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Anti-CD3 antibodies, bispecific antigen-binding molecules that bind CD3 and CD20, and uses thereof

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(54) Title: ANTI-CD3 ANTIBODIES, BISPECIFIC ANTIGEN-BINDING MOLECULES THAT BIND CD3 AND CD20, AND USES THEREOF

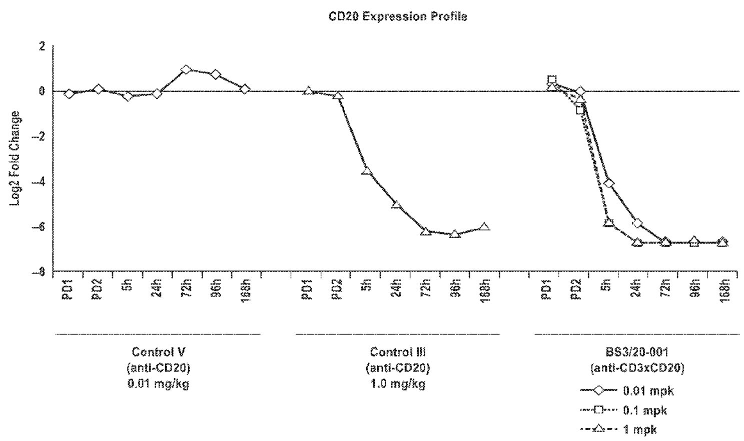

FIG. 6

(57) **Abstract**: The present invention provides antibodies that bind to CD3 and methods of using the same. According to certain embodiments, the antibodies of the invention bind human CD3 with high affinity and induce human T cell proliferation. The invention includes antibodies that bind CD3 and induce T cell-mediated killing of tumor cells. According to certain embodiments, the present invention provides bispecific antigen-binding molecules comprising a first antigen-binding domain that specifically binds human CD3, and a second antigen-binding molecule that specifically binds human CD20. In certain embodiments, the bispecific antigen-binding molecules of the present invention are capable of inhibiting the growth of B-cell tumors expressing CD20. The antibodies and bispecific antigen-binding molecules of the invention are useful for the treatment of diseases and disorders in which an up-regulated or induced targeted immune response is desired and/or therapeutically beneficial. For example, the antibodies of the invention are useful for the treatment of various cancers as well as other CD20-related diseases and disorders.

WO 2014/047231 A1

ANTI-CD3 ANTIBODIES, BISPECIFIC ANTIGEN-BINDING MOLECULES THAT BIND CD3 AND CD20, AND USES THEREOF

FIELD OF THE INVENTION

[0001] The present invention relates to antibodies, and antigen-binding fragments thereof, which are specific for CD3, and methods of use thereof. The present invention also relates to bispecific antigen-binding molecules that bind CD3 and a target molecule such as CD20, and methods of use thereof.

BACKGROUND

[0002] CD3 is a homodimeric or heterodimeric antigen expressed on T cells in association with the T cell receptor complex (TCR) and is required for T cell activation. Functional CD3 is formed from the dimeric association of two of four different chains: epsilon, zeta, delta and gamma. The CD3 dimeric arrangements include gamma/epsilon, delta/epsilon and zeta/zeta. Antibodies against CD3 have been shown to cluster CD3 on T cells, thereby causing T cell activation in a manner similar to the engagement of the TCR by peptide-loaded MHC molecules. Thus, anti-CD3 antibodies have been proposed for therapeutic purposes involving the activation of T cells. In addition, bispecific antibodies that are capable of binding CD3 and a target antigen have been proposed for therapeutic uses involving targeting T cell immune responses to tissues and cells expressing the target antigen.

[0003] CD20 is a non-glycosylated phosphoprotein expressed on the cell membranes of mature B cells. CD20 is considered a B cell tumor-associated antigen because it is expressed by more than 95% of B-cell non-Hodgkin lymphomas (NHLs) and other B-cell malignancies, but it is absent on precursor B-cells, dendritic cells and plasma cells. Methods for treating cancer by targeting CD20 are known in the art. For example, the chimeric anti-CD20 monoclonal antibody rituximab has been used or suggested for use in treating cancers such as NHL, chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). CD20 is believed to kill CD20-expressing tumor cells by complement dependent cytotoxicity (CDC), antibody-dependent cell mediated cytotoxicity (ADCC) and/or induction of apoptosis and sensitization to chemotherapy. Although anti-CD20 tumor targeting strategies have shown great promise in clinical settings, not all patients respond to anti-CD20 therapy, and some patients have been shown to develop resistance to or exhibit incomplete responses to anti-CD20 therapy (*e.g.*, resistance to rituximab).

[0004] Bispecific antigen-binding molecules that bind both CD3 and a target antigen (such as CD20) would be useful in therapeutic settings in which specific targeting and T cell-mediated killing of cells that express the target antigen is desired.

BRIEF SUMMARY OF THE INVENTION

[0005] In a first aspect, the present invention provides antibodies and antigen-binding fragments thereof that bind human CD3. The antibodies according to this aspect of the invention are useful, *inter alia*, for targeting T cells expressing CD3, and for stimulating T cell activation, *e.g.*, under circumstances where T cell-mediated killing is beneficial or desirable. The anti-CD3 antibodies of the invention, or antigen-binding portions thereof, may be included as part of a bispecific antibody that directs CD3-mediated T cell activation to specific cell types such as tumor cells or infectious agents.

[0006] Exemplary anti-CD3 antibodies of the present invention are listed in Tables 1 and 2 herein. Table 1 sets forth the amino acid sequence identifiers of the heavy chain variable regions (HCVRs) and light chain variable regions (LCVRs), as well as heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3), and light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) of the exemplary anti-CD3 antibodies. Table 2 sets forth the sequence identifiers of the nucleic acid molecules encoding the HCVRs, LCVRs, HCDR1, HCDR2 HCDR3, LCDR1, LCDR2 and LCDR3 of the exemplary anti-CD3 antibodies.

[0007] The present invention provides antibodies, or antigen-binding fragments thereof, comprising an HCVR comprising an amino acid sequence selected from any of the HCVR amino acid sequences listed in Table 1, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0008] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising an LCVR comprising an amino acid sequence selected from any of the LCVR amino acid sequences listed in Table 1, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0009] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising an HCVR and an LCVR amino acid sequence pair (HCVR/LCVR) comprising any of the HCVR amino acid sequences listed in Table 1 paired with any of the LCVR amino acid sequences listed in Table 1. According to certain embodiments, the present invention provides antibodies, or antigen-binding fragments thereof, comprising an HCVR/LCVR amino acid sequence pair contained within any of the exemplary anti-CD3 antibodies listed in Table 1. In certain embodiments, the HCVR/LCVR amino acid sequence pair is selected from the group consisting of SEQ ID NOs: 2/10 (*e.g.*, H1H2712N); 114/122 (*e.g.*, H2M2609N); 514/522 (*e.g.*, H2M3563N); 770/778 (*e.g.*, H1H5778P); 1050/1234 (*e.g.*, H1H7195B); and 1090/1234 (*e.g.*, H1H7208B).

[0010] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a heavy chain CDR1 (HCDR1) comprising an amino acid sequence selected from any of the HCDR1 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0011] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a heavy chain CDR2 (HCDR2) comprising an amino acid sequence selected from any of the HCDR2 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0012] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a heavy chain CDR3 (HCDR3) comprising an amino acid sequence selected from any of the HCDR3 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0013] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a light chain CDR1 (LCDR1) comprising an amino acid sequence selected from any of the LCDR1 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0014] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a light chain CDR2 (LCDR2) comprising an amino acid sequence selected from any of the LCDR2 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0015] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a light chain CDR3 (LCDR3) comprising an amino acid sequence selected from any of the LCDR3 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0016] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising an HCDR3 and an LCDR3 amino acid sequence pair (HCDR3/LCDR3) comprising any of the HCDR3 amino acid sequences listed in Table 1 paired with any of the LCDR3 amino acid sequences listed in Table 1. According to certain embodiments, the present invention provides antibodies, or antigen-binding fragments thereof, comprising an HCDR3/LCDR3 amino acid sequence pair contained within any of the exemplary anti-CD3 antibodies listed in Table 1. In certain embodiments, the HCDR3/LCDR3 amino acid sequence pair is selected from the group consisting of SEQ ID NOs: 8/16 (*e.g.*, H1H2712N); 120/128 (*e.g.*, H2M2609N); 520/528 (*e.g.*, H2M3563N); 776/784 (*e.g.*, H1H5778P); 1056/1240 (*e.g.*, H1H7195B); and 1096/1240 (*e.g.*, H1H7208B).

[0017] The present invention also provides antibodies, or antigen-binding fragments thereof, comprising a set of six CDRs (*i.e.*, HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3) contained within any of the exemplary anti-CD3 antibodies listed in Table 1. In certain embodiments, the HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 amino acid sequences set is selected from the group consisting of SEQ ID NOs: 4-6-8-12-14-16 (*e.g.*, H1H2712N); 116-118-120-124-126-128 (*e.g.*, H2M2609N); 516-518-520-524-526-528 (*e.g.*, H2M3563N); 772-774-776-780-782-784 (*e.g.*, H1H5778P); 1052-1054-1056-1236-1238-1240 (*e.g.*, H1H7195B); and 1092-1094-1096-1236-1238-1240 (*e.g.*, H1H7208B).

[0018] In a related embodiment, the present invention provides antibodies, or antigen-binding fragments thereof, comprising a set of six CDRs (*i.e.*, HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-

LCDR3) contained within an HCVR/LCVR amino acid sequence pair as defined by any of the exemplary anti-CD3 antibodies listed in Table 1. For example, the present invention includes antibodies, or antigen-binding fragments thereof, comprising the HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 amino acid sequences set contained within an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10 (*e.g.*, H1H2712N); 114/122 (*e.g.*, H2M2609N); 514/522 (*e.g.*, H2M3563N); 770/778 (*e.g.*, H1H5778P); 1050/1234 (*e.g.*, H1H7195B); and 1090/1234 (*e.g.*, H1H7208B). Methods and techniques for identifying CDRs within HCVR and LCVR amino acid sequences are well known in the art and can be used to identify CDRs within the specified HCVR and/or LCVR amino acid sequences disclosed herein. Exemplary conventions that can be used to identify the boundaries of CDRs include, *e.g.*, the Kabat definition, the Chothia definition, and the AbM definition. In general terms, the Kabat definition is based on sequence variability, the Chothia definition is based on the location of the structural loop regions, and the AbM definition is a compromise between the Kabat and Chothia approaches. *See*, *e.g.*, Kabat, "Sequences of Proteins of Immunological Interest," National Institutes of Health, Bethesda, Md. (1991); Al-Lazikani *et al.*, *J. Mol. Biol. 273*:927-948 (1997); and Martin *et al.*, *Proc. Natl. Acad. Sci. USA 86*:9268-9272 (1989). Public databases are also available for identifying CDR sequences within an antibody.

