys	Ala	Asp	Ser 155	Ser	Pro	Val	Lys	Ala 160
Gly	Val	Glu	Thr 165	Thr	Thr	Pro	Ser	Lys	Gln 170	Ser	Asn	Asn	Lys	Tyr 175	Ala
Ala	Ser	Ser	Tyr 180	Leu	Ser	Leu	Thr	Pro 185	Glu	Gln	Trp	Lys	Ser 190	His	Arg
Ser	Tyr	Ser	Cys 195	Gln	Val	Thr	His 200	Glu	Gly	Ser	Thr	Val	Glu	Lys	Thr

-continued

Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 440
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 440

```

cagggtcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaa cgtccgata taccttact tcttacgaca tccattgggt gcgccaggcc    120
ccgggccagg gcctcgatg gatgggccc atcgaccgt actctggcaa cacgaactac    180
gcgcagaaat ttcagggcc ggtgacctg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgc tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgt tggggccaag gcaccctggt gactgttagc    360
tcagcctcca ccaagggtcc atcgggtctc cccctggcac cctcctccaa gagcacctct    420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg    480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc    540
tcaggactct actccctcag cagcgtggtg accgtgcct ccagcagctt gggcaccag    600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag    660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg    720
ggaccgtcag tcttctctt ccccccaaaa cccaaggaca ccctcatgat ctcccgacc    780
cctgaggtca catgctggtt ggtggacgtg agccacgaag accctgaggt caagttcaac    840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac    900
aacagcacgt accgggtggt cagcgtctc accgtcctgc accaggactg gctgaatggc    960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc   1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca cctgcccc atcccgagg    1080
gagatgacca agaaccaggt cagcctgacc tgctgtgtca aagccttcta tcccagcgac   1140
atgcgcgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc   1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg   1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggetctgca caaccactac   1320
acgcagaaga gcctctccct gtctcgggt aaa                               1353

```

<210> SEQ ID NO 441
 <211> LENGTH: 645
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 441

```

gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgcgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg    180

```

-continued

```

agcaaccggt ttagcggtat caaaagcggc aacaccgcca gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc ggttctcgta cttctcataa ctgggtgttt 300
ggcgcgcgga cgaagttaac cgtcctaggt cagcccaagg ctgccccctc ggctactctg 360
ttcccgccct cctctgagga gcttcaagcc aacaaggcca cactgggtgtg tctcataagt 420
gaattctacc cgggagccgt gacagtggcc tgggaaggcag atagcagccc cgtaaggcg 480
ggagtggaga ccaccacacc ctccaacaa agcaacaaca agtacgcggc cagcagctat 540
ctgagcctga cgctgagca gtggaagtcc cacagaagct acagctgcca ggtaacgcat 600
gaagggagca ccgtggagaa gacagtggcc cctacagaat gtcca 645

```

```

<210> SEQ ID NO 442
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 442

```

```

Ser Tyr Asp Ile His
1           5

```

```

<210> SEQ ID NO 443
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 443

```

```

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1           5           10           15

```

```

Gly

```

```

<210> SEQ ID NO 444
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 444

```

```

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1           5           10

```

```

<210> SEQ ID NO 445
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 445

```

```

Gly Tyr Thr Phe Thr Ser Tyr
1           5

```

```

<210> SEQ ID NO 446
<211> LENGTH: 6

```

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 446

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 447
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 447

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 448
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 448

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 449
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 449

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 450
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 450

Ala Val Arg Gly Ser Gln Thr Leu Val
1 5

<210> SEQ ID NO 451
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 451

-continued

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 452
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 452

Gly Val Ser
1

<210> SEQ ID NO 453
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 453

Arg Gly Ser Gln Thr Leu
1 5

<210> SEQ ID NO 454
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 454

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 455
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 455

-continued

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15
 Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Val Arg Gly Ser Gln
 85 90 95
 Thr Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105

<210> SEQ ID NO 456
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polynucleotide

<400> SEQUENCE: 456

```

cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccggggccagg gcctcgagtg gatggggcgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tca                                                                                   363
  
```

<210> SEQ ID NO 457
 <211> LENGTH: 327
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polynucleotide

<400> SEQUENCE: 457

```

gatatcgcg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgac tacgggtgtt ctaaacgtcc gagcggcgtg      180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc gctgttcgtg gttctcagac tctgggtgtt      300
ggcggcgga cgaagttaac cgtccta                                                                                   327
  
```

<210> SEQ ID NO 458
 <211> LENGTH: 451
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

-continued

polypeptide

<400> SEQUENCE: 458

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro

-continued

385	390	395	400
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val	405	410	415
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met	420	425	430
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser	435	440	445
Pro Gly Lys	450		

<210> SEQ ID NO 459
 <211> LENGTH: 215
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 459

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln	1	5	10	15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr	20	25	30	
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu	35	40	45	
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe	50	55	60	
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu	65	70	75	80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Val Arg Gly Ser Gln	85	90	95	
Thr Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro	100	105	110	
Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu	115	120	125	
Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro	130	135	140	
Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala	145	150	155	160
Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala	165	170	175	
Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg	180	185	190	
Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr	195	200	205	
Val Ala Pro Thr Glu Cys Ser	210	215		

<210> SEQ ID NO 460
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 460

-continued

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgtccggata taccttctact tcttacgaca tccattgggt gcgccaggcc	120
ccgggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa cacgaactac	180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctcg tagcgaagat acggccctgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctgggt gactgttagc	360
tcagcctcca ccaagggtcc atcgggtcttc cccctggcac cctcctccaa gacacctct	420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg	480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtc	540
tcaggactct actccctcag cagcgtgggt accgtgccct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660
cccaaattct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720
ggaccgtcag tcttctctct cccccaaaa cccaaggaca cctcatgat ctcccgacc	780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag acctgaggt caagttcaac	840
tggtagctgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag	900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc	1020
tccaaagcca aagggcagcc ccgagaacca cagggtgtaca ccctgcccc atcccgggag	1080
gagatgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac	1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200
gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggtcttgca caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 461

<211> LENGTH: 645

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 461

gatatcgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcgccgaa actgatgatc tacgggtgtt ctaaacgtcc gagcggcgtg	180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcca gcctgacct tagcggcctg	240
caagcggaag acgaagcgga ttattactgc gctgttcgtg gttctcagac tctggtgtt	300
ggcggcgcca cgaagttaac cgtcctaggt cagcccaagg ctgccccctc ggtcactctg	360
ttccgcacct cctctgagga gcttcaagcc aacaaggcca cactggtgtg tctcataagt	420
gacttctacc cgggagccgt gacagtggcc tggaaggcag atagcagccc cgtcaaggcg	480
ggagtggaga ccaccacacc ctccaacaaa agcaacaaca agtacgggc cagcagctat	540
ctgagcctga cgctgagca gtggaagtcc cacagaagct acagctgcca ggtcacgcat	600

-continued

gaagggagca ccgtggagaa gacagtggcc cctacagaat gttca

645

<210> SEQ ID NO 462
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 462

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 463
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 463

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 464
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 464

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 465
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 465

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 466
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 466

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 467

-continued

<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 467

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 468
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 468

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 469
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 469

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 470
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 470

Gly Ser Arg Asp Ser Trp Ala His Val
1 5

<210> SEQ ID NO 471
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 471

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 472
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 472

Gly Val Ser
1

<210> SEQ ID NO 473

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 473

Arg Asp Ser Trp Ala His
1 5

<210> SEQ ID NO 474

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 474

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 475

<211> LENGTH: 109

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 475

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

-continued

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gly Ser Arg Asp Ser Trp
85 90 95

Ala His Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 476

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 476

```
cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc    120
ccggggccagg gcctcgagtg gatgggccgt atcgaccgt actctggcaa cacgaactac    180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc    360
tca                                          363
```

<210> SEQ ID NO 477

<211> LENGTH: 327

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 477

```
gatatcgcg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg    180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc gggtctcgtg actcttgggc tcatgtgttt    300
ggcggcgcca cgaagttaac cgtccta                                          327
```

<210> SEQ ID NO 478

<211> LENGTH: 451

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 478

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

[illegible]

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<210> SEQ ID NO 479
 <211> LENGTH: 215
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 479

```

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
          20           25           30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
          35           40           45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
          50           55           60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65           70           75           80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gly Ser Arg Asp Ser Trp
          85           90           95
Ala His Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro
          100          105          110
Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu
          115          120          125
Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro
          130          135          140
Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala
145          150          155          160
Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala
          165          170          175
Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg
          180          185          190
Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr
          195          200          205
Val Ala Pro Thr Glu Cys Ser
          210          215

```

<210> SEQ ID NO 480
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 480

```

cagggtgcaat tgggtgcagag cggtgcgga gtaaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaa gctccggata taccttca ctctacgaca tccattgggt gcgccaggcc    120
ccgggccagg gcctcgatg gatgggccgt atcgaccctg actctggcaa cacgaactac    180
gcgcagaaat ttcaggggcc ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgc tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgt tggggccaag gcaccctggt gactgttagc    360

```

-continued

tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct	420
gggggcacag cggccctggg ctgcttggtc aaggactact tccccgaacc ggtgacggtg	480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgtg cctacagtcc	540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720
ggaccgtcag tcttctctt cccccaaaa cccaaggaca ccctcatgat ctcccgacc	780
cctgaggtca catgctggtt ggtggacgtg agccacgaag accctgaggt caagttcaac	840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac	900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgaa gaaaaccatc	1020
tccaagcca aagggcagcc ccgagaacca caggtgtaca cctgcccc atcccgagg	1080
gagatgacca agaaccaggt cagcctgacc tgcttggtca aaggcttcta tcccagcgac	1140
atgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200
gtgtggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 481

<211> LENGTH: 645

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 481

gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcgcgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg	180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcca gcctgacat tagcggcctg	240
caagcggaag acgaagcgga ttattactgc ggttctcgtg actcttgggc tcatgtgttt	300
ggcggcgcca cgaagttaac cgtcctaggt cagcccaagg ctgccccctc ggtcactctg	360
ttcccgccct cctctgagga gcttcaagcc aacaaggcca cactggtgtg tctcataagt	420
gaactctacc cgggagccgt gacagtggcc tgggaaggcag atagcagccc cgtcaaggcg	480
ggagtggaga ccaccacacc ctccaacaaa agcaacaaca agtacgcggc cagcagctat	540
ctgagcctga cgctgagca gtggaagtcc cacagaagct acagctgcca ggtcacgcat	600
gaaggagca ccgtggagaa gacagtggcc cctacagaat gttca	645

<210> SEQ ID NO 482

<211> LENGTH: 5

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 482

-continued

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 483
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 483

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 484
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 484

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 485
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 485

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 486
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 486

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 487
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 487

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

-continued

<210> SEQ ID NO 488
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 488

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 489
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 489

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 490
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 490

Tyr Ser Arg Ala Lys Thr His Trp Thr Asp Val
1 5 10

<210> SEQ ID NO 491
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 491

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 492
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 492

Gly Val Ser
1

<210> SEQ ID NO 493
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 493

Arg Ala Lys Thr His Trp Thr Asp
1 5

<210> SEQ ID NO 494

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 494

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 495

<211> LENGTH: 111

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 495

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Tyr Ser Arg Ala Lys Thr
85 90 95His Trp Thr Asp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 496

<211> LENGTH: 363

<212> TYPE: DNA

-continued

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 496
caggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaaag cgcccgata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagt gatgggccgt atcgaccgt actctggcaa caggaactac      180
gcgcagaaat ttcagggcgg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctggt gactgttagc      360
tca                                                                                   363

<210> SEQ ID NO 497
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 497
gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc tactctcgtg ctaaaactca ttggactgac      300
gtgtttggcg gcggcacgaa gttaaccgtc cta                                                                                   333

<210> SEQ ID NO 498
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

<400> SEQUENCE: 498
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser

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115	120	125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala		
130	135	140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val		
145	150	155
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala		
165	170	175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val		
180	185	190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His		
195	200	205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys		
210	215	220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
225	230	235
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met		
245	250	255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His		
260	265	270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val		
275	280	285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr		
290	295	300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly		
305	310	315
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile		
325	330	335
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val		
340	345	350
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser		
355	360	365
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
370	375	380
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
385	390	395
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
405	410	415
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
420	425	430
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
435	440	445
Pro Gly Lys		
450		

<210> SEQ ID NO 499

<211> LENGTH: 217

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 499

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln

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1	5	10	15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr	20	25	30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu	35	40	45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe	50	55	60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu	65	70	75
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Tyr Ser Arg Ala Lys Thr	85	90	95
His Trp Thr Asp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly	100	105	110
Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu	115	120	125
Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe	130	135	140
Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val	145	150	155
Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys	165	170	175
Tyr Ala Ala Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser	180	185	190
His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu	195	200	205
Lys Thr Val Ala Pro Thr Glu Cys Ser	210	215	

<210> SEQ ID NO 500

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 500

```

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaaag cgctccgata taccttact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gacacacctc      420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc      540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaattct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720
ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccgacc      780

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cctgagggtca catgctgtgt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac 900
aacagcacgt accgggtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgaa gaaaaccatc 1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgggag 1080
gagatgacca agaaccaggt cagcctgacc tgcttggtca aagccttcta tcccagcgac 1140
atcgccgtgg agtgggagag caatgggcag ccgagaacca actacaagac cagcctccc 1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcatgtctc gtgatgcatg aggtctctga caaccactac 1320
acgcagaaga gcctctcctt gtctccgggt aaa 1353

<210> SEQ ID NO 501
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polynucleotide

<400> SEQUENCE: 501

gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tactctcgtg ctaaaactca ttggactgac 300
gtgtttggcg gcggcacgaa gttaaccgtc ctaggtcagc ccaaggctgc cccctcggtc 360
actctgttcc cgccctctc tgaggagctt caagccaaca aggccacact ggtgtgtctc 420
ataagtgact tctaccgggg agccgtgaca gtggcctgga aggcagatag cagccccgtc 480
aaggcgggag tggagaccac cacaccctcc aaacaaagca acaacaagta cgcggccagc 540
agctatctga gcctgacgcc tgagcagtg aagtcccaca gaagctacag ctgccaggtc 600
acgcatagaag ggagcaccgt ggagaagaca gtggccccta cagaatgttc a 651

<210> SEQ ID NO 502
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 502

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 503
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

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<400> SEQUENCE: 503

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 504

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 504

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 505

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 505

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 506

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 506

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 507

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 507

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 508

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 508

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

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<210> SEQ ID NO 509
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 509

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 510
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 510

Ser Val Trp Thr Ser Ile Lys Val Phe Val
1 5 10

<210> SEQ ID NO 511
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 511

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 512
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 512

Gly Val Ser
1

<210> SEQ ID NO 513
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 513

Trp Thr Ser Ile Lys Val Phe
1 5

<210> SEQ ID NO 514
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

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polypeptide

<400> SEQUENCE: 514

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30
 Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 515

<211> LENGTH: 110

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 515

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15
 Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Val Trp Thr Ser Ile
 85 90 95
 Lys Val Phe Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

<210> SEQ ID NO 516

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 516

cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60
 agctgcaaaag cgctccgata taccttcaact tcttacgaca tccattgggt gcgccaggcc 120
 ccgggccagg gcctcgagtg gatggggcgt atcgaccctg actctggcaa caggaactac 180

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gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat   240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct   300
ttctacactc gtgactctta cttcgatggt tggggccaag gcaccctggt gactgttagc   360
tca                                                                    363

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<210> SEQ ID NO 517
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

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<400> SEQUENCE: 517
gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt   60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag  120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaactgcc gagcggcgtg  180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg  240
caagcggaag acgaagcgga ttattactgc tctgtttgga cttctatcaa agttttcgtg  300
tttggcggcg gcacgaagtt aaccgtccta                                     330

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<210> SEQ ID NO 518
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

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<400> SEQUENCE: 518
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190

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Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
  195                200                205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
  210                215                220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
  225                230                235                240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                250                255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
                260                265                270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
  275                280                285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
  290                295                300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
  305                310                315                320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                330                335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
  340                345                350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
  355                360                365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
  370                375                380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
  385                390                395                400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                410                415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
                420                425                430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
  435                440                445

Pro Gly Lys
  450

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<210> SEQ ID NO 519

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 519

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Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
  1             5             10             15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
                20             25             30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
                35             40             45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
  50             55             60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
  65             70             75             80

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Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Val Trp Thr Ser Ile
 85 90 95

Lys Val Phe Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
 100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
 115 120 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
 130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
 145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
 165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
 180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
 195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
 210 215

<210> SEQ ID NO 520

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 520

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cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaaag cgtccgdata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagtg gatgggcccgt atcgaccctgt actctggcaa cacgaactac      180
gcgcagaaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct      420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc      540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaattctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720
ggaccgtcag tcttctctct ccccccaaaa cccaaggaca ccctcatgat ctcccgacc      780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840
tggtacgtgg acggcggtga ggtgcataat gccaaagaaa agccgcggga ggagcagtac      900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc      960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgga gaaaaccatc     1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg      1080
gagatgacca agaaccaggt cagcctgacc tgccgtgtca aaggcttcta tcccagcgac     1140

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atcgccgtgg agtgggagag caatgggcag cgggagaaca actacaagac cagcctccc 1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcattgtcc gtgatgcatg aggctctgca caaccactac 1320
acgcagaaga gcctctccct gtctccgggt aaa 1353

<210> SEQ ID NO 521
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 521

gatatcgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccgtt ttagcggatc caaagcggc aacaccgcga gcctgacct tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tctgtttgga cttctatcaa agttttcgtg 300
tttggcggcg gcacgaagt aaccgtccta ggtcagccca aggetgcccc ctgggtcact 360
ctgttcccg cctcctctga ggagcttcaa gccacaagg ccacactggt gtgtctcata 420
agtgaattct acccgggagc cgtgacagt gcctggaagg cagatagcag ccccgtaag 480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc gccagcagc 540
tatctgagcc tgacgcctga gcagtggaag tcccacagaa gctacagctg ccaggtcacg 600
catgaaggga gcaccgtgga gaagacagt gccctacag aatgttca 648

<210> SEQ ID NO 522
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 522

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 523
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 523

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 524
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 524

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 525

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 525

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 526

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 526

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 527

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 527

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 528

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 528

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 529

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 529

Gly Val Ser Lys Arg Pro Ser
1 5

-continued

<210> SEQ ID NO 530
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 530

Ser Ala Tyr Asp Ala Ser Thr Gln Val Val
1 5 10

<210> SEQ ID NO 531
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 531

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 532
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 532

Gly Val Ser
1

<210> SEQ ID NO 533
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 533

Tyr Asp Ala Ser Thr Gln Val
1 5

<210> SEQ ID NO 534
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 534

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 535
 <211> LENGTH: 110
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polypeptide

<400> SEQUENCE: 535

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ala Tyr Asp Ala Ser
 85 90 95

Thr Gln Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

<210> SEQ ID NO 536
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 polynucleotide

<400> SEQUENCE: 536

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60

agctgcaaaag cgctccgata taccttact tcttacgaca tccattgggt gcgccaggcc 120

ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac 180

gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat 240

atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct 300

ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc 360

tca 363

<210> SEQ ID NO 537
 <211> LENGTH: 330
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polynucleotide

<400> SEQUENCE: 537

gatatcgcgc tgacccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc attacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaactgcc gagcggcgtg      180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc tctgcttacg acgtttctac tcaggttgtg      300
tttggcggcg gcacgaagtt aaccgtccta                                     330


<210> SEQ ID NO 538
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

<400> SEQUENCE: 538

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130         135         140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145         150         155         160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165         170         175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180         185         190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195         200         205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210         215         220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245         250         255

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Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
      260                      265                      270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
      275                      280                      285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
      290                      295                      300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
      305                      310                      315                      320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
      325                      330                      335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
      340                      345                      350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
      355                      360                      365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
      370                      375                      380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
      385                      390                      395                      400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
      405                      410                      415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
      420                      425                      430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
      435                      440                      445

Pro Gly Lys
      450