[0018a] In one embodiment, there is provided an isolated human antibody or antigen-binding fragment thereof that binds human CD3 with a binding dissociation equilibrium constant (K_D) of less than 2 nM as measured in a surface plasmon resonance assay at 25ºC in an antigen-capture format, wherein the antibody or antigen-binding fragment comprises six complementarity determining regions (CDRs) within a heavy chain variable region (HCVR)/light chain variable region (LCVR) amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346, 354/362, 386/394, 402/410, 418/426, 434/442, 466/474, 482/490, 514/522, 594/602, 610/618, 626/634, 722/730, 770/778, 786/794, 802/810, 850/858, 882/890, 898/906, 930/938, 946/954, 1042/1234, 1050/1234, 1066/1234, 1074/1234, 1098/1234, 1106/1234, 1114/1234, 1122/1234, 1138/1234, 1146/1234, 1162/1234, and 1178/1234, and

wherein the CDRs are identified by the Kabat definition, the Chothia definition or the AbM definition

[0019] The present invention also provides nucleic acid molecules encoding anti-CD3 antibodies or portions thereof. For example, the present invention provides nucleic acid molecules encoding any of the HCVR amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCVR nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0020] The present invention also provides nucleic acid molecules encoding any of the LCVR amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCVR nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0021] The present invention also provides nucleic acid molecules encoding any of the HCDR1 amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCDR1 nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0022] The present invention also provides nucleic acid molecules encoding any of the HCDR2 amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCDR2 nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at

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least 95%, at least 98% or at least 99% sequence identity thereto.

[0023] The present invention also provides nucleic acid molecules encoding any of the HCDR3 amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCDR3 nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0024] The present invention also provides nucleic acid molecules encoding any of the LCDR1 amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCDR1 nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0025] The present invention also provides nucleic acid molecules encoding any of the LCDR2 amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCDR2 nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0026] The present invention also provides nucleic acid molecules encoding any of the LCDR3 amino acid sequences listed in Table 1; in certain embodiments the nucleic acid molecule comprises a polynucleotide sequence selected from any of the LCDR3 nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

[0027] The present invention also provides nucleic acid molecules encoding an HCVR, wherein the HCVR comprises a set of three CDRs (*i.e.*, HCDR1-HCDR2-HCDR3), wherein the HCDR1-HCDR2-HCDR3 amino acid sequence set is as defined by any of the exemplary anti-CD3 antibodies listed in Table 1.

[0028] The present invention also provides nucleic acid molecules encoding an LCVR, wherein the LCVR comprises a set of three CDRs (*i.e.*, LCDR1-LCDR2-LCDR3), wherein the LCDR1-LCDR2-LCDR3 amino acid sequence set is as defined by any of the exemplary anti-CD3 antibodies listed in Table 1.

[0029] The present invention also provides nucleic acid molecules encoding both an HCVR and an LCVR, wherein the HCVR comprises an amino acid sequence of any of the HCVR amino acid sequences listed in Table 1, and wherein the LCVR comprises an amino acid sequence of any of the LCVR amino acid sequences listed in Table 1. In certain embodiments, the nucleic acid molecule comprises a polynucleotide sequence selected from any of the HCVR nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto, and a polynucleotide sequence selected from any of the LCVR nucleic acid sequences listed in Table 2, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto. In certain embodiments according to this aspect of the invention, the nucleic acid molecule encodes an HCVR and LCVR, wherein the HCVR and LCVR are both derived from the same anti-CD3 antibody listed in Table 1.

[0030] The present invention also provides recombinant expression vectors capable of expressing a polypeptide comprising a heavy or light chain variable region of an anti-CD3 antibody. For example, the present invention includes recombinant expression vectors comprising any of the nucleic acid molecules mentioned above, *i.e.*, nucleic acid molecules encoding any of the HCVR, LCVR, and/or CDR sequences as set forth in Table 1. Also included within the scope of the present invention are host cells into which such vectors have been introduced, as well as methods of producing the antibodies or portions thereof by culturing the host cells under conditions permitting production of the antibodies or antibody fragments, and recovering the antibodies and antibody fragments so produced.

[0031] The present invention includes anti-CD3 antibodies having a modified glycosylation pattern. In some embodiments, modification to remove undesirable glycosylation sites may be useful, or an antibody lacking a fucose moiety present on the oligosaccharide chain, for example, to increase antibody dependent cellular cytotoxicity (ADCC) function (see Shield et al. (2002) JBC 277:26733). In other applications, modification of galactosylation can be made in order to modify complement dependent cytotoxicity (CDC).

[0032] In another aspect, the invention provides a pharmaceutical composition comprising a recombinant human antibody or fragment thereof which specifically binds CD3 and a pharmaceutically acceptable carrier. In a related aspect, the invention features a composition which is a combination of an anti-CD3 antibody and a second therapeutic agent. In one embodiment, the second therapeutic agent is any agent that is advantageously combined with an anti-CD3 antibody. Exemplary agents that may be advantageously combined with an anti-CD3 antibody include, without limitation, other agents that bind and/or activate CD3 signaling (including other antibodies or antigen-binding fragments thereof, etc.) and/or agents which do not directly bind CD3 but nonetheless activate or stimulate immune cell activation. Additional combination therapies and co-formulations involving the anti-CD3 antibodies of the present invention are disclosed elsewhere herein.

[0033] In yet another aspect, the invention provides therapeutic methods for stimulating T cell activation using an anti-CD3 antibody or antigen-binding portion of an antibody of the invention, wherein the therapeutic methods comprise administering a therapeutically effective amount of a pharmaceutical composition comprising an antibody or antigen-binding fragment of an antibody of the invention to a subject in need thereof. The disorder treated is any disease or condition which is improved, ameliorated, inhibited or prevented by stimulation of CD3 activity or signaling.

[0034] According to another aspect, the present invention provides bispecific antigen-binding molecules that bind CD3 and a target antigen. According to certain exemplary embodiments, the bispecific antigen-binding molecules bind CD3 and CD20; such bispecific antigen-binding molecules are also referred to herein as "anti-CD3/anti-CD20 bispecific molecules." The anti-CD20 portion of the anti-CD3/anti-CD20 bispecific molecule is useful for targeting tumor cells that express CD20 (*e.g.*, B-cell tumors), and the anti-CD3 portion of the bispecific molecule is useful for activating T-cells. The simultaneous binding of CD20 on a tumor cell and CD3 on a T-cell facilitates directed killing (cell lysis) of the targeted tumor cell by the activated T-cell. The anti-CD3/anti-CD20 bispecific molecules of the invention are therefore useful, *inter alia*, for treating diseases and disorders related to or caused by CD20-expressing tumors (*e.g.*, lymphomas).

[0035] The bispecific antigen-binding molecules according to this aspect of the present invention comprise a first antigen-binding domain that specifically binds human CD3, and a second antigen-binding domain that specifically binds CD20. The present invention includes anti-CD3/anti-CD20 bispecific molecules (*e.g.*, bispecific antibodies) wherein each antigen-binding domain comprises a heavy chain variable region (HCVR) paired with a light chain variable region (LCVR). In certain exemplary embodiments of the invention, the anti-CD3 antigen-binding domain and the anti-CD20 antigen binding domain each comprise different, distinct HCVRs paired with a common LCVR. For example, as illustrated in Example 7 herein, bispecific antibodies were constructed comprising a first antigen-binding domain that specifically binds CD3, wherein the first antigen-binding domain comprises an HCVR/LCVR pair derived from an anti-CD3 antibody; and a second antigen-binding domain that specifically binds CD20, wherein the second antigen-binding domain comprises an HCVR derived from an anti-CD20 antibody paired with an LCVR derived from an anti-CD3 antibody (*e.g.*, the same LCVR that is included in the anti-CD3 antigen-binding domain). In other words, in the exemplary molecules disclosed herein, the pairing of an HCVR from an anti-CD20 antibody with an LCVR from an anti-CD3 antibody creates an antigen-binding domain that specifically binds CD20 (but does not bind CD3). In such embodiments, the first and second antigen-binding domains comprise distinct anti-CD3 and anti-CD20 HCVRs but share a common anti-CD3 LCVR.

[0036] The present invention provides anti-CD3/anti-CD20 bispecific molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises any of the HCVR amino acid sequences as set forth in Table 1 or Table 18. The first antigen-binding domain that specifically binds CD3 may also comprise any of the LCVR amino acid sequences as set forth in Table 1 or Table 19. According to certain embodiments, the first antigen-binding domain that specifically binds CD3 comprises any of the HCVR/LCVR amino acid sequence pairs as set forth in Table 1 or Table 17. The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises any of the heavy chain CDR1-CDR2-CDR3 amino acid sequences as set forth in Table 1 or Table 18, and/or any of the light chain CDR1-CDR2-CDR3 amino acid sequences as set forth in Table 1 or Table 19.

[0037] According to certain embodiments, the present invention provides anti-CD3/anti-CD20 bispecific molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises a heavy chain variable region (HCVR) having an amino acid sequence selected from the group consisting of SEQ ID NOs:1250, 1266, 1282, 1298, 1314 and 1329 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0038] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises a light chain variable region (LCVR) having an amino acid sequence selected from the group consisting of SEQ ID NOs:1258, 1274, 1290, 1306, 1322 and 1333, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0039] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises a HCVR and LCVR (HCVR/LCVR) amino acid sequence pair selected from the group consisting of SEQ ID NOs:1250/1258, 1266/1274, 1282/1290, 1298/1306, 1314/1322, and 1329/1333.

[0040] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises a heavy chain CDR3 (HCDR3) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs:1256, 1272, 1288, 1304, 1320 and 1332, or a substantially similar sequence thereto having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; and a light chain CDR3 (LCDR3) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs:1264, 1280, 1296, 1312, 1328 and 1336, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0041] In certain embodiments, the first antigen-binding domain that specifically binds CD3 comprises a HCDR3/LCDR3 amino acid sequence pair selected from the group consisting of SEQ ID NOs: 1256/1264, 1272/1280, 1288/1296, 1304/1312, 1320/1328 and 1332/1336.

[0042] The present invention also provides anti-CD3/anti-CD20 bispecific antigen-binding molecules, wherein the first antigen-binding domain that specifically binds CD3 comprises a heavy chain CDR1 (HCDR1) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs:1252, 1268, 1284, 1300, 1316 and 1330, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; a heavy chain CDR2 (HCDR2) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs:1254, 1270, 1286, 1302, 1318 and 1331, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; a light chain CDR1 (LCDR1) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs:1260, 1276, 1292, 1308, 1324 and 1334, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; and a light chain CDR2 (LCDR2) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs:1262, 1278, 1294, 1310, 1326 and

1335, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0043] Certain non-limiting, exemplary anti-CD3/anti-CD20 bispecific antigen-binding molecules of the invention include a first antigen-binding domain that specifically binds CD3 comprising HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 domains, respectively, having the amino acid sequences selected from the group consisting of: SEQ ID NOs: 1252-1254-1256-1260-1262-1264 (*e.g.* BS3/20-001); 1268-1270-1272-1276-1278-1280 (*e.g.* BS3/20-002); 1284-1286-1288-1292-1294-1296 (*e.g.* BS3/20-003); 1300-1302-1304-1308-1310-1312 (*e.g.* BS3/20-004); 1316-1318-1320-1324-1326-1328 (*e.g.* BS3-20-005); and 1330-1331-1332-1334-1335-1336 (*e.g.* BS3/20-007).