```

<210> SEQ ID NO 539

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 539

```

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10           15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
      20           25           30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
      35           40           45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
      50           55           60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
      65           70           75           80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ala Tyr Asp Ala Ser
      85           90           95

Thr Gln Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
      100          105          110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
      115          120          125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
      130          135          140

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Pro	Gly	Ala	Val	Thr	Val	Ala	Trp	Lys	Ala	Asp	Ser	Ser	Pro	Val	Lys
145					150					155					160

Ala	Gly	Val	Glu	Thr	Thr	Thr	Pro	Ser	Lys	Gln	Ser	Asn	Asn	Lys	Tyr
				165					170					175	

Ala	Ala	Ser	Ser	Tyr	Leu	Ser	Leu	Thr	Pro	Glu	Gln	Trp	Lys	Ser	His
		180						185					190		

Arg	Ser	Tyr	Ser	Cys	Gln	Val	Thr	His	Glu	Gly	Ser	Thr	Val	Glu	Lys
		195					200					205			

Thr	Val	Ala	Pro	Thr	Glu	Cys	Ser
210						215	

<210> SEQ ID NO 540

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 540

```

cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaa cgtccgata taccttact tttacgaca tccattgggt gcgccaggcc      120
ccggggccagg gcctcgagt gatgggccc atcgaccgt actctggcaa caggaactac      180
gcgcagaaat ttcagggcc ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgc tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta ctctgatgt tggggccaag gcaccctggt gactgttagc      360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct      420
gggggcacag cggccctggg ctgctgtgtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcgc gtgcacacct tcccggtgt cctacagtcc      540
tcaggactct actcctcag cagcgtggtg accgtgcct ccagcagctt gggcaccacg      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720
ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccgacc      780
cctgagggtc catgctggtt ggtggacgtg agccacgaag accctgaggt caagttcaac      840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag      900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc      960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc     1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca cctgcccc atcccgagg      1080
gagatgacca agaaccaggt cagcctgacc tgctgtgtca aaggttcta tcccagcgac      1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc      1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg      1260
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggtctgca caaccactac      1320
acgcagaaga gcctctccct gtctccgggt aaa                                1353

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<210> SEQ ID NO 541

<211> LENGTH: 648

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 541

gatatcgcgc	tgaccagacc	ggcgagcgtg	agcggtagcc	cgggccagag	cattaccatt	60
agctgcaccg	gcaccagcag	cgatgtgggc	acttacaacc	aggtgtcttg	gtaccagcag	120
catccgggca	aggcgccgaa	actgatgac	tacggtgttt	ctaaacgtcc	gagcggcgtg	180
agcaaccgtt	ttagcggatc	caaaagcggc	aacaccgcga	gcctgaccat	tagcggcctg	240
caagcggaag	acgaagcgga	ttattactgc	tctgcttacg	acgtttctac	tcaggttgtg	300
tttggcggcg	gcacgaagt	aaccgtccta	ggtcagccca	aggctgcccc	ctcggtcact	360
ctgttcccg	cctcctctga	ggagcttcaa	gccaacaagg	ccacactgg	gtgtctcata	420
agtgacttct	acccggggag	cgtgacagtg	gcctggaagg	cagatagcag	ccccgtcaag	480
gcgggagtgg	agaccaccac	accctccaaa	caaagcaaca	acaagtacgc	ggccagcagc	540
tatctgagcc	tgacgcctga	gcagtggaag	tcccacagaa	gctacagctg	ccaggtcacg	600
catgaaggga	gcaccgtgga	gaagacagtg	gccctacag	aatgttca		648

<210> SEQ ID NO 542
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 542

Ser	Tyr	Asp	Ile	His
1			5	

<210> SEQ ID NO 543
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 543

Arg	Ile	Asp	Pro	Tyr	Ser	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> SEQ ID NO 544
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 544

Gly	Ser	Phe	Tyr	Thr	Arg	Asp	Ser	Tyr	Phe	Asp	Val
1				5					10		

<210> SEQ ID NO 545
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 545

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 546
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 546

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 547
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 547

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 548
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 548

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 549
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 549

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 550
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 550

Gln Ser Ala Ala Ile Ala Thr Ser Val

-continued

1 5

<210> SEQ ID NO 551
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 551

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 552
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 552

Gly Val Ser
1

<210> SEQ ID NO 553
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 553

Ala Ala Ile Ala Thr Ser
1 5

<210> SEQ ID NO 554
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 554

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

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115	120	
<210> SEQ ID NO 555		
<211> LENGTH: 109		
<212> TYPE: PRT		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide		
<400> SEQUENCE: 555		
Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln		
1 5 10 15		
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr		
20 25 30		
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu		
35 40 45		
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe		
50 55 60		
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu		
65 70 75 80		
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Ala Ile Ala		
85 90 95		
Thr Ser Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu		
100 105		
<210> SEQ ID NO 556		
<211> LENGTH: 363		
<212> TYPE: DNA		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide		
<400> SEQUENCE: 556		
cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt		60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc		120
ccggggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa cacgaactac		180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat		240
atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct		300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc		360
tca		363
<210> SEQ ID NO 557		
<211> LENGTH: 327		
<212> TYPE: DNA		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide		
<400> SEQUENCE: 557		
gatatcgcgc tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt		60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc agtgtcttg gtaccagcag		120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaactgcc gagcggcgtg		180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg		240

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caagcggaag acgaagcgga ttattactgc cagtctgctg ctatcgctac ttctgtgtt 300
ggcggcggca cgaagttaac cgtccta 327

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<210> SEQ ID NO 558
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
      polypeptide

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<400> SEQUENCE: 558

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10           15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20           25           30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35           40           45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50           55           60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65           70           75           80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85           90           95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100          105          110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115          120          125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130          135          140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145          150          155          160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165          170          175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180          185          190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195          200          205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210          215          220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225          230          235          240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245          250          255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260          265          270
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275          280          285
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290          295          300
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305          310          315          320
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile

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210	215	
<210> SEQ ID NO 560		
<211> LENGTH: 1353		
<212> TYPE: DNA		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide		
<400> SEQUENCE: 560		
cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60	
agctgcaaaag cgtccggata taccttcact tcttacgaca tccattgggt gcgccaggcc	120	
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa caggaactac	180	
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240	
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct	300	
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctgggt gactgttagc	360	
tcagcctcca ccaagggtcc atcgggtcttc cccctggcac cctcctccaa gacacctct	420	
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg	480	
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtc	540	
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccag	600	
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660	
cccaaattct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720	
ggaccgtcag tcttctctct cccccaaaa cccaaggaca cctcatgat ctcccgacc	780	
cctgagggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac	840	
tggtagctgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag	900	
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc	960	
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc	1020	
tccaaagcca aagggcagcc ccgagaacca cagggtgtaca ccctgcccc atcccgagg	1080	
gagatgacca agaaccagggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac	1140	
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200	
gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg	1260	
tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggtctctga caaccactac	1320	
acgcagaaga gcctctccct gtctccgggt aaa	1353	

<210> SEQ ID NO 561		
<211> LENGTH: 645		
<212> TYPE: DNA		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide		
<400> SEQUENCE: 561		
gatatacgcg tgaccagcc gccgagcgtg agcggtagcc cgggccagag cattaccatt	60	
agctgcaccc gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120	
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg	180	
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg	240	

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caagcggaag acgaagcgga ttattactgc cagtctgctg ctatcgctac ttctgtgttt 300
ggcggcgga cgaagttaac cgtcctaggt cagcccaagg ctgccccctc ggctcactctg 360
ttcccgcct cctctgagga gcttcaagcc aacaaggcca cactgggtgtg tctcataagt 420
gacttctacc cgggagccgt gacagtggcc tggaaggcag atagcagccc cgtaaggcg 480
ggagtggaga ccaccacacc ctocaaacaa agcaacaaca agtacgcggc cagcagctat 540
ctgagcctga cgctgagca gtggaagtcc cacagaagct acagctgccca ggtaacgcat 600
gaagggagca ccgtggagaa gacagtggcc cctacagaat gttca 645

<210> SEQ ID NO 562
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 562

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 563
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 563

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 564
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 564

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 565
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 565

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 566
<211> LENGTH: 6
<212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 566

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 567
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 567

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 568
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 568

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 569
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 569

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 570
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 570

Ser Thr Thr Thr Tyr Ser Phe His Met Val
1 5 10

<210> SEQ ID NO 571
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 571

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Thr	Ser	Ser	Asp	Val	Gly	Thr	Tyr	Asn	Gln
1				5					10

<210> SEQ ID NO 572
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 572

Gly Val Ser
1

<210> SEQ ID NO 573
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 573

Thr	Thr	Tyr	Ser	Phe	His	Met
1				5		

<210> SEQ ID NO 574
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 574

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Ser	Tyr
			20						25					30	

Asp	Ile	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
		35					40					45			

Gly	Arg	Ile	Asp	Pro	Tyr	Ser	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe
	50						55				60				

Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65					70					75				80	

Met	Glu	Leu	Ser	Arg	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	

Ala	Arg	Gly	Ser	Phe	Tyr	Thr	Arg	Asp	Ser	Tyr	Phe	Asp	Val	Trp	Gly
			100					105					110		

Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
		115					120	

<210> SEQ ID NO 575
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 575

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Asp	Ile	Ala	Leu	Thr	Gln	Pro	Ala	Ser	Val	Ser	Gly	Ser	Pro	Gly	Gln
1				5					10					15	
Ser	Ile	Thr	Ile	Ser	Cys	Thr	Gly	Thr	Ser	Ser	Asp	Val	Gly	Thr	Tyr
			20					25					30		
Asn	Gln	Val	Ser	Trp	Tyr	Gln	Gln	His	Pro	Gly	Lys	Ala	Pro	Lys	Leu
		35						40				45			
Met	Ile	Tyr	Gly	Val	Ser	Lys	Arg	Pro	Ser	Gly	Val	Ser	Asn	Arg	Phe
	50					55					60				
Ser	Gly	Ser	Lys	Ser	Gly	Asn	Thr	Ala	Ser	Leu	Thr	Ile	Ser	Gly	Leu
65					70					75				80	
Gln	Ala	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	Ser	Thr	Thr	Thr	Tyr	Ser
				85					90					95	
Phe	His	Met	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu		
			100					105					110		

<210> SEQ ID NO 576
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 576

cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc	120
ccggggccagg gcctcgagtg gatgggcccgt atcgaccctg actctggcaa cacgaactac	180
gcgcagaaat ttcagggccg ggtgacctg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctgag tagcgaagat acggccgtgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc	360
tca	363

<210> SEQ ID NO 577
 <211> LENGTH: 330
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 577

gatatcgcg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcggcgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg	180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgacct tagcggcctg	240
caagcggaag acgaagcgga ttattactgc tctactacta cttactcttt ccatatggtg	300
tttgccggcg gcacgaagtt aaccgtccta	330

<210> SEQ ID NO 578
 <211> LENGTH: 451
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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<400> SEQUENCE: 578

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30
 Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400

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Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> SEQ ID NO 579

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 579

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Thr Thr Thr Tyr Ser
85 90 95

Phe His Met Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
115 120 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 580

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 580

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caggtgcaat	tggtgcagag	cgggtcggaa	gtgaaaaaac	cgggtgccag	cgtgaaagtt	60
agctgcaaag	cgtccggata	taccttcaact	tcttacgaca	tccattgggt	gcgccaggcc	120
ccgggccagg	gcctcgagtg	gatgggccgt	atcgaccctg	actctggcaa	cacgaactac	180
gcgcagaaat	ttcagggccg	ggtgaccatg	accctgata	ccagcattag	caccgcgtat	240
atggaactga	gcctctcg	tagcgaagat	acggccgtgt	attattgcgc	gcgtggttct	300
ttctacactc	gtgactctta	cttcgatgtt	tggggccaag	gcaccctggt	gactgttagc	360
tcagcctcca	ccaagggtcc	atcgggtctc	cccctggcac	cctcctccaa	gagcacctct	420
gggggcacag	cggccctggg	ctgcctggtc	aaggactact	tccccgaacc	ggtgacggtg	480
tcgtggaact	caggcgccct	gaccagcggc	gtgcacacct	tcccggtgtg	cctacagtcc	540
tcaggactct	actccctcag	cagcgtggtg	accgtgccct	ccagcagctt	gggcacccag	600
acctacatct	gcaacgtgaa	tcacaagccc	agcaacacca	aggtggacaa	gagagttgag	660
cccaaatctt	gtgacaaaac	tcacacatgc	ccaccgtgcc	cagcacctga	actcctgggg	720
ggaccgtcag	tcttctctct	ccccccaaaa	cccaaggaca	ccctcatgat	ctcccgacc	780
cctgaggtca	catgcgtggt	ggtggacgtg	agccacgaag	accctgaggt	caagttcaac	840
tggtacgtgg	acggcgtgga	ggtgcataat	gccaaagaca	agccgcggga	ggagcagtac	900
aacgacacgt	accgggtggt	cagcgtcttc	accgtcctgc	accaggactg	gctgaatggc	960
aaggagtaca	agtgcaaggt	ctccaacaaa	gccctcccag	cccccatcga	gaaaaccatc	1020
tccaagcca	aaggcgagcc	ccgagaacca	caggtgtaca	ccctgcccc	atcccgagg	1080
gagatgacca	agaaccaggt	cagcctgacc	tgcttggtca	aaggcttcta	tcccagcgac	1140
atgcgcgtgg	agtgggagag	caatgggcag	ccggagaaca	actacaagac	cacgcctccc	1200
gtgttgact	ccgacggctc	cttcttcttc	tacagcaagc	tcaccgtgga	caagagcagg	1260
tggcagcagg	ggaacgtctt	ctcatgctcc	gtgatgcatg	aggctctgca	caaccactac	1320
acgcagaaga	gcctctccct	gtctccgggt	aaa			1353

<210> SEQ ID NO 581

<211> LENGTH: 648

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 581

gatatacgcg	tgaccagcc	ggcgagcgtg	agcggtagcc	cgggccagag	cattaccatt	60
agctgcaccg	gcaccagcag	cgatgtgggc	acttacaacc	aggtgtcttg	gtaccagcag	120
catccgggca	aggcgccgaa	actgatgatc	tacggtgttt	ctaaacgtcc	gagcggcgtg	180
agcaaccgtt	ttagcggatc	caaaagcggc	aacaccgcga	gcctgaccat	tagcggcctg	240
caagcggaag	acgaagcggg	ttattactgc	tctactacta	cttactcttt	ccatatggtg	300
tttggcggcg	gcacgaagtt	aaccgtccta	ggtcagccca	aggctgcccc	ctcggctact	360
ctgttcccg	cctcctctga	ggagcttcaa	gccaaacagg	ccacactggt	gtgtctcata	420
agtgacttct	acccgggagc	cgtgacagtg	gcctggaagg	cagatagcag	ccccgtcaag	480
gcgggagtg	agaccaccac	accctccaaa	caaagcaaca	acaagtacgc	ggccagcagc	540
tatctgagcc	tgacgcctga	gcagtggaag	tcccacagaa	gctacagctg	ccaggtcacg	600

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catgaagggga gcaccgtgga gaagacagtg gccctacag aatgttca 648

<210> SEQ ID NO 582
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 582

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 583
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 583

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 584
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 584

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 585
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 585

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 586
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 586

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 587
<211> LENGTH: 12

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 587

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 588
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 588

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 589
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 589

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 590
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 590

Gln Ala Trp Asp Tyr Arg Gln Thr Ile Val
1 5 10

<210> SEQ ID NO 591
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 591

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 592
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 592

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Gly Val Ser
1

<210> SEQ ID NO 593
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 593

Trp Asp Tyr Arg Gln Thr Ile
1 5

<210> SEQ ID NO 594
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 594

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 595
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 595

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu

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65	70	75	80
Gln Ala Glu Asp	Glu Ala Asp Tyr Tyr	Cys Gln Ala Trp Asp	Tyr Arg
	85	90	95
Gln Thr Ile Val Phe	Gly Gly Gly Thr	Lys Leu Thr Val Leu	
	100	105	110

<210> SEQ ID NO 596
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 596

cagggtgcaat tgggtgcagag cgggtgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgtccggata taccttcact tcttacgaca tccattgggt gcgccaggcc	120
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac	180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctcgc tagcgaagat acggccctgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta cttegatgtt tggggccaag gcaccctggt gactgttagc	360
tca	363

<210> SEQ ID NO 597
 <211> LENGTH: 330
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 597

gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg	180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg	240
caagcggaag acgaagcgga ttattactgc caggcttggg actaccgtca gactatcgtg	300
tttggcggcg gcacgaagtt aaccgtccta	330