[0044] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the second antigen-binding domain that specifically binds CD20 comprises a heavy chain variable region (HCVR) having the amino acid sequence of SEQ ID NO:1242, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0045] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the second antigen-binding domain that specifically binds CD20 comprises a light chain variable region (LCVR) having the amino acid sequence selected from the group consisting of SEQ ID NOs:1258, 1274, 1290, 1306, 1322 and 1333, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0046] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the second antigen-binding domain that specifically binds CD20 comprises a HCVR and LCVR (HCVR/LCVR) amino acid sequence pair selected from the group consisting of SEQ ID NOs: 1242/1258, 1242/1274, 1242/1290, 1242/1306, 1242/1322 and 1242/1333.

[0047] The present invention also provides anti-CD3/anti-CD20 bispecific molecules, wherein the second antigen-binding domain that specifically binds CD20 comprises a heavy chain CDR3 (HCDR3) domain having the amino acid sequence of SEQ ID NO:1248, or a substantially similar sequence thereto having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; and a light chain CDR3 (LCDR3) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1264, 1280, 1296, 1312, 1328 and 1336, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0048] In certain embodiments, the second antigen-binding domain that specifically binds CD20 comprises a HCDR3/LCDR3 amino acid sequence pair selected from the group consisting of SEQ ID NOs: 1248/1264, 1248/1280, 1248/1296, 1248/1312, 1248/1328 and 1248/1336.

[0049] The present invention also provides anti-CD3/anti-CD20 bispecific antigen-binding molecules, wherein the second antigen-binding domain that specifically binds CD20 comprises a heavy chain CDR1 (HCDR1) domain having the amino acid sequence of SEQ ID NO:1244, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; a heavy chain CDR2 (HCDR2) domain having the amino acid sequence of SEQ ID NO:1246, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; a light chain CDR1 (LCDR1) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1260, 1276, 1292, 1308, 1324 and 1334, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; and a light chain CDR2 (LCDR2) domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1262, 1278, 1294, 1310, 1326 and 1335, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0050] Certain non-limiting, exemplary anti-CD3/anti-CD20 bispecific antigen-binding molecules of the invention include a second antigen-binding domain that specifically binds CD20 comprising HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 domains, respectively, having the amino acid sequences selected from the group consisting of: SEQ ID NOs: 1244-1246-1248-1260-1262-1264 (*e.g.* BS3/20-001); 1244-1246-1248-1276-1278-1280 (*e.g.* BS3/20-002); 1244-1246-1248-1292-1294-1296 (*e.g.* BS3/20-003); 1244-1246-1248-1308-1310-1312 (*e.g.* BS3/20-004); 1244-1246-1248-1324-1326-1328 (*e.g.* BS3-20-005); and 1244-1246-1248-1334-1335-1336 (*e.g.* BS3/20-007).

[0051] In a related embodiment, the invention includes anti-CD3/anti-CD20 bispecific antigen-binding molecules wherein the second antigen-binding domain that specifically binds CD20 comprises the heavy and light chain CDR domains contained within heavy and light chain variable region (HCVR/LCVR) sequences selected from the group consisting of SEQ ID NOs: 1242/1258, 1242/1274, 1242/1290, 1242/1306, 1242/1322 and 1242/1333.

[0052] In another aspect, the present invention provides nucleic acid molecules encoding any of the HCVR, LCVR or CDR sequences of the anti-CD3/anti-CD20 bispecific antigen-binding molecules disclosed herein, including nucleic acid molecules comprising the polynucleotide sequences as set forth in Tables 20 and 21 herein, as well as nucleic acid molecules comprising two or more of the polynucleotide sequences as set forth in Tables 20 and 21 in any functional combination or arrangement thereof. Recombinant expression vectors carrying the nucleic acids of the invention, and host cells into which such vectors have been introduced, are also encompassed by the invention, as are methods of producing the antibodies by culturing the host cells under conditions permitting production of the antibodies, and recovering the antibodies produced.

[0053] The present invention includes anti-CD3/anti-CD20 bispecific antigen-binding molecules wherein any of the aforementioned antigen-binding domains that specifically bind CD3 is combined, connected or otherwise associated with any of the aforementioned antigen-binding domains that specifically bind CD20 to form a bispecific antigen-binding molecule that binds CD3 and CD20.

[0054] The present invention includes anti-CD3/anti-CD20 bispecific antigen-binding molecules having a modified glycosylation pattern. In some applications, modification to remove undesirable glycosylation sites may be useful, or an antibody lacking a fucose moiety present on the oligosaccharide chain, for example, to increase antibody dependent cellular cytotoxicity (ADCC) function (see Shield et al. (2002) JBC 277:26733). In other applications, modification of galactosylation can be made in order to modify complement dependent cytotoxicity (CDC).

[0055] In another aspect, the invention provides a pharmaceutical composition comprising an anti-CD3/anti-CD20 bispecific antigen-binding molecule as disclosed herein and a pharmaceutically acceptable carrier. In a related aspect, the invention features a composition which is a combination of an anti-CD3/anti-CD20 bispecific antigen-binding molecule and a second therapeutic agent. In one embodiment, the second therapeutic agent is any agent that is advantageously combined with an anti-CD3/anti-CD20 bispecific antigen-binding molecule. Exemplary agents that may be advantageously combined with an anti-CD3/anti-CD20 bispecific antigen-binding molecule are discussed in detail elsewhere herein.

[0056] In yet another aspect, the invention provides therapeutic methods for targeting/killing tumor cells expressing CD20 using an anti-CD3/anti-CD20 bispecific antigen-binding molecule of the invention, wherein the therapeutic methods comprise administering a therapeutically effective amount of a pharmaceutical composition comprising an anti-CD3/anti-CD20 bispecific antigen-binding molecule of the invention to a subject in need thereof.

[0057] The present invention also includes the use of an anti-CD3/anti-CD20 bispecific antigen-binding molecule of the invention in the manufacture of a medicament for the treatment of a disease or disorder related to or caused by CD20 expression.

[0058] Other embodiments will become apparent from a review of the ensuing detailed description.

BRIEF DESCRIPTION OF THE FIGURES

[0059] **Figure 1** shows the tumor volume (in mm^3) over time in NOD/SCID mice implanted subcutaneously with a mixture of Raji tumor cells and PBMCs following tumor implantation and treatment, starting the day of tumor implantation, with either human Fc (hFc, solid line) or CD3xCD20 bispecific antibody (BS3/20-007, dashed line).

[0060] **Figure 2** shows the tumor volume (in mm^3) over time in NOD/SCID mice implanted subcutaneously with a mixture of Raji tumor cells and PBMCs following tumor implantation and treatment, starting 7 days after tumor implantation, with either human Fc (hFc, solid line) or CD3xCD20 bispecific antibody (BS3/20-007, dashed line).

[0061] **Figure 3** shows a plot of B-cell numbers (x1000/µL) over time in blood samples from cynomolgus monkeys treated with three different doses of bispecific antibody BS3/20-001 (0.01, 0.1 or 1.0 mg/kg); low-dose anti-CD20 control antibody (Control V, 0.01 mg/kg); or high-dose anti-CD20 control antibody (Control III (1.0 mg/kg).

[0062] **Figure 4** shows a plot of T-cell numbers (x1000/μL) over time in blood samples from cynomolgus monkeys treated with three different doses of bispecific antibody BS3/20-001 (0.01, 0.1 or 1.0 mg/kg); low-dose anti-CD20 control antibody (Control V, 0.01 mg/kg); or high-dose anti-CD20 control antibody (Control III (1.0 mg/kg).

[0063] **Figures 5A, 5B, 5C** and **5D** show the pre-dose and post-dose levels (pg/mL) of IFN-gamma, IL-2, IL-6, and TNF-alpha, respectively, for cynomolgous monkeys treated with a single dose of BS3/20-001 (0.01, 0.1 or 1.0 mg/kg), low dose anti-CD20 control antibody (0.01 mg/kg Control V), or high-dose anti-CD20 control antibody (1.0 mg/kg Control III).

[0064] **Figure 6** shows the CD20 expression profile (expressed in terms of Log2 fold change in expression) determined from blood samples taken at various time points from cynomolgus monkeys treated with 0.01 mg/kg Control V (anti-CD20 antibody); 1.0 mg/kg Control III (anti-CD20 antibody); and 0.01 mg/kg, 0.1 mg/kg and 1.0 mg/kg BS3/20-001 (anti-CD3xCD20 bispecific antibody).

[0065] **Figure 7** shows the total serum concentration (μg/mL) of CD3xCD20 bispecific antibody (BS3/20-001) over time in blood samples from cynomolgus monkeys treated with 1.0 mg/kg (open triangles), 0.1 mg/kg (open squares) or 0.01 mg/kg (open diamonds) of CD3xCD20 bispecific antibody.

DETAILED DESCRIPTION

[0066] Before the present invention is described, it is to be understood that this invention is not limited to particular methods and experimental conditions described, as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0067] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. As used herein, the term "about," when used in reference to a particular recited numerical value, means that the value may vary from the recited value by no more than 1%. For example, as used herein, the expression "about 100" includes 99 and 101 and all values in between (*e.g.*, 99.1, 99.2, 99.3, 99.4, etc.).

[0068] Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described.

Definitions

[0069] The expression "CD3," as used herein, refers to an antigen which is expressed on T cells as part of the multimolecular T cell receptor (TCR) and which consists of a homodimer or heterodimer formed from the association of two of four receptor chains: CD3-epsilon, CD3-delta, CD3-zeta, and CD3-gamma. Human CD3-epsilon comprises the amino acid sequence as set forth in SEQ ID NO:1370; human CD3-delta comprises the amino acid sequence as set forth in SEQ ID NO:1371. All references to proteins, polypeptides and protein fragments herein are intended to refer to the human version of the respective protein, polypeptide or protein fragment unless explicitly specified as being from a non-human species. Thus, the expression "CD3" means human CD3 unless specified as being from a non-human species, *e.g.*, "mouse CD3," "monkey CD3," etc.

[0070] As used herein, "an antibody that binds CD3" or an "anti-CD3 antibody" includes antibodies and antigen-binding fragments thereof that specifically recognize a single CD3 subunit (*e.g.*, epsilon, delta, gamma or zeta), as well as antibodies and antigen-binding fragments thereof that specifically recognize a dimeric complex of two CD3 subunits (*e.g.*, gamma/epsilon, delta/epsilon, and zeta/zeta CD3 dimers). The antibodies and antigen-binding fragments of the present invention may bind soluble CD3 and/or cell surface expressed CD3. Soluble CD3 includes natural CD3 proteins as well as recombinant CD3 protein variants such as, *e.g.*, monomeric and dimeric CD3 constructs, that lack a transmembrane domain or are otherwise unassociated with a cell membrane.