<210> SEQ ID NO 598
 <211> LENGTH: 451
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 598

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala	
1	15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr	
20	30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	
35	45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe	

[illegible]

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<210> SEQ ID NO 599
 <211> LENGTH: 216
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 599

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Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1           5           10          15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
          20          25          30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
          35          40          45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
          50          55          60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
          65          70          75          80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Tyr Arg
          85          90          95
Gln Thr Ile Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
          100         105         110
Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
          115         120         125
Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
          130         135         140
Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
          145         150         155         160
Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
          165         170         175
Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
          180         185         190
Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
          195         200         205
Thr Val Ala Pro Thr Glu Cys Ser
          210         215

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<210> SEQ ID NO 600
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 600

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cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt    60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc    120
ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac    180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat    240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc    360
tcagcctcca ccaagggtcc atcgtgtcttc ccctggcac cctcctccaa gagcacctct    420

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gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc 540
tcaggactct actccctcag cagcgtgggtg accgtgccct ccagcagctt gggcacccag 600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttag 660
cccaaattct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg 720
ggaccgtcag tcttctctt cccccaaaa cccaaggaca ccctcatgat ctcccgacc 780
cctgagggtca catgctgggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtac 900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc 960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc 1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgagg 1080
gagatgacca agaaccaggt cagcctgacc tgcttggtca aaggcttcta tcccagcagc 1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc 1200
gtgctggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcatgtctc gtgatgcag aggtctctga caaccactac 1320
acgcagaaga gcctctccct gtctccgggt aaa 1353

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<210> SEQ ID NO 601
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

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<400> SEQUENCE: 601

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gatatcgccg tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgccgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc cagccttggg actaccgtca gactatcgtg 300
tttggcggcg gcacgaagtt aaccgtctca ggtcagccca aggtgcccc ctcggtcact 360
ctgttccccg cctcctctga ggagcttcaa gccaaacaagg ccacactggg gtgtctcata 420
agtgaattct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag 480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc 540
tatctgagcc tgacgcctga gcagtggaag tcccacagaa gctacagctg ccaggtcacg 600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca 648

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<210> SEQ ID NO 602
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

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<400> SEQUENCE: 602

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-continued

Ser Tyr Asp Ile His
1 5

<210> SEQ ID NO 603
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 603

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 604
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 604

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 605
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 605

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 606
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 606

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 607
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 607

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 608

-continued

<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 608

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 609
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 609

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 610
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 610

Gln Val Trp Asp Ser Asp Gln Ala Met Val
1 5 10

<210> SEQ ID NO 611
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 611

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 612
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 612

Gly Val Ser
1

<210> SEQ ID NO 613
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

-continued

<400> SEQUENCE: 613

Trp Asp Ser Asp Gln Ala Met
1 5

<210> SEQ ID NO 614

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 614

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 615

<211> LENGTH: 110

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 615

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30

Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Asp
85 90 95

Gln Ala Met Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 616

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 616

caggtgcaat tggcgagag cggcgaggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgagtg gatggggcgt atcgaccctg actctggcaa cacgaactac      180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc      360
tca                                                                 363

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<210> SEQ ID NO 617
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

<400> SEQUENCE: 617

gatatcgcgc tgaccagacc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgacg tacgggtgttt ctaaactgcc gagcggcgtg      180
agcaaccgtt ttagcggatc caaaagcggc aacaccgcga gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc caggtttggg actctgacca ggctatgggtg      300
tttggcggcg gcacgaagtt aaccgtccta                                     330

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<210> SEQ ID NO 618
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

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<400> SEQUENCE: 618

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20          25          30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100         105         110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115         120         125

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Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130                      135                      140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145                      150                      155                      160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                      170                      175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
                180                      185                      190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                      200                      205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210                      215                      220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225                      230                      235                      240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                      250                      255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        260                      265                      270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275                      280                      285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290                      295                      300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305                      310                      315                      320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                      330                      335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340                      345                      350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355                      360                      365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370                      375                      380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385                      390                      395                      400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                      410                      415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420                      425                      430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435                      440                      445

Pro Gly Lys
 450

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<210> SEQ ID NO 619

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 619

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Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1              5              10              15

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Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Asp
 85 90 95
 Gln Ala Met Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
 100 105 110
 Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
 115 120 125
 Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
 130 135 140
 Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
 145 150 155 160
 Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
 165 170 175
 Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
 180 185 190
 Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
 195 200 205
 Thr Val Ala Pro Thr Glu Cys Ser
 210 215

<210> SEQ ID NO 620

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 620

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cagggtgcaat tgggtcgagag cgggtcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt ggcgcaggcc      120
ccgggccagg gcctcgagtg gatgggcccgt atcgacccgt actctggcaa cacgaactac      180
gcgcagaaat ttcagggccg ggtgacctg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggg gactgttagc      360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct      420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc      540
tcaggactct actcctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaattctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720
ggaccgtcag tcttctctct cccccaaaaa cccaaggaca ccctcatgat ctcccggacc      780

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cctgaggtca catgctgtgt ggtggacgtg agccacgaag accctgaggt caagttcaac      840
tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac      900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc      960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcgaa gaaaaccatc     1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgggag      1080
gagatgacca agaaccaggt cagcctgacc tgcttggtca aaggcttcta tcccagcgac      1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc      1200
gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg      1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggcctctga caaccactac      1320
acgcagaaga gcctctccct gtctccgggt aaa                                  1353

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<210> SEQ ID NO 621
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
                        polynucleotide

```

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<400> SEQUENCE: 621
gatatcgcgc tgaccagccc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgccgaa actgatgacg tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccgtt ttagcgggac caaaagcggc aacaccgcga gcctgaccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc caggtttggg actctgacca ggctatgggt      300
tttggcggcg gcacgaagtt aaccgtccta ggtcagcccc aggetgcccc ctgggtcact      360
ctgttcccgc cctcctctga ggagcttcaa gccaacaagg ccacactggt gtgtctcata      420
agtgaacttc acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag      480
gctgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc      540
tatctgagcc tgacgcctga gcagtggaag tcccacagaa gctacagctg ccaggtcacg      600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca                    648

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<210> SEQ ID NO 622
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
                        peptide

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<400> SEQUENCE: 622

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Ser Tyr Asp Ile His
1           5

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<210> SEQ ID NO 623
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
                        peptide

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<400> SEQUENCE: 623

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Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> SEQ ID NO 624
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 624

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 625
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 625

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 626
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 626

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 627
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 627

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 628
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 628

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

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<210> SEQ ID NO 629
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 629

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 630
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 630

Ser Thr Ala Thr Ala Met Thr Val Ser Leu Val
1 5 10

<210> SEQ ID NO 631
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 631

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 632
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 632

Gly Val Ser
1

<210> SEQ ID NO 633
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 633

Ala Thr Ala Met Thr Val Ser Leu
1 5

<210> SEQ ID NO 634
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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<400> SEQUENCE: 634

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30
 Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 635

<211> LENGTH: 111

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 635

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15
 Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Thr Ala Thr Ala Met
 85 90 95
 Thr Val Ser Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

<210> SEQ ID NO 636

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 636

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60
 agctgcaaaag cgtccggata taccttcact tcttacgaca tccattgggt gcgccaggcc 120
 ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac 180
 gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat 240

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atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct    300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggg gactgttagc    360
tca                                                                    363

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<210> SEQ ID NO 637
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 637
gatatcgcgc tgaccagacc gccgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgccgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg    180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc tctactgcta ctgctatgac tgtttctctg    300
gtgtttggcg gcggcacgaa gtaaccgtc cta                                333

```

```

<210> SEQ ID NO 638
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polypeptide

```

```

<400> SEQUENCE: 638
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20        25        30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35        40        45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50        55        60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65        70        75        80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85        90        95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100       105       110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115       120       125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130       135       140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145       150       155       160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165       170       175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180       185       190

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Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His
	195						200					205			
Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys
	210					215					220				
Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
225					230					235					240
Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
				245					250					255	
Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
			260					265					270		
Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
	275						280					285			
His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
	290					295					300				
Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
305					310					315					320
Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile
				325					330					335	
Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
			340					345					350		
Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
		355					360					365			
Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
	370					375					380				
Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
385					390					395					400
Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val
				405					410					415	
Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met
			420				425					430			
His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser
		435					440					445			
Pro	Gly	Lys													
	450														

<210> SEQ ID NO 639

<211> LENGTH: 217

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 639

Asp	Ile	Ala	Leu	Thr	Gln	Pro	Ala	Ser	Val	Ser	Gly	Ser	Pro	Gly	Gln
1				5					10					15	
Ser	Ile	Thr	Ile	Ser	Cys	Thr	Gly	Thr	Ser	Ser	Asp	Val	Gly	Thr	Tyr
			20				25					30			
Asn	Gln	Val	Ser	Trp	Tyr	Gln	Gln	His	Pro	Gly	Lys	Ala	Pro	Lys	Leu
		35				40					45				
Met	Ile	Tyr	Gly	Val	Ser	Lys	Arg	Pro	Ser	Gly	Val	Ser	Asn	Arg	Phe
	50				55					60					
Ser	Gly	Ser	Lys	Ser	Gly	Asn	Thr	Ala	Ser	Leu	Thr	Ile	Ser	Gly	Leu
65					70				75					80	

-continued

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Thr Ala Thr Ala Met
85 90 95

Thr Val Ser Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu
115 120 125

Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
130 135 140

Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
145 150 155 160

Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
165 170 175

Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
180 185 190

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
195 200 205

Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> SEQ ID NO 640

<211> LENGTH: 1353

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 640

```

cagggtcaat tgggtgcagag cggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt      60
agctgcaaa cgtccgata taccttact tcttacgaca tccattgggt gcgccaggcc      120
ccgggccagg gcctcgatg gatgggccgt atcgaccgt actctggcaa cagcaactac      180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat      240
atggaactga gccgtctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttct      300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctggt gactgttagc      360
tcagcctcca ccaagggtcc atcgggtcttc cccctggcac cctcctccaa gagcacctct      420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc      540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccacg      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag      660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg      720
ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc      780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840
tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac      900
aacagcacgt accgggtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc      960
aaggagtaca agtgcaaggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc     1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgcccc atcccgggag     1080
gagatgacca agaaccaggt cagcctgacc tgctggtca aagccttcta tcccagcgac     1140
atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc     1200

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```

gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcatg aggctctgca caaccactac 1320
acgcagaaga gcctctccct gtctcgggt aaa 1353

```

```

<210> SEQ ID NO 641
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        polynucleotide

```

```

<400> SEQUENCE: 641

```

```

gatatcgcg tgacccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc atttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcggcga actgatgac tacggtgttt ctaaacgtcc gagcgcgctg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgacat tagcggcctg 240
caagcggaag acgaagcgga ttattactgc tctactgcta ctgctatgac tgtttctctg 300
gtgtttggcg gcggcacgaa gttaacgtc ctaggtcagc ccaaggctgc cccctcggtc 360
actctgttcc cgccctcttc tgaggagctt caagccaaca aggccacact ggtgtgtctc 420
ataagtgact tctacccggg agccgtgaca gtggcctgga aggcagatag cagccccgtc 480
aaggcgggag tggagaccac cacacctcc aaacaaagca acaacaagta cgcggccagc 540
agctatctga gcctgacgcc tgagcagtg aagtcaccaca gaagctacag ctgccaggtc 600
acgcatgaag ggagcacctg ggagaagaca gtggccccta cagaatgttc a 651

```

```

<210> SEQ ID NO 642
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 642

```

```

Ser Tyr Asp Ile His
1           5

```

```

<210> SEQ ID NO 643
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
        peptide

```

```

<400> SEQUENCE: 643

```

```

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1           5           10           15

```

```

Gly

```

```

<210> SEQ ID NO 644
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

```

-continued

peptide

<400> SEQUENCE: 644

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 645

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 645

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 646

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 646

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 647

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 647

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 648

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 648

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 649

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

<400> SEQUENCE: 649

Gly Val Ser Lys Arg Pro Ser
1 5

-continued

<210> SEQ ID NO 650
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 650

Gln Val Ala Asp Gln Gly Trp His Gln Val
1 5 10

<210> SEQ ID NO 651
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 651

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 652
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 652

Gly Val Ser
1

<210> SEQ ID NO 653
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 653

Ala Asp Gln Gly Trp His Gln
1 5

<210> SEQ ID NO 654
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 654

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe

-continued

50	55	60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr		
65	70	75 80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys		
	85	90 95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly		
	100	105 110
Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 655
 <211> LENGTH: 110
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 655

Asp Ile Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln	
1	5 10 15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr	
	20 25 30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu	
	35 40 45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe	
	50 55 60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu	
65	70 75 80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Val Ala Asp Gln Gly	
	85 90 95
Trp His Gln Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu	
	100 105 110

<210> SEQ ID NO 656
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 656

cagggtgcaat tgggtgcagag cgggtgcgaa gtgaaaaaac cgggtgccag cgtgaaagtt agctgcaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc ccggggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc tca	60 120 180 240 300 360 363

<210> SEQ ID NO 657
 <211> LENGTH: 330
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

-continued

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 657

```

gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt      60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag      120
catccgggca aggcgcgaa actgatgac tacggtgttt ctaaacgtcc gagcggcgtg      180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgacccat tagcggcctg      240
caagcggaag acgaagcgga ttattactgc caggttgctg accagggttg gcatcaggtg      300
tttggcggcg gcacgaagtt aaccgtccta                                     330

```

<210> SEQ ID NO 658

<211> LENGTH: 451

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 658

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala      15
1          5          10          15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr      30
20          25          30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met      45
35          40          45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe      60
50          55          60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr      80
65          70          75          80
Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys      95
85          90          95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly     110
100          105          110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser     125
115          120          125
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala     140
130          135          140
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val     160
145          150          155          160
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala     175
165          170          175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val     190
180          185          190
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His     205
195          200          205
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys     220
210          215          220
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly     240
225          230          235          240
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met     255
245          250          255
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His

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-continued

260					265					270					
Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
275					280					285					
His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr
290					295					300					
Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
305					310					315					
Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile
325					330					335					
Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
340					345					350					
Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
355					360					365					
Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
370					375					380					
Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
385					390					395					
Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val
405					410					415					
Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met
420					425					430					
His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser
435					440					445					
Pro	Gly	Lys													
450															

<210> SEQ ID NO 659

<211> LENGTH: 216

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 659

Asp	Ile	Ala	Leu	Thr	Gln	Pro	Ala	Ser	Val	Ser	Gly	Ser	Pro	Gly	Gln
1				5					10					15	
Ser	Ile	Thr	Ile	Ser	Cys	Thr	Gly	Thr	Ser	Ser	Asp	Val	Gly	Thr	Tyr
		20					25						30		
Asn	Gln	Val	Ser	Trp	Tyr	Gln	Gln	His	Pro	Gly	Lys	Ala	Pro	Lys	Leu
		35					40					45			
Met	Ile	Tyr	Gly	Val	Ser	Lys	Arg	Pro	Ser	Gly	Val	Ser	Asn	Arg	Phe
	50					55					60				
Ser	Gly	Ser	Lys	Ser	Gly	Asn	Thr	Ala	Ser	Leu	Thr	Ile	Ser	Gly	Leu
65					70					75				80	
Gln	Ala	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	Gln	Val	Ala	Asp	Gln	Gly
		85							90					95	
Trp	His	Gln	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu	Gly	Gln
		100						105						110	
Pro	Lys	Ala	Ala	Pro	Ser	Val	Thr	Leu	Phe	Pro	Pro	Ser	Ser	Glu	Glu
		115					120					125			
Leu	Gln	Ala	Asn	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ile	Ser	Asp	Phe	Tyr
	130					135					140				
Pro	Gly	Ala	Val	Thr	Val	Ala	Trp	Lys	Ala	Asp	Ser	Ser	Pro	Val	Lys

-continued

145	150	155	160
Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr			
	165	170	175
Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His			
	180	185	190
Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys			
	195	200	205
Thr Val Ala Pro Thr Glu Cys Ser			
	210	215	

<210> SEQ ID NO 660
 <211> LENGTH: 1353
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 660

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt	60
agctgcaaaag cgtccggata taccttcaact tcttacgaca tccattgggt gcgccaggcc	120
ccgggccagg gcctcgatgt gatgggccgt atcgaccctg actctggcaa caggaactac	180
gcgcagaaat ttcaggggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctcgc tagcgaagat acggccgtgt attattgcgc gcgtggttct	300
ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctgggt gactgttagc	360
tcagcctcca ccaagggtcc atcgggtcttc cccctggcac cctcctccaa gacacctct	420
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg	480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggtgt cctacagtcc	540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660
cccaaactct gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg	720
ggaccgtcag tcttctctct cccccaaaa cccaaggaca ccctcatgat ctcccgacc	780
cctgagggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac	840
tggtagctgg acggcgtgga ggtgcataat gccaaagaaa agccgcggga ggagcagtag	900
aacagcacgt accgggtggt cagcgtcttc accgtcctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaagggt ctccaacaaa gccctcccag ccccatcga gaaaaccatc	1020
tccaaagcca aagggcagcc ccgagaacca cagggtgtaca ccctgcccc atcccgagg	1080
gagatgacca agaaccagggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac	1140
atgcgcgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc	1200
gtgctggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcagtctcc gtgatgcag aggtctctgca caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 661
 <211> LENGTH: 648
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 661

```
gatatcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt    60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag    120
catccgggca aggcgcgcaa actgatgac tacggtgttt ctaaactgcc gagcggcgtg    180
agcaaccggt ttagcggatc caaaagcggc aacaccgcca gcctgaccat tagcggcctg    240
caagcggaag acgaagcgga ttattactgc caggttgctg accagggttg gcatcaggtg    300
tttggcggcg gcacgaagt aaccgtccta ggtagccca aggctgcccc ctggtcact    360
ctgttccccg cctcctctga ggagcttcaa gccacaagg ccacactggt gtgtctcata    420
agtgaattct acccgggagc cgtgacagtg gcctggaagg cagatagcag ccccgtaag    480
gcgggagtg agaccaccac accctccaaa caaagcaaca acaagtacgc ggccagcagc    540
tatctgagcc tgacgcctga gcagtgaag tcccacagaa gctacagctg ccaggtcagc    600
catgaaggga gcaccgtgga gaagacagtg gccctacag aatgttca    648
```

<210> SEQ ID NO 662

<211> LENGTH: 5

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 662