[0071] As used herein, the expression "cell surface-expressed CD3" means one or more CD3 protein(s) that is/are expressed on the surface of a cell *in vitro* or *in vivo*, such that at least a portion of a CD3 protein is exposed to the extracellular side of the cell membrane and is accessible to an antigen-binding portion of an antibody. "Cell surface-expressed CD3" includes CD3 proteins contained within the context of a functional T cell receptor in the membrane of a cell. The expression "cell surface-expressed CD3" includes CD3 protein expressed as part of a homodimer or heterodimer on the surface of a cell (*e.g.*, gamma/epsilon, delta/epsilon, and zeta/zeta CD3 dimers). The expression, "cell surface-expressed CD3" also includes a CD3 chain (*e.g.*, CD3-epsilon, CD3-delta or CD3-gamma) that is expressed by itself, without other CD3 chain types, on the surface of a cell. A "cell surface-expressed CD3" can comprise or consist of a CD3 protein expressed on the surface of a cell which normally expresses CD3 protein. Alternatively, "cell surface-expressed CD3" can comprise or consist of CD3 protein expressed on the surface of a cell that normally does not express human CD3 on its surface but has been artificially engineered to express CD3 on its surface.

[0072] As used herein, the expression "anti-CD3 antibody" includes both monovalent antibodies with a single specificity, as well as bispecific antibodies comprising a first arm that binds CD3 and a second arm that binds a second (target) antigen, wherein the anti-CD3 arm comprises any of the HCVR/LCVR or CDR sequences as set forth in Table 1 or Tables 18/19 herein. Examples of anti-CD3 bispecific antibodies are described elsewhere herein. The term "antigen-binding molecule" includes antibodies and antigen-binding fragments of antibodies, including, *e.g.*, bispecific antibodies.

[0073] The term "antibody", as used herein, means any antigen-binding molecule or molecular complex comprising at least one complementarity determining region (CDR) that specifically binds to or interacts with a particular antigen (*e.g.*, CD3). The term "antibody" includes immunoglobulin molecules comprising four polypeptide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, as well as multimers thereof (*e.g.*, IgM). Each heavy chain comprises a heavy chain variable region (abbreviated herein as HCVR or V_H) and a heavy chain constant region. The heavy chain constant region comprises three domains, C_H1, C_H2 and C_H3. Each light chain comprises a light chain variable region (abbreviated herein as LCVR or V_L) and a light chain constant region. The light chain constant region comprises one domain (C_L1). The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FR). Each V_H and V_L 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. In different embodiments of the invention, the FRs of the anti-CD3 antibody (or antigen-binding portion thereof) may be identical to the human germline sequences, or may be naturally or artificially modified. An amino acid consensus sequence may be defined based on a side-by-side analysis of two or more CDRs.

[0074] The term "antibody", as used herein, also includes antigen-binding fragments of full antibody molecules. The terms "antigen-binding portion" of an antibody, "antigen-binding fragment" of an antibody, and the like, as used herein, include any naturally occurring, enzymatically obtainable, synthetic, or genetically engineered polypeptide or glycoprotein that specifically binds an antigen to form a complex. Antigen-binding fragments of an antibody may be derived, *e.g.*, from full antibody molecules using any suitable standard techniques such as proteolytic digestion or recombinant genetic engineering techniques involving the manipulation and expression of DNA encoding antibody variable and optionally constant domains. Such DNA is known and/or is readily available from, *e.g.*, commercial sources, DNA libraries (including, *e.g.*, phage-antibody libraries), or can be synthesized. The DNA may be sequenced and manipulated chemically or by using molecular biology techniques, for example, to arrange one or more variable and/or constant domains into a suitable configuration, or to introduce codons, create cysteine residues, modify, add or delete amino acids, etc.

[0075] Non-limiting examples of antigen-binding fragments include: (i) Fab fragments; (ii) F(ab')2 fragments; (iii) Fd fragments; (iv) Fv fragments; (v) single-chain Fv (scFv) molecules; (vi) dAb fragments; and (vii) minimal recognition units consisting of the amino acid residues that mimic the hypervariable region of an antibody (*e.g.*, an isolated complementarity determining region (CDR) such as a CDR3 peptide), or a constrained FR3-CDR3-FR4 peptide. Other engineered molecules, such as domain-specific antibodies, single domain antibodies, domain-deleted antibodies, chimeric antibodies, CDR-grafted antibodies, diabodies, triabodies, tetrabodies, minibodies, nanobodies (*e.g.* monovalent nanobodies, bivalent nanobodies, etc.), small modular immunopharmaceuticals (SMIPs), and shark variable IgNAR domains, are also encompassed within the expression "antigen-binding fragment," as used herein.

[0076] An antigen-binding fragment of an antibody will typically comprise at least one variable domain. The variable domain may be of any size or amino acid composition and will generally comprise at least one CDR which is adjacent to or in frame with one or more framework sequences. In antigen-binding fragments having a V_H domain associated with a V_L domain, the V_H and V_L domains may be situated relative to one another in any suitable arrangement. For example, the variable region may be dimeric and contain V_H-V_H, V_H-V_L or V_L-V_L dimers. Alternatively, the antigen-binding fragment of an antibody may contain a monomeric V_H or V_L domain.

[0077] In certain embodiments, an antigen-binding fragment of an antibody may contain at least one variable domain covalently linked to at least one constant domain. Non-limiting, exemplary configurations of variable and constant domains that may be found within an antigen-binding fragment of an antibody of the present invention include: (i) V_H-C_H1; (ii) V_H-C_H2; (iii) V_H-C_H3; (iv) V_H-C_H1-C_H2; (v) V_H-C_H1-C_H2-C_H3; (vi) V_H-C_H2-C_H3; (vii) V_H-C_L; (viii) V_L-C_H1; (ix) V_L-C_H2; (x) V_L-C_H3; (xi) V_L-C_H1-C_H2; (xii) V_L-C_H1-C_H2-C_H3; (xiii) V_L-C_H2-C_H3; and (xiv) V_L-C_L. In any configuration of variable and constant domains, including any of the exemplary configurations listed above, the variable and constant domains may be either directly linked to one another or may be linked by a full or partial hinge or linker region. A hinge region may consist of at least 2 (*e.g.*, 5, 10, 15, 20, 40, 60 or more) amino acids which result in a flexible or semi-flexible linkage between adjacent variable and/or constant domains in a single polypeptide molecule. Moreover, an antigen-binding fragment of an antibody of the present invention may comprise a homo-dimer or hetero-dimer (or other multimer) of any of the variable and constant domain configurations listed above in non-covalent association with one another and/or with one or more monomeric V_H or V_L domain (*e.g.*, by disulfide bond(s)).

[0078] As with full antibody molecules, antigen-binding fragments may be monospecific or multispecific (*e.g.*, bispecific). A multispecific antigen-binding fragment of an antibody will typically comprise at least two different variable domains, wherein each variable domain is capable of specifically binding to a separate antigen or to a different epitope on the same antigen. Any multispecific antibody format, including the exemplary bispecific antibody formats disclosed herein, may be adapted for use in the context of an antigen-binding fragment of an antibody of the present invention using routine techniques available in the art.

[0079] The antibodies of the present invention may function through complement-dependent cytotoxicity (CDC) or antibody-dependent cell-mediated cytotoxicity (ADCC). "Complement-dependent cytotoxicity" (CDC) refers to lysis of antigen-expressing cells by an antibody of the invention in the presence of complement. "Antibody-dependent cell-mediated cytotoxicity" (ADCC) refers to a cell-mediated reaction in which nonspecific cytotoxic cells that express Fc receptors (FcRs) (*e.g.*, Natural Killer (NK) cells, neutrophils, and macrophages) recognize bound antibody on a target cell and thereby lead to lysis of the target cell. CDC and ADCC can be measured using assays that are well known and available in the art. (*See*, *e.g.*, U.S. Patent Nos 5,500,362 and 5,821,337, and Clynes *et al.* (1998) Proc. Natl. Acad. Sci. (USA) *95*:652-656). The constant region of an antibody is important in the ability of an antibody to fix complement and mediate cell-dependent cytotoxicity. Thus, the isotype of an antibody may be selected on the basis of whether it is desirable for the antibody to mediate cytotoxicity.

[0080] In certain embodiments of the invention, the anti-CD3 antibodies of the invention (monospecific or bispecific) are human antibodies. The term "human antibody", as used herein, is intended to include antibodies having variable and constant regions derived from human germline immunoglobulin sequences. The human antibodies of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*), for example in the CDRs and in particular CDR3. However, the term "human antibody", as used herein, is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

[0081] The antibodies of the invention may, in some embodiments, be recombinant human antibodies. The term "recombinant human antibody", as used herein, is intended to include all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as antibodies expressed using a recombinant expression vector transfected into a host cell (described further below), antibodies isolated from a recombinant, combinatorial human antibody library (described further below), antibodies isolated from an animal (e.g., a mouse) that is transgenic for human immunoglobulin genes (see e.g., Taylor et al. (1992) Nucl. Acids Res. 20:6287-6295) or antibodies prepared, expressed, created or isolated by any other means that involves splicing of human immunoglobulin gene sequences to other DNA sequences. Such recombinant human antibodies have variable and constant regions derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies are 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*.

[0082] Human antibodies can exist in two forms that are associated with hinge heterogeneity. In one form, an immunoglobulin molecule comprises a stable four chain construct of approximately 150-160 kDa in which the dimers are held together by an interchain heavy chain disulfide bond. In a second form, the dimers are not linked via inter-chain disulfide bonds and a molecule of about 75-80 kDa is formed composed of a covalently coupled light and heavy chain (half-antibody). These forms have been extremely difficult to separate, even after affinity purification.

[0083] The frequency of appearance of the second form in various intact IgG isotypes is due to, but not limited to, structural differences associated with the hinge region isotype of the antibody. A single amino acid substitution in the hinge region of the human IgG4 hinge can significantly reduce the appearance of the second form (Angal et al. (1993) Molecular Immunology 30:105) to levels typically observed using a human IgG1 hinge. The instant invention encompasses antibodies having one or more mutations in the hinge, C_H2 or C_H3 region which may be desirable, for example, in production, to improve the yield of the desired antibody form.

[0084] The antibodies of the invention may be isolated antibodies. An "isolated antibody," as used herein, means an antibody that has been identified and separated and/or recovered from at least one component of its natural environment. For example, an antibody that has been separated or removed from at least one component of an organism, or from a tissue or cell in which the antibody naturally exists or is naturally produced, is an "isolated antibody" for purposes of the present invention. An isolated antibody also includes an antibody *in situ* within a recombinant cell. Isolated antibodies are antibodies that have been subjected to at least one purification or isolation step. According to certain embodiments, an isolated antibody may be substantially free of other cellular material and/or chemicals.

[0085] The present invention also includes one-arm antibodies that bind CD3. As used herein, a "one-arm antibody" means an antigen-binding molecule comprising a single antibody heavy chain and a single antibody light chain. The one-arm antibodies of the present invention may comprise any of the HCVR/LCVR or CDR amino acid sequences as set forth in Table 1 or Tables 18/19 herein.

[0086] The anti-CD3 antibodies disclosed herein may comprise one or more amino acid substitutions, insertions and/or deletions in the framework and/or CDR regions of the heavy and light chain variable domains as compared to the corresponding germline sequences from which the antibodies were derived. Such mutations can be readily ascertained by comparing the amino acid sequences disclosed herein to germline sequences available from, for example, public antibody sequence databases. The present invention includes antibodies, and antigen-binding fragments thereof, which are derived from any of the amino acid sequences disclosed herein, wherein one or more amino acids within one or more framework and/or CDR regions are mutated to the corresponding residue(s) of the germline sequence from which the antibody was derived, or to the corresponding residue(s) of another human germline sequence, or to a conservative amino acid substitution of the corresponding germline residue(s) (such sequence changes are referred to herein collectively as "germline mutations"). A person of ordinary skill in the art, starting with the heavy and light chain variable region sequences disclosed herein, can easily produce numerous antibodies and antigen-binding fragments which comprise one or more individual germline mutations or combinations thereof. In certain embodiments, all of the framework and/or CDR residues within the V_H and/or V_L domains are mutated back to the residues found in the original germline sequence from which the antibody was derived. In other embodiments, only certain residues are mutated back to the original germline sequence, *e.g.*, only the mutated residues found within the first 8 amino acids of FR1 or within the last 8 amino acids of FR4, or only the mutated residues found within CDR1, CDR2 or CDR3. In other embodiments, one or more of the framework and/or CDR residue(s) are mutated to the corresponding residue(s) of a different germline sequence (*i.e.*, a germline sequence that is different from the germline sequence from which the antibody was originally derived). Furthermore, the antibodies of the present invention may contain any combination of two or more germline mutations within the framework and/or CDR regions, *e.g.*, wherein certain individual residues are mutated to the corresponding residue of a particular germline sequence while certain other residues that differ from the original germline sequence are maintained or are mutated to the corresponding residue of a different germline sequence. Once obtained, antibodies and antigen-binding fragments that contain one or more germline mutations can be easily tested for one or more desired property such as, improved binding specificity, increased binding affinity, improved or enhanced antagonistic or agonistic biological properties (as the case may be), reduced immunogenicity, etc. Antibodies and antigen-binding fragments obtained in this general manner are encompassed within the present invention.

[0087] The present invention also includes anti-CD3 antibodies comprising variants of any of the HCVR, LCVR, and/or CDR amino acid sequences disclosed herein having one or more conservative substitutions. For example, the present invention includes anti-CD3 antibodies having HCVR, LCVR, and/or CDR amino acid sequences with, *e.g.*, 10 or fewer, 8 or fewer, 6 or fewer, 4 or fewer, etc. conservative amino acid substitutions relative to any of the HCVR, LCVR, and/or CDR amino acid sequences set forth in Table 1 herein.

[0088] The term "epitope" refers to an antigenic determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. A single antigen may have more than one epitope. Thus, different antibodies may bind to different areas on an antigen and may have different biological effects. Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. In certain circumstance, an epitope may include moieties of saccharides, phosphoryl groups, or sulfonyl groups on the antigen.

[0089] The term "substantial identity" or "substantially identical," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 95%, and more preferably at least about 96%, 97%, 98% or 99% of the nucleotide bases, as measured by any well-known algorithm of sequence identity, such as FASTA, BLAST or Gap, as discussed below. A nucleic acid molecule having substantial identity to a reference nucleic acid molecule may, in certain instances, encode a polypeptide having the same or substantially similar amino acid sequence as the polypeptide encoded by the reference nucleic acid molecule.

[0090] As applied to polypeptides, the term "substantial similarity" or "substantially similar" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 95% sequence identity, even more preferably at least 98% or 99% sequence identity. Preferably, residue positions which are not identical differ by conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well-known to those of skill in the art. *See, e.g.*, Pearson (1994) Methods Mol. Biol. 24: 307-331. Examples of groups of amino acids that have side chains with similar chemical properties include (1) aliphatic side chains: glycine, alanine, valine, leucine and isoleucine; (2) aliphatic-hydroxyl side chains: serine and threonine; (3) amide-containing side chains: asparagine and glutamine; (4) aromatic side chains: phenylalanine, tyrosine, and tryptophan; (5) basic side chains: lysine, arginine, and histidine; (6) acidic side chains: aspartate and glutamate, and (7) sulfur-containing side chains are cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamate-aspartate, and asparagine-glutamine. Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet *et al.* (1992) Science 256: 1443-1445. A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

[0091] Sequence similarity for polypeptides, which is also referred to as sequence identity, is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG software contains programs such as Gap and Bestfit which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild type protein and a mutein thereof. *See, e.g.*, GCG Version 6.1. Polypeptide sequences also can be compared using FASTA using default or recommended parameters, a program in GCG Version 6.1. FASTA (e.g., FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (2000) supra). Another preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially BLASTP or TBLASTN, using default parameters. *See, e.g.*, Altschul *et al.* (1990) J. Mol. Biol. 215:403-410 and Altschul *et al.* (1997) Nucleic Acids Res. 25:3389-402.

Bispecific Antigen-Binding Molecules

[0092] The antibodies of the present invention may be monospecific, bi-specific, or multispecific. Multispecific antibodies may be specific for different epitopes of one target polypeptide or may contain antigen-binding domains specific for more than one target polypeptide. See, e.g., Tutt et al., 1991, J. Immunol. 147:60-69; Kufer *et al.*, 2004, Trends Biotechnol. 22:238-244. The anti-CD3 antibodies of the present invention can be linked to or co-expressed with another functional molecule, e.g., another peptide or protein. For example, an antibody or fragment thereof can be functionally linked (e.g., by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody or antibody fragment to produce a bi-specific or a multispecific antibody with a second binding specificity.

[0093] Use of the expression "anti-CD3 antibody" herein is intended to include both monospecific anti-CD3 antibodies as well as bispecific antibodies comprising a CD3-binding arm and a second arm that binds a target antigen. Thus, the present invention includes bispecific antibodies wherein one arm of an immunoglobulin binds human CD3, and the other arm of the immunoglobulin is specific for a target antigen. The target antigen that the other arm of the CD3 bispecific antibody binds can be any antigen expressed on or in the vicinity of a cell, tissue, organ, microorganism or virus, against which a targeted immune response is desired. The CD3-binding arm can comprise any of the HCVR/LCVR or CDR amino acid sequences as set forth in Table 1 or Tables 18/19 herein. In certain embodiments, the CD3-binding arm binds human CD3 and induces human T cell proliferation.

[0094] In the context of bispecific antibodies of the present invention wherein one arm of the antibody binds CD3 and the other arm binds a target antigen, the target antigen can be a tumor-associated antigen. Non-limiting examples of specific tumor-associated antigens include, *e.g.*, AFP, ALK, BAGE proteins, β-catenin, brc-abl, BRCA1, BORIS, CA9, carbonic anhydrase IX, caspase-8, CCR5, CD19, CD20, CD30, CD40, CDK4, CEA, CTLA4, cyclin-B1, CYP1B1, EGFR, EGFRvIII, ErbB2/Her2, ErbB3, ErbB4, ETV6-AML, EpCAM, EphA2, Fra-1, FOLR1, GAGE proteins (*e.g.*, GAGE-1, -2), GD2, GD3, GloboH, glypican-3, GM3, gp100, Her2, HLA/B-raf, HLA/k-ras, HLA/MAGE-A3, hTERT, LMP2, MAGE proteins (*e.g.*, MAGE-1, -2, -3, -4, -6, and -12), MART-1, mesothelin, ML-IAP, Muc1, Muc2, Muc3, Muc4, Muc5, Muc16 (CA-125), MUM1, NA17, NY-BR1, NY-BR62, NY-BR85, NY-ESO1, OX40, p15, p53, PAP, PAX3, PAX5, PCTA-1, PLAC1, PRLR, PRAME, PSMA (FOLH1), RAGE proteins, Ras, RGS5, Rho, SART-1, SART-3, Steap-1, Steap-2, survivin, TAG-72, TGF-β, TMPRSS2, Tn, TRP-1, TRP-2, tyrosinase, and uroplakin-3.

[0095] In the context of bispecific antibodies of the present invention wherein one arm of the antibody binds CD3 and the other arm binds a target antigen, the target antigen can be an infectious disease-associated antigen. Non-limiting examples of infectious disease-associated antigens include, *e.g.*, an antigen that is expressed on the surface of a virus particle, or preferentially expressed on a cell that is infected with a virus, wherein the virus is selected from the group consisting of HIV, hepatitis (A, B or C), herpes virus (*e.g.*, HSV-1, HSV-2, CMV, HAV-6, VZV, Epstein Barr virus), adenovirus, influenza virus, flavivirus, echovirus, rhinovirus, coxsackie virus, coronavirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus, and arboviral encephalitis virus. Alternatively, the target antigen can be an antigen that is expressed on the surface of a bacterium, or preferentially expressed on a cell that is infected with a bacterium, wherein the bacterium is selected from the group consisting of chlamydia, rickettsia, mycobacteria, staphylococci, streptococci, pneumonococci, meningococci, gonococci, klebsiella, proteus, serratia, pseudomonas, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospira, and Lyme disease bacteria. In certain embodiments, the target antigen is an antigen that is expressed on the surface of a fungus, or preferentially expressed on a cell that is infected with a fungus, wherein the fungus is selected from the group consisting of Candida (albicans, krusei, glabrata, tropicalis, etc.), Crytococcus neoformans, Aspergillus (fumigatus, niger, etc.), Mucorales (mucor, absidia, rhizopus, etc.), Sporothrix schenkii, Blastomyces dermatitidis, Paracoccidioides brasiliensis, Coccidioides immitis, and Histoplasma capsulatum. In certain embodiments, the target antigen is an antigen that is expressed on the surface of a parasite, or preferentially expressed on a cell that is infected with a parasite, wherein the parasite is selected from the group consisting of Entamoeba histolytica, Balantidium coli, Naegleriafowleri, Acanthamoeba sp., Giardia lambia, Cryptosporidium sp., Pneumocystis carinii, Plasmodium vivax, Babesia microti, Trypanosoma brucei, Trypanosoma cruzi, Leishmania donovani, Toxoplasma gondii, Nippostrongylus brasiliensis, Taenia crassiceps, and Brugia malayi. Non-limiting examples of specific pathogen-associated antigens include, *e.g.*,HIV gp120, HIV CD4, hepatitis B glucoprotein L, hepatitis B glucoprotein M, hepatitis B glucoprotein S, hepatitis C E1, hepatitis C E2, hepatocyte-specific protein, herpes simplex virus gB, cytomegalovirus gB, and HTLV envelope protein.

[0096] According to certain exemplary embodiments, the present invention includes bispecific antigen-binding molecules that specifically bind CD3 and CD20. Such molecules may be referred to herein as, *e.g.*, "anti-CD3/anti-CD20," or "anti-CD3xCD20" or "CD3xCD20" bispecific molecules, or other similar terminology.