```
Ser Tyr Asp Ile His
1           5
```

<210> SEQ ID NO 663

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 663

```
Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1           5           10          15
```

Gly

<210> SEQ ID NO 664

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 664

```
Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1           5           10
```

<210> SEQ ID NO 665

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 665

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> SEQ ID NO 666

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 666

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 667

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 667

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 668

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 668

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 669

<211> LENGTH: 7

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 669

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 670

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 670

Ser Ser Ala Thr Gln Lys Pro Asp Val Thr Val
1 5 10

-continued

<210> SEQ ID NO 671
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 671

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln
1 5 10

<210> SEQ ID NO 672
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 672

Gly Val Ser
1

<210> SEQ ID NO 673
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 673

Ala Thr Gln Lys Pro Asp Val Thr
1 5

<210> SEQ ID NO 674
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 674

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

-continued

<210> SEQ ID NO 675
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 675

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
20 25 30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Ala Thr Gln Lys
85 90 95
Pro Asp Val Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 676
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 676

cagggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60
agctgcaaa cgtccgata taccttcaact tcttacgaca tccattgggt gcgccaggcc 120
ccgggccagg gcctcgatg gatgggcccgt atcgaccgt actctggcaa cacgaactac 180
gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat 240
atggaactga gccgtctgcg tagcgacgat acggccgtgt attattgcgc gcgtggttct 300
ttctacactc gtgactctta ctctgatgtt tggggccaag gcaccctggt gactgttagc 360
tca 363

<210> SEQ ID NO 677
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 677

cagagcgcgc tgaccagacc gccgagcgtg agcggtagcc cgggccagag cattaccatt 60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag 120
catccgggca aggcgcgaa actgatgatc tacggtgttt ctaaacgtcc gagcggcgtg 180
agcaaccggt ttagcggatc caaaagcggc aacaccgcga gcctgacat tagcggcctg 240

-continued

caagcggaag acgaagcgga ttattactgc tttctgcta ctcagaaacc ggacgttact 300

gtgtttggcg gcggcacgaa gttaaccgtc cta 333

<210> SEQ ID NO 678

<211> LENGTH: 451

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 678

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

-continued

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445
 Pro Gly Lys
 450

<210> SEQ ID NO 679

<211> LENGTH: 217

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 679

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
 1 5 10 15
 Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr
 20 25 30
 Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
 35 40 45
 Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Ala Thr Gln Lys
 85 90 95
 Pro Asp Val Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
 100 105 110
 Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu
 115 120 125
 Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
 130 135 140
 Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
 145 150 155 160
 Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
 165 170 175
 Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
 180 185 190
 His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
 195 200 205
 Lys Thr Val Ala Pro Thr Glu Cys Ser
 210 215

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<210> SEQ ID NO 680
<211> LENGTH: 1353
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 680

caggtgcaat tggcgagag cggcgagaa gtgaaaaaac cgggtgagag cgtgaaagt	60
agctgcagg cgtccggata taccttact tcttacgaca tccattgggt gcgccaggcc	120
ccgggccagg gcctcgagt gatgggagc atcgaccggt actctggcaa cacgaactac	180
gcgcagaaat ttcaggggcg ggtgacctg acccgtgata ccagcattag caccgcgtat	240
atggaactga gccgtctgc tagcgagat acggccgtgt attattgcgc gcgtggtct	300
ttctacactc gtgactctta cttcgatgt tggggccaag gcacctgggt gactgttagc	360
tcagcctcca ccaagggtcc atcggtcttc cccctggcac cctcctccaa gagcacctct	420
gggggcacag cggccctggg ctgctgggtc aaggactact tccccgaacc ggtgacgggt	480
tcgtggaact caggcgccct gaccagggc gtgcacacct tccgggtgt cctacagtc	540
tcaggactct actccctcag cagcgtgggt accgtgccct ccagcagctt gggcaccag	600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag	660
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctggg	720
ggaccgtcag tcttctctt ccccccaaaa ccaaggaca ccctcatgat ctcccgacc	780
cctgaggtca catgcgtggt ggtggagctg agccacgaag accctgaggt caagttcaac	840
tggtagctgg acggcggtga ggtgcataat gccaaagaca agccgcggga ggagcagtag	900
aacagcacgt accgggtggt cagcgtcttc accgtctgc accaggactg gctgaatggc	960
aaggagtaca agtgcaaggt ctccaacaaa gccctccag ccccatcga gaaaaccatc	1020
tccaagcca aaggcgagcc ccgagaacca caggtgtaca cctgcccc atccgggag	1080
gagatgacca agaaccaggt cagcctgacc tgctgtgca aaggcttcta tccagcgac	1140
atcgccgtgg agtgggagag caatgggag ccggagaaca actacaagac cagcctccc	1200
gtgtggact ccgacggctc cttcttctc tacagcaagc tcaccgtgga caagagcagg	1260
tggcagcagg ggaacgtctt ctcagctcc gtgatgcatg aggtctgca caaccactac	1320
acgcagaaga gcctctccct gtctccgggt aaa	1353

<210> SEQ ID NO 681
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 681

cagagcgcg tgaccagcc ggcgagcgtg agcggtagcc cgggccagag cattaccatt	60
agctgcaccg gcaccagcag cgatgtgggc acttacaacc aggtgtcttg gtaccagcag	120
catccgggca aggcggcga actgatgatc tacggtgttt ctaaacgtcc gagcgcgctg	180
agcaaccgtt ttagcggatc caaaagcgcc aacaccgga gcctgacct tagcggcctg	240

-continued

```

caagcggaag acgaagcgga ttattactgc tttctgcta ctcagaaacc ggacgttact 300
gtgtttggcg gcggcacgaa gttaaccgtc ctaggtcagc ccaaggctgc cccctcggtc 360
actctgttcc cgcctctctc tgaggagctt caagccaaca aggccacact ggtgtgtctc 420
ataagtgact tctaccggg agccgtgaca gtggcctgga aggcagatag cagccccgtc 480
aaggcgggag tggagaccac cacacctcc aaacaaagca acaacaagta cgcggccagc 540
agctatctga gcctgacgcc tgagcagtg aagtcaccaca gaagctacag ctgccaggtc 600
acgcatgaag ggagcaccgt ggagaagaca gtggccccta cagaatgttc a 651

```

```

<210> SEQ ID NO 682
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 682

```

```

Ser Tyr Asp Ile His
1             5

```

```

<210> SEQ ID NO 683
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 683

```

```

Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1             5             10             15

```

```

Gly

```

```

<210> SEQ ID NO 684
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 684

```

```

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1             5             10

```