[0097] The term "CD20," as used herein, refers to the human CD20 protein unless specified as being from a non-human species (*e.g.*, "mouse CD20," "monkey CD20," etc.). The human CD20 protein has the amino acid sequence shown in SEQ ID NO:1369.

[0098] As used herein, the expression "antigen-binding molecule" means a protein, polypeptide or molecular complex comprising or consisting of at least one complementarity determining region (CDR) that alone, or in combination with one or more additional CDRs and/or framework regions (FRs), specifically binds to a particular antigen. In certain embodiments, an antigen-binding molecule is an antibody or a fragment of an antibody, as those terms are defined elsewhere herein.

[0099] As used herein, the expression "bispecific antigen-binding molecule" means a protein, polypeptide or molecular complex comprising at least a first antigen-binding domain and a second antigen-binding domain. Each antigen-binding domain within the bispecific antigen-binding molecule comprises at least one CDR that alone, or in combination with one or more additional CDRs and/or FRs, specifically binds to a particular antigen. In the context of the present invention, the first antigen-binding domain specifically binds a first antigen (*e.g.*, CD3), and the second antigen-binding domain specifically binds a second, distinct antigen (*e.g.*, CD20).

[0100] In certain exemplary embodiments of the present invention, the bispecific antigen-binding molecule is a bispecific antibody. Each antigen-binding domain of a bispecific antibody comprises a heavy chain variable domain (HCVR) and a light chain variable domain (LCVR). In the context of a bispecific antigen-binding molecule comprising a first and a second antigen-binding domain (*e.g.*, a bispecific antibody), the CDRs of the first antigen-binding domain may be designated with the prefix "A1" and the CDRs of the second antigen-binding domain may be designated with the prefix "A2". Thus, the CDRs of the first antigen-binding domain may be referred to herein as A1-HCDR1, A1-HCDR2, and A1-HCDR3; and the CDRs of the second antigen-binding domain may be referred to herein as A2-HCDR1, A2-HCDR2, and A2-HCDR3.

[0101] The first antigen-binding domain and the second antigen-binding domain may be directly or indirectly connected to one another to form a bispecific antigen-binding molecule of the present invention. Alternatively, the first antigen-binding domain and the second antigen-binding domain may each be connected to a separate multimerizing domain. The association of one multimerizing domain with another multimerizing domain facilitates the association between the two antigen-binding domains, thereby forming a bispecific antigen-binding molecule. As used herein, a "multimerizing domain" is any macromolecule, protein, polypeptide, peptide, or amino acid that has the ability to associate with a second multimerizing domain of the same or similar structure or constitution. For example, a multimerizing domain may be a polypeptide comprising an immunoglobulin C_H3 domain. A non-limiting example of a multimerizing component is an Fc portion of an immunoglobulin (comprising a C_H2-C_H3 domain), *e.g.*, an Fc domain of an IgG selected from the isotypes IgG1, IgG2, IgG3, and IgG4, as well as any allotype within each isotype group.

[0102] Bispecific antigen-binding molecules of the present invention will typically comprise two multimerizing domains, *e.g.*, two Fc domains that are each individually part of a separate antibody heavy chain. The first and second multimerizing domains may be of the same IgG isotype such as, *e.g.*, IgG1/IgG1, IgG2/IgG2, IgG4/IgG4. Alternatively, the first and second multimerizing domains may be of different IgG isotypes such as, *e.g.*, IgG1/IgG2, IgG1/IgG4, IgG2/IgG4, etc.

[0103] In certain embodiments, the multimerizing domain is an Fc fragment or an amino acid sequence of 1 to about 200 amino acids in length containing at least one cysteine residues. In other embodiments, the multimerizing domain is a cysteine residue, or a short cysteine-containing peptide. Other multimerizing domains include peptides or polypeptides comprising or consisting of a leucine zipper, a helix-loop motif, or a coiled-coil motif.

[0104] Any bispecific antibody format or technology may be used to make the bispecific antigen-binding molecules of the present invention. For example, an antibody or fragment thereof having a first antigen binding specificity can be functionally linked (e.g., by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody or antibody fragment having a second antigen-binding specificity to produce a bispecific antigen-binding molecule. Specific exemplary bispecific formats that can be used in the context of the present invention include, without limitation, *e.g.*, scFv-based or diabody bispecific formats, IgG-scFv fusions, dual variable domain (DVD)-Ig, Quadroma, knobs-into-holes, common light chain (*e.g.*, common light chain with knobs-into-holes, etc.), CrossMab, CrossFab, (SEED)body, leucine zipper, Duobody, IgG1/IgG2, dual acting Fab (DAF)-IgG, and Mab^2 bispecific formats (*see*, *e.g.*, Klein *et al.* 2012, mAbs 4:6, 1-11, and references cited therein, for a review of the foregoing formats).

[0105] In the context of bispecific antigen-binding molecules of the present invention, the multimerizing domains, *e.g.*, Fc domains, may comprise one or more amino acid changes (*e.g.*, insertions, deletions or substitutions) as compared to the wild-type, naturally occurring version of the Fc domain. For example, the invention includes bispecific antigen-binding molecules comprising one or more modifications in the Fc domain that results in a modified Fc domain having a modified binding interaction (*e.g.*, enhanced or diminished) between Fc and FcRn. In one embodiment, the bispecific antigen-binding molecule comprises a modification in a C_H2 or a C_H3 region, wherein the modification increases the affinity of the Fc domain to FcRn in an acidic environment (*e.g.,* in an endosome where pH ranges from about 5.5 to about 6.0). Non-limiting examples of such Fc modifications include, *e.g.*, a modification at position 250 (*e.g.,* E or Q); 250 and 428 (*e.g.,* L or F); 252 (*e.g.,* L/Y/F/W or T), 254 (*e.g.,* S or T), and 256 (*e.g.,* S/R/Q/E/D or T); or a modification at position 428 and/or 433 (*e.g.,* L/R/S/P/Q or K) and/or 434 (*e.g.,* H/F or Y); or a modification at position 250 and/or 428; or a modification at position 307 or 308 (*e.g.,* 308F, V308F), and 434. In one embodiment, the modification comprises a 428L (*e.g.,* M428L) and 434S (*e.g.,* N434S) modification; a 428L, 259I (*e.g.,* V259I), and 308F (*e.g.,* V308F) modification; a 433K (*e.g.,* H433K) and a 434 (*e.g.,* 434Y) modification; a 252, 254, and 256 (*e.g.,* 252Y, 254T, and 256E) modification; a 250Q and 428L modification (*e.g.,* T250Q and

M428L); and a 307 and/or 308 modification (*e.g.,* 308F or 308P).

[0106] The present invention also includes bispecific antigen-binding molecules comprising a first C_H3 domain and a second Ig C_H3 domain, wherein the first and second Ig C_H3 domains differ from one another by at least one amino acid, and wherein at least one amino acid difference reduces binding of the bispecific antibody to Protein A as compared to a bi-specific antibody lacking the amino acid difference. In one embodiment, the first Ig C_H3 domain binds Protein A and the second Ig C_H3 domain contains a mutation that reduces or abolishes Protein A binding such as an H95R modification (by IMGT exon numbering; H435R by EU numbering). The second C_H3 may further comprise a Y96F modification (by IMGT; Y436F by EU). Further modifications that may be found within the second C_H3 include: D16E, L18M, N44S, K52N, V57M, and V82I (by IMGT; D356E, L358M, N384S, K392N, V397M, and V422I by EU) in the case of IgG1 antibodies; N44S, K52N, and V82I (IMGT; N384S, K392N, and V422I by EU) in the case of IgG2 antibodies; and Q15R, N44S, K52N, V57M, R69K, E79Q, and V82I (by IMGT; Q355R, N384S, K392N, V397M, R409K, E419Q, and V422I by EU) in the case of IgG4 antibodies.

[0107] In certain embodiments, the Fc domain may be chimeric, combining Fc sequences derived from more than one immunoglobulin isotype. For example, a chimeric Fc domain can comprise part or all of a C_H2 sequence derived from a human IgG1, human IgG2 or human IgG4 C_H2 region, and part or all of a C_H3 sequence derived from a human IgG1, human IgG2 or human IgG4. A chimeric Fc domain can also contain a chimeric hinge region. For example, a chimeric hinge may comprise an "upper hinge" sequence, derived from a human IgG1, a human IgG2 or a human IgG4 hinge region, combined with a "lower hinge" sequence, derived from a human IgG1, a human IgG2 or a human IgG4 hinge region. A particular example of a chimeric Fc domain that can be included in any of the antigen-binding molecules set forth herein comprises, from N- to C-terminus: [IgG4 C_H1] - [IgG4 upper hinge] - [IgG2 lower hinge] - [IgG4 CH2] - [IgG4 CH3]. Another example of a chimeric Fc domain that can be included in any of the antigen-binding molecules set forth herein comprises, from N- to C-terminus: [IgG1 C_H1] - [IgG1 upper hinge] - [IgG2 lower hinge] - [IgG4 CH2] - [IgG1 CH3]. These and other examples of chimeric Fc domains that can be included in any of the antigen-binding molecules of the present invention are described in US Provisional Application No. 61/759,578, filed February 1, 2013. Chimeric Fc domains having these general structural arrangements, and variants thereof, can have altered Fc receptor binding, which in turn affects Fc effector function.

Sequence Variants

[0108] The antibodies and bispecific antigen-binding molecules of the present invention may comprise one or more amino acid substitutions, insertions and/or deletions in the framework and/or CDR regions of the heavy and light chain variable domains as compared to the corresponding germline sequences from which the individual antigen-binding domains were derived. Such mutations can be readily ascertained by comparing the amino acid sequences disclosed herein to germline sequences available from, for example, public antibody sequence databases. The antigen-binding molecules of the present invention may comprise antigen-binding domains which are derived from any of the exemplary amino acid sequences disclosed herein, wherein one or more amino acids within one or more framework and/or CDR regions are mutated to the corresponding residue(s) of the germline sequence from which the antibody was derived, or to the corresponding residue(s) of another human germline sequence, or to a conservative amino acid substitution of the corresponding germline residue(s) (such sequence changes are referred to herein collectively as "germline mutations"). A person of ordinary skill in the art, starting with the heavy and light chain variable region sequences disclosed herein, can easily produce numerous antibodies and antigen-binding fragments which comprise one or more individual germline mutations or combinations thereof. In certain embodiments, all of the framework and/or CDR residues within the V_H and/or V_L domains are mutated back to the residues found in the original germline sequence from which the antigen-binding domain was originally derived. In other embodiments, only certain residues are mutated back to the original germline sequence, *e.g.*, only the mutated residues found within the first 8 amino acids of FR1 or within the last 8 amino acids of FR4, or only the mutated residues found within CDR1, CDR2 or CDR3. In other embodiments, one or more of the framework and/or CDR residue(s) are mutated to the corresponding residue(s) of a different germline sequence (*i.e.*, a germline sequence that is different from the germline sequence from which the antigen-binding domain was originally derived). Furthermore, the antigen-binding domains may contain any combination of two or more germline mutations within the framework and/or CDR regions, *e.g.*, wherein certain individual residues are mutated to the corresponding residue of a particular germline sequence while certain other residues that differ from the original germline sequence are maintained or are mutated to the corresponding residue of a different germline sequence. Once obtained, antigen-binding domains that contain one or more germline mutations can be easily tested for one or more desired property such as, improved binding specificity, increased binding affinity, improved or enhanced antagonistic or agonistic biological properties (as the case may be), reduced immunogenicity, etc. Bispecific antigen-binding molecules comprising one or more antigen-binding domains obtained in this general manner are encompassed within the present invention.

[0109] The present invention also includes antigen-binding molecules wherein one or both antigen-binding domains comprise variants of any of the HCVR, LCVR, and/or CDR amino acid sequences disclosed herein having one or more conservative substitutions. For example, the present invention includes antigen-binding molecules comprising an antigen-binding domain having HCVR, LCVR, and/or CDR amino acid sequences with, *e.g.*, 10 or fewer, 8 or fewer, 6 or fewer, 4 or fewer, etc. conservative amino acid substitutions relative to any of the HCVR, LCVR, and/or CDR amino acid sequences disclosed herein. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. Examples of groups of amino acids that have side chains with similar chemical properties include (1) aliphatic side chains: glycine, alanine, valine, leucine and isoleucine; (2) aliphatic-hydroxyl side chains: serine and threonine; (3) amide-containing side chains: asparagine and glutamine; (4) aromatic side chains: phenylalanine, tyrosine, and tryptophan; (5) basic side chains: lysine, arginine, and histidine; (6) acidic side chains: aspartate and glutamate, and (7) sulfur-containing side chains are cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamate-aspartate, and asparagine-glutamine. Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet *et al.* (1992) Science 256: 1443-1445. A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

[0110] The present invention also includes antigen-binding molecules comprising an antigen-binding domain with an HCVR, LCVR, and/or CDR amino acid sequence that is substantially identical to any of the HCVR, LCVR, and/or CDR amino acid sequences disclosed herein. The term "substantial identity" or "substantially identical," when referring to an amino acid sequence means that two amino acid sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 95% sequence identity, even more preferably at least 98% or 99% sequence identity. Preferably, residue positions which are not identical differ by conservative amino acid substitutions. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well-known to those of skill in the art. *See, e.g.*, Pearson (1994) Methods Mol. Biol. 24: 307-331.

[0111] Sequence similarity for polypeptides, which is also referred to as sequence identity, is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG software contains programs such as Gap and Bestfit which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild type protein and a mutein thereof. *See, e.g.*, GCG Version 6.1. Polypeptide sequences also can be compared using FASTA using default or recommended parameters, a program in GCG Version 6.1. FASTA (e.g., FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (2000) supra). Another preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially BLASTP or TBLASTN, using default parameters. *See, e.g.*, Altschul *et al.* (1990) J. Mol. Biol. 215:403-410 and Altschul *et al.* (1997) Nucleic Acids Res. 25:3389-402.

pH-Dependent Binding

[0112] The present invention includes anti-CD3 antibodies, and anti-CD3/anti-CD20 bispecific antigen-binding molecules, with pH-dependent binding characteristics. For example, an anti-CD3 antibody of the present invention may exhibit reduced binding to CD3 at acidic pH as compared to neutral pH. Alternatively, anti-CD3 antibodies of the invention may exhibit enhanced binding to CD3 at acidic pH as compared to neutral pH. The expression "acidic pH" includes pH values less than about 6.2, *e.g.*, about 6.0, 5.95, 5,9, 5.85, 5.8, 5.75, 5.7, 5.65, 5.6, 5.55, 5.5, 5.45, 5.4, 5.35, 5.3, 5.25, 5.2, 5.15, 5.1, 5.05, 5.0, or less. As used herein, the expression "neutral pH" means a pH of about 7.0 to about 7.4. The expression "neutral pH" includes pH values of about 7.0, 7.05, 7.1, 7.15, 7.2, 7.25, 7.3, 7.35, and 7.4.

[0113] In certain instances, "reduced binding ... at acidic pH as compared to neutral pH" is expressed in terms of a ratio of the K_D value of the antibody binding to its antigen at acidic pH to the K_D value of the antibody binding to its antigen at neutral pH (or vice versa). For example, an antibody or antigen-binding fragment thereof may be regarded as exhibiting "reduced binding to CD3 at acidic pH as compared to neutral pH" for purposes of the present invention if the antibody or antigen-binding fragment thereof exhibits an acidic/neutral K_D ratio of about 3.0 or greater. In certain exemplary embodiments, the acidic/neutral K_D ratio for an antibody or antigen-binding fragment of the present invention can be about 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, 9.5, 10.0, 10.5, 11.0, 11.5, 12.0, 12.5, 13.0, 13.5, 14.0, 14.5, 15.0, 20.0. 25.0, 30.0, 40.0, 50.0, 60.0, 70.0, 100.0 or greater.

[0114] Antibodies with pH-dependent binding characteristics may be obtained, *e.g.*, by screening a population of antibodies for reduced (or enhanced) binding to a particular antigen at acidic pH as compared to neutral pH. Additionally, modifications of the antigen-binding domain at the amino acid level may yield antibodies with pH-dependent characteristics. For example, by substituting one or more amino acids of an antigen-binding domain (*e.g.*, within a CDR) with a histidine residue, an antibody with reduced antigen-binding at acidic pH relative to neutral pH may be obtained.

Antibodies Comprising Fc Variants

[0115] According to certain embodiments of the present invention, anti-CD3 antibodies, and anti-CD3/anti-CD20 bispecific antigen-binding molecules, are provided comprising an Fc domain comprising one or more mutations which enhance or diminish antibody binding to the FcRn receptor, *e.g.*, at acidic pH as compared to neutral pH. For example, the present invention includes antibodies comprising a mutation in the C_H2 or a C_H3 region of the Fc domain, wherein the mutation(s) increases the affinity of the Fc domain to FcRn in an acidic environment (*e.g.,* in an endosome where pH ranges from about 5.5 to about 6.0). Such mutations may result in an increase in serum half-life of the antibody when administered to an animal. Non-limiting examples of such Fc modifications include, *e.g.*, a modification at position 250 (e.g., E or Q); 250 and 428 (e.g., L or F); 252 (e.g., L/Y/F/W or T), 254 (e.g., S or T), and 256 (e.g., S/R/Q/E/D or T); or a modification at position 428 and/or 433 (e.g., H/L/R/S/P/Q or K) and/or 434 (*e.g.,* H/F or Y); or a modification at position 250 and/or 428; or a modification at position 307 or 308 (*e.g.,* 308F, V308F), and 434. In one embodiment, the modification comprises a 428L (*e.g.,* M428L) and 434S (*e.g.,* N434S) modification; a 428L, 259I (*e.g.,* V259I), and 308F (*e.g.,* V308F) modification; a 433K (*e.g.,* H433K) and a 434 (*e.g.,* 434Y) modification; a 252, 254, and 256 (*e.g.,* 252Y, 254T, and 256E) modification; a 250Q and 428L modification (*e.g.,* T250Q and M428L); and a 307 and/or 308 modification (*e.g.,* 308F or 308P).

[0116] For example, the present invention includes anti-CD3 antibodies, and anti-CD3/anti-CD20 bispecific antigen-binding molecules, comprising an Fc domain comprising one or more pairs or groups of mutations selected from the group consisting of: 250Q and 248L (*e.g.*, T250Q and M248L); 252Y, 254T and 256E (*e.g.*, M252Y, S254T and T256E); 428L and 434S (*e.g.*, M428L and N434S); and 433K and 434F (*e.g.*, H433K and N434F). All possible combinations of the foregoing Fc domain mutations, and other mutations within the antibody variable domains disclosed herein, are contemplated within the scope of the present invention.

Biological Characteristics of the Antibodies and Bispecific Antigen-Binding Molecules

[0117] The present invention includes antibodies and antigen-binding fragments thereof that bind human CD3 and induce T cell proliferation. For example, the present invention includes anti-CD3 antibodies that induce human T cell proliferation with an EC_{50} value of less than about 0.33 pM, as measured by an *in vitro* T cell proliferation assay, *e.g.*, using the assay format as defined in Example 4 herein (*e.g.*, assessing the proliferation of Jurkat cells or human PBMCs in the presence of anti-CD3 antibodies), or a substantially similar assay. In certain embodiments, the antibodies or antigen-binding fragments of the present invention induce human T cell proliferation (*e.g.*, Jurkat cell proliferation and/or PBMC proliferation) with an EC_{50} value of less than about 0.32 pM, less than about 0.31 pM, less than about 0.30 pM, less than about 0.28 pM, less than about 0.26 pM, less than about 0.24 pM, less than about 0.22 pM, or less than about 0.20 pM, as measured by an *in vitro* T cell proliferation assay, *e.g.*, using the assay format as defined in Example 4 herein, or a substantially similar assay.

[0118] The present invention also includes antibodies and antigen-binding fragments thereof that bind human CD3 and induce T cell-mediated killing of tumor cells. For example, the present invention includes anti-CD3 antibodies that induce T cell-mediated killing of tumor cells with an EC_{50} of less than about 2.3 pM, as measured in an *in vitro* T cell-mediated tumor cell killing assay, *e.g.*, using the assay format as defined in Example 6 herein (*e.g.*, assessing the extent of U937 tumor cell killing by human PBMCs in the presence of anti-CD3 antibodies), or a substantially similar assay. In certain embodiments, the antibodies or antigen-binding fragments of the present invention induce T cell-mediated tumor cell killing (*e.g.*, PBMC-mediated killing of U937 cells) with an EC_{50} value of less than about 2.3 pM, less than about 2.2 pM, less than about 2.1 pM, less than about 2.0 pM, less than about 1.8 pM, less than about 1.6 pM, less than about 1.4 pM, less than about 1.2 pM, less than about 1.0 pM, less than about 0.8 pM, less than about 0.6 pM, or less than about 0.5 pM, as measured by an *in vitro* T cell-mediated tumor cell killing assay, *e.g.*, using the assay format as defined in Example 6 herein, or a substantially similar assay.

[0119] The present invention includes antibodies and antigen-binding fragments thereof that bind human CD3 with high affinity. The present invention also includes antibodies and antigen-binding fragments thereof that bind human CD3 with medium or low affinity, depending on the therapeutic context and particular targeting properties that are desired. For example, in the context of a bispecific antigen-binding molecule, wherein one arm binds CD3 and another arm binds a target antigen (*e.g.*, CD20), it may be desirable for the target antigen-binding arm to bind the target antigen with high affinity while the anti-CD3 arm binds CD3 with only moderate or low affinity. In this manner, preferential targeting of the antigen-binding molecule to cells expressing the target antigen may be achieved while avoiding general/untargeted CD3 binding and the consequent adverse side effects associated therewith.