```

<210> SEQ ID NO 685
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

```

```

<400> SEQUENCE: 685

```

```

Gly Tyr Thr Phe Thr Ser Tyr
1             5

```

```

<210> SEQ ID NO 686
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

```

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 686

Asp Pro Tyr Ser Gly Asn
1 5

<210> SEQ ID NO 687
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 687

Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 688
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 688

Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln Val Ser
1 5 10

<210> SEQ ID NO 689
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 689

Gly Val Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 690
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 690

Ala Ser Ala Asp His Ser Tyr His Thr Val
1 5 10

<210> SEQ ID NO 691
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 691

Thr Ser Ser Asp Val Gly Thr Tyr Asn Gln

-continued

1 5 10

<210> SEQ ID NO 692
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 692

Gly Val Ser
1

<210> SEQ ID NO 693
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 693

Ala Asp His Ser Tyr His Thr
1 5

<210> SEQ ID NO 694
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 694

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 695
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 695

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln

-continued

1	5	10	15
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Thr Tyr	20	25	30
Asn Gln Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu	35	40	45
Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe	50	55	60
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu	65	70	75
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Ala Asp His Ser	85	90	95
Tyr His Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu	100	105	110

<210> SEQ ID NO 696
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polynucleotide

<400> SEQUENCE: 696
 caggtgcaat tgggtgcagag cgggtgcggaa gtgaaaaaac cgggtgccag cgtgaaagtt 60
 agctgcaaaag cgctccgata taccttcact tcttacgaca tccattgggt gcgccaggcc 120
 ccgggccagg gcctcgagtg gatgggccgt atcgaccctg actctggcaa cacgaactac 180
 gcgcagaaat ttcagggccg ggtgaccatg acccgtgata ccagcattag caccgcgtat 240
 atggaactga gccgtctcgc tagcgacgat acggccgtgt attattgcgc gcgtggttct 300
 ttctacactc gtgactctta cttcgatgtt tggggccaag gcaccctggt gactgttagc 360
 tca 363

<210> SEQ ID NO 697
 <211> LENGTH: 330
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
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<210> SEQ ID NO 698
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<400> SEQUENCE: 698

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 35 40 45
 Gly Arg Ile Asp Pro Tyr Ser Gly Asn Thr Asn Tyr Ala Gln Lys Phe
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 Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Ser Phe Tyr Thr Arg Asp Ser Tyr Phe Asp Val Trp Gly
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 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
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 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
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 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
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 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
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 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
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 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
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Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
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Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
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Met Ile Tyr Gly Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
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Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Ala Asp His Ser
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Tyr His Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
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Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
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Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
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Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
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<210> SEQ ID NO 700

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<210> SEQ ID NO 701

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<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

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<210> SEQ ID NO 702
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<400> SEQUENCE: 702

His His His His His His
1             5

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1. An isolated antibody or fragment thereof that recognizes a non-linear epitope of a HER3 receptor, wherein the non-linear epitope comprises amino acid residues within domain 3 of the HER3 receptor, wherein the antibody or fragment thereof binds to a binding surface comprising at least one amino acid residue selected from binding surface B, and wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

2. The isolated antibody or fragment thereof of claim 1, wherein binding surface B comprises at least one amino acid residue selected from amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455.

3. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment further binds to binding surface A.

4. The isolated antibody or fragment thereof of claim 3, wherein binding surface A comprises at least one amino acid residue selected from the group consisting of amino acid residues 362-376.

5. An isolated antibody or fragment thereof that recognizes a non-linear epitope of a HER3 receptor, wherein the non-linear epitope comprises amino acid residues within domain 3 of the HER3 receptor, wherein the antibody or fragment thereof binds to a binding surface comprising at least one amino acid residue selected from binding surface A and at least one amino acid residue selected from binding surface B, and wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

6. The isolated antibody or fragment thereof of claim 5, wherein the antibody or fragment thereof blocks HER3 ligand binding on the HER3 receptor.

7. The isolated antibody or fragment thereof of claim 6, wherein the HER3 ligand is selected from the group consisting of neuregulin 1 (NRG), neuregulin 2, betacellulin, heparin-binding epidermal growth factor, and ephregrin. 8. The isolated antibody or fragment thereof of claim 5, wherein the antibody or fragment thereof has any one of the characteristics selected from the group consisting of binding to the inactive state of the HER3 receptor, preventing HER3 adopting an active conformation due to steric hindrance between the antibody or fragment thereof and domains of HER3, preventing HER3 adopting an active conformation by reducing the degree of flexibility in domain 3, inducing a conformational change in domain 3 residues 371-377 that prevents HER3 from adopting an active conformation, destabilizing HER3 such that it is susceptible to degradation, accelerating down regulation of cell surface HER3, and generating an

un-natural HER3 dimer that is susceptible to proteolytic degradation or unable to dimerize with other receptor tyrosine kinases.

9. The isolated antibody or fragment thereof of claim 5, wherein the binding surface A comprises amino acid residues 362-376.

10. The isolated antibody or fragment thereof of claim 5, wherein the binding surface B comprises amino acid residues 335-342, 398, 400, 424-428, 431, 433-434 and 455.

11. The isolated antibody of claim 5, wherein the non-linear epitope comprises amino acid residues 335-342, 362-376, 398, 400, 424-428, 431, 433-434 and 455 (within domain 3), or a subset thereof.

12. The isolated antibody of claim 5, wherein the VH of the antibody or fragment thereof binds to at least one of the following HER3 residues: Ile365, Thr366, Asn369, Gly370, Asp371, Pro372, Trp373, His374, Lys375, Gln400, and Lys434.

13. The isolated antibody of claim 5, wherein the VL of the antibody or fragment thereof binds to at least one of the following HER3 residues: Gly335, Ser336, Gly337, Ser338, Phe340, Gln341, Asp362, Leu364, Ile365, Thr366, His374, Ile376, Asn398, Gln400, Tyr424, Asn425, Arg426, Phe428, Leu431, Met433, Lys434, Tyr455.

14. The isolated antibody or fragment of claim 5, wherein binding of the antibody or fragment thereof to the HER3 receptor in the absence of a HER3 ligand reduces ligand-independent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3.

15. The isolated antibody or fragment thereof of claim 5, wherein the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by a HER3 ligand-independent phosphorylation assay.

16. The isolated antibody or fragment thereof of claim 15, wherein the HER3 ligand-independent phosphorylation assay uses HER2 amplified cells, wherein the HER2 amplified cells are SK-BR-3 cells and BT-474.

17. The isolated antibody or fragment of claim 5, wherein binding of the antibody or fragment thereof to the HER3 receptor in the presence of a HER3 ligand reduces ligand-dependent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3.

18. The isolated antibody or fragment thereof of claim 5, wherein the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by HER3 ligand-dependent phosphorylation assay.

19. The isolated antibody or fragment thereof of claim **18**, wherein the HER3 ligand-dependent phosphorylation assay uses stimulated MCF7 cells in the presence of neuregulin (NRG).

20. The isolated antibody or fragment thereof of claim **5**, wherein the antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a chimeric antibody, a humanized antibody, and a synthetic antibody.

21. An isolated antibody or fragment thereof that recognizes an epitope of a HER3 receptor, wherein the epitope comprises amino acid residues within domains 3-4 of the HER3 receptor, and wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

22. The isolated antibody of claim **21**, wherein the epitope comprises at least one amino acid residue selected from the group consisting of amino acid residues: 329-498 (domain 3) of SEQ ID NO: 1, and at least one amino acid residue selected from the group consisting of amino acid residues 499-642 (domain 4) of SEQ ID NO: 1.

23. The isolated antibody of claim **21**, wherein the epitope comprising amino acid residues within domains 3-4 is selected from the group consisting of a linear epitope, a non-linear epitope, and a conformational epitope.

24. The isolated antibody of claim **21**, wherein binding of the antibody or fragment thereof to the HER3 receptor in the absence of a HER3 ligand reduces ligand-independent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3.

25. The isolated antibody or fragment thereof of claim **21**, wherein the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by a HER3 ligand-independent phosphorylation assay.

26. The isolated antibody or fragment thereof of claim **25**, wherein the HER3 ligand-independent phosphorylation assay uses HER2 amplified cells, wherein the HER2 amplified cells are SK-Br-3 cells and BT-474.

27. The isolated antibody or fragment thereof of claim **21**, wherein binding of the antibody or fragment thereof to the HER3 receptor in the presence of a HER3 ligand reduces ligand-dependent formation of a HER2-HER3 protein complex in a cell which expresses HER2 and HER3.

28. The isolated antibody or fragment thereof of claim **21**, wherein the antibody or fragment thereof inhibits phosphorylation of HER3 as assessed by HER3 ligand-dependent phosphorylation assay.

29. The isolated antibody or fragment thereof of claim **28**, wherein the HER3 ligand-dependent phosphorylation assay uses stimulated MCF7 cells in the presence of neuregulin (NRG).

30. An isolated antibody or fragment thereof to a HER3 receptor, having a dissociation (K_D) of at least $1 \times 10^7 \text{ M}^{-1}$, 10^8 M^{-1} , 10^9 M^{-1} , 10^{10} M^{-1} , 10^{11} M^{-1} , 10^{12} M^{-1} , 10^{13} M^{-1} , wherein the antibody or fragment thereof blocks both ligand-dependent and ligand-independent signal transduction.

31. The isolated antibody or fragment thereof of claim **30**, wherein the antibody or fragment thereof inhibits phosphorylation of HER3 as measured by an in vitro phosphorylation assay selected from the group consisting of phospho-HER3 and phospho-Akt.

32. The isolated antibody or fragment thereof of claim **30**, wherein the antibody or fragment thereof binds to the same non-linear epitope within domain 3 of HER3 as an antibody described in Table 1.

33. The isolated antibody or fragment thereof of claim **30**, wherein the antibody or fragment thereof, binds to the same amino acid residues within domains 3-4 of HER3 as an antibody described in Table 2.

34. A fragment of an antibody that binds to HER3 selected from the group consisting of; Fab, $F(ab)_2$, $F(ab)_2'$, scFv, VHH, VH, VL, dAbs, wherein the fragment of the antibody blocks both ligand-dependent and ligand-independent signal transduction.

35. A pharmaceutical composition comprising an antibody or fragment thereof and a pharmaceutically acceptable carrier.

36. The pharmaceutical composition of claim **35**, further comprising an additional therapeutic agent.

37. The pharmaceutical composition of claim **36**, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

38. The pharmaceutical composition of claim **37**, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix®/Panitumumab, mAb 806, Nimotuzumab, Iressa®/Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb®/Lapatinib Ditosylate, Tarceva®/Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate/Tykerb®; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203 (Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

39. The pharmaceutical composition of claim **37**, wherein the additional therapeutic agent is a HER3 inhibitor, wherein the HER3 inhibitor is MOR10703.

40. The pharmaceutical composition of claim **37**, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus/Deforolimus, AP23573, MK8669, everolimus/Affinitor®.

41. The pharmaceutical composition of claim **37**, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BKM120 and BYL719.

42. A method of treating a cancer comprising selecting a subject having an HER3 expressing cancer, administering to the subject an effective amount of a composition comprising an antibody or fragment thereof disclosed in Table 1 or Table 2.

43. The method of claim **42**, wherein the subject is a human and the cancer is selected from the group consisting of breast cancer, colorectal cancer, lung cancer, multiple myeloma, ovarian cancer, liver cancer, gastric cancer, acute myeloid leukemia, chronic myeloid leukemia, osteosarcoma, squamous cell carcinoma, peripheral nerve sheath tumors, schwannoma, head and neck cancer, bladder cancer, esophageal cancer, Barretts esophageal cancer, glioblastoma, clear cell sarcoma of soft tissue, malignant mesothelioma, neurofibromatosis, renal cancer, and melanoma, prostate cancer, benign prostatic hyperplasia (BPH), gynaecomastia, and endometriosis.