[0120] According to certain embodiments, the present invention includes antibodies and antigen-binding fragments of antibodies that bind human CD3 (*e.g.*, at 25ºC) with a K_D of less than about 15 nM as measured by surface plasmon resonance, *e.g.*, using an assay format as defined in Example 3 herein. In certain embodiments, the antibodies or antigen-binding fragments of the present invention bind CD3 with a K_D of less than about 5 nM, less than about 2 nM, less than about 1 nM, less than about 800 pM, less than about 600 pM, less than about 500 pM, less than about 400 pM, less than about 300 pM, less than about 200 pM, less than about 180 pM, less than about 160 pM, less than about 140 pM, less than about 120 pM, less than about 100 pM, less than about 80 pM, less than about 60 pM, less than about 40 pM, less than about 20 pM, or less than about 10 pM, as measured by surface plasmon resonance, *e.g.*, using an assay format as defined in Example 3 herein (*e.g.*, mAb-capture or antigen-capture format), or a substantially similar assay.

[0121] The present invention also includes antibodies and antigen-binding fragments thereof that bind CD3 with a dissociative half-life (t½) of greater than about 10 minutes as measured by surface plasmon resonance at 25°C or 37°C, *e.g.*, using an assay format as defined in Example 3 herein, or a substantially similar assay. In certain embodiments, the antibodies or antigen-binding fragments of the present invention bind CD3 with a t½ of greater than about 20 minutes, greater than about 30 minutes, greater than about 40 minutes, greater than about 50 minutes, greater than about 60 minutes, greater than about 70 minutes, greater than about 80 minutes, greater than about 90 minutes, greater than about 100 minutes, greater than about 200 minutes, greater than about 300 minutes, greater than about 400 minutes, greater than about 500 minutes, greater than about 600 minutes, greater than about 700 minutes, greater than about 800 minutes, greater than about 900 minutes, greater than about 1000 minutes, or greater than about 1200 minutes, as measured by surface plasmon resonance at 25°C or 37°C, *e.g.*, using an assay format as defined in Example 3 herein (*e.g.*, mAb-capture or antigen-capture format), or a substantially similar assay.

[0122] The present invention includes bispecific antigen-binding molecules (*e.g.*, bispecific antibodies) which are capable of simultaneously binding to human CD3 and human CD20. According to certain embodiments, the bispecific antigen-binding molecules of the invention specifically interact with cells that express CD3 and/or CD20. The extent to which a bispecific antigen-binding molecule binds cells that express CD3 and/or CD20 can be assessed by fluorescence activated cell sorting (FACS), as illustrated in Example 8 herein. For example, the present invention includes bispecific antigen-binding molecules which specifically bind human T-cell lines which express CD3 but not CD20 (*e.g.*, Jurkat), human B-cell lines which express CD20 but not CD3 (*e.g.*, Raji), and/or primate T-cells (*e.g.*, cynomolgus peripheral blood mononuclear cells [PBMCs]). The present invention includes bispecific antigen-binding molecules which bind any of the aforementioned cells and cell lines with an EC_{50} value of from about $9.0x10^{-6}$ to about $2.0x10^{-9}$, or less, as determined using a FACS assay as set forth in Example 8 or a substantially similar assay.

[0123] The present invention also includes anti-CD3/anti-CD20 bispecific antigen-binding molecules which bind to CD3-expressing human T-cells (*e.g.*, Jurkat) with an EC_{50} value of between 1.0 pM and 1000 nM. In certain embodiments, the anti-CD3/anti-CD20 bispecific antigen-binding molecules bind to CD3-expressing human T-cells with an EC50 value of between 1 nM and 60 nM. For example, the present invention includes anti-CD3/anti-CD20 bispecific antigen-binding molecules which bind to CD3-expressing human T-cells (*e.g.*, Jurkat) with an EC_{50} value of about 1 pM. about 10 pM, about 100 pM, about 500 pM, about 1 nM, about 2 nM, about 5 nM, about 10 nM, about 20 nM, about 30 nM, about 40 nM, about 50 nM about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 200 nM, about 300 nM, about 500 nM, about 800 nM, about 1000 nM, or more.

[0124] The present invention also includes anti-CD3/anti-CD20 bispecific antigen-binding molecules which exhibit one or more characteristics selected from the group consisting of: (a) inducing PBMC proliferation in vitro (*see*, *e.g.*, Example 9 herein); (b) activating T-cells, inducing IFN-gamma release and CD25 up-regulation in human whole blood (*see*, *e.g.*, Example 10 herein); (c) inducing T-cell mediated cytotoxicity on anti-CD20-resistant cell lines (*see*, *e.g.*, Example 11 herein); (d) inducing cytotoxicity to human B-cells (*e.g.*, Raji; *see*, *e.g.*, Example 13 herein); (e) depleting B-cells (*e.g.*, CD19+ B-cells) in mice reconstituted with human immune cells (*see*, *e.g.*, Example 14 herein); and (f) decreasing B-cell tumor volume (*e.g.*, Raji tumor volume) in mouse xenografts (*see*, *e.g.*, Example 15).

[0125] The present invention includes anti-CD3/anti-CD20 bispecific antigen-binding molecules which are capable of depleting B cells in a subject (*see*, *e.g.*, Example 16). For example, according to certain embodiments, anti-CD3/anti-CD20 bispecific antigen-binding molecules are provided, wherein a single administration of the bispecific antigen-binding molecule to a subject (*e.g.*, at a dose of about 0.1 mg/kg, about 0.08 mg/kg, about 0.06 mg/kg about 0.04 mg/kg, about 0.04 mg/kg, about 0.02 mg/kg, about 0.01 mg/kg, or less) causes a reduction in the number of B cells in the subject (*e.g.*, in a blood sample taken from the subject) below detectable levels. In certain embodiments, a single administration of the anti-CD3/anti-CD20 bispecific antigen-binding molecule at a dose of about 0.1 mg/kg causes a reduction in the number of B cells in the subject below detectable levels by about day 7, about day 6, about day 5, about day 4, about day 3, about day 2, or about day 1 after administration of the bispecific antigen-binding molecule to the subject. According to certain embodiments, a single administration of an anti-CD3/anti-CD20 bispecific antigen-binding molecule of the invention, at a dose of about 0.01 mg/kg, causes the number of B-cells to remain below detectable levels until at least about 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days or more, following the administration. As used herein, the expression "below detectable levels" means that no B cells can be directly or indirectly detected in a blood sample drawn from a subject using standard B-cell detection assays, *e.g.*, a FACS assay for B-cell markers, as set forth in Example 16, herein.

[0126] In related embodiments, an anti-CD3/anti-CD20 bispecific antigen-binding molecule is provided, wherein the number of B-cells per microliter of blood drawn from a subject at about day 1 through about day 28 after administration of a single dose of about 0.01 mg/kg of the antigen-binding molecule to the subject is less than 25% the number of B-cells per microliter of blood drawn from the subject prior to the administration. In certain other embodiments, an anti-CD3/anti-CD20 bispecific antigen-binding molecule is provided, wherein the number of B-cells per microliter of blood drawn from a subject at about day 1 through about day 56 after administration of a single dose of about 0.01 mg/kg of the antigen-binding molecule to the subject is less than 50% the number of B-cells per microliter of blood drawn from the subject prior to the administration.

[0127] The present invention also provides anti-CD3/anti-CD20 bispecific antigen-binding molecules that, when administered to a subject, cause no more than a transient decrease in T cells. For example, anti-CD3/anti-CD20 bispecific antigen-binding molecules are provided that, when administered to a subject at a dose of about 0.01 mg/kg cause the number of T cells to decline at day 1 following administration, but wherein the number of T cells per microliter of blood rebounds at timepoints thereafter (*e.g.*, by about day 2, day 7, day 14, day 28, day 42, day 56 or later following the administration). For example the present invention provides an anti-CD3/anti-CD20 bispecific antigen-binding molecule, wherein the number of T cells per microliter of blood drawn from the subject at about day 14 through about day 56 after administration of the antigen binding molecule to the subject at a dose of about 0.01 mg/kg is equal to or greater than the number of T cells per microliter of blood drawn from the subject prior to administration of the bispecific antigen-binding molecule.

Epitope Mapping and Related Technologies

[0128] The epitope on CD3 to which the antigen-binding molecules of the present invention bind may consist of a single contiguous sequence of 3 or more (*e.g.*, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) amino acids of a CD3 protein. Alternatively, the epitope may consist of a plurality of non-contiguous amino acids (or amino acid sequences) of CD3. The antibodies of the invention may interact with amino acids contained within a single CD3 chain (*e.g.*, CD3-epsilon, CD3-delta or CD3-gamma), or may interact with amino acids on two or more different CD3 chains. The term "epitope," as used herein, refers to an antigenic determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. A single antigen may have more than one epitope. Thus, different antibodies may bind to different areas on an antigen and may have different biological effects. Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. In certain circumstance, an epitope may include moieties of saccharides, phosphoryl groups, or sulfonyl groups on the antigen.

[0129] Various techniques known to persons of ordinary skill in the art can be used to determine whether an antigen-binding domain of an antibody "interacts with one or more amino acids" within a polypeptide or protein. Exemplary techniques include, *e.g.*, routine cross-blocking assay such as that described <u>Antibodies</u>, Harlow and Lane (Cold Spring Harbor Press, Cold Spring Harb., NY), alanine scanning mutational analysis, peptide blots analysis (Reineke, 2004, Methods Mol Biol 248:443-463), and peptide cleavage analysis. In addition, methods such as epitope excision, epitope extraction and chemical modification of antigens can be employed (Tomer, 2000, Protein Science 9:487-496). Another method that can be used to identify the amino acids within a polypeptide with which an antigen-binding domain of an antibody interacts is hydrogen/deuterium exchange detected by mass spectrometry. In general terms, the hydrogen/deuterium exchange method involves deuterium-labeling the protein of interest, followed by binding the antibody to the deuterium-labeled protein. Next, the protein/antibody complex is transferred to water to allow hydrogen-deuterium exchange to occur at all residues except for the residues protected by the antibody (which remain deuterium-labeled). After dissociation of the antibody, the target protein is subjected to protease cleavage and mass spectrometry analysis, thereby revealing the deuterium-labeled residues which correspond to the specific amino acids with which the antibody interacts. *See, e.g.*, Ehring (1999) *Analytical Biochemistry* 267(2):252-259; Engen and Smith (2001) *Anal. Chem. 73*:256A-265A. X-ray crystallography of the antigen/antibody complex may also be used for epitope mapping purposes.

[0130] The present invention further includes anti-CD3 antibodies that bind to the same epitope as any of the specific exemplary antibodies described herein (*e.g.* antibodies comprising any of the amino acid sequences as set forth in Table 1 herein). Likewise, the present invention also includes anti-CD3 antibodies that compete for binding to CD3 with any of the specific exemplary antibodies described herein (*e.g.* antibodies comprising any of the amino acid sequences as set forth in Table 1 herein).

[0131] The present invention also includes bispecific antigen-binding molecules comprising a first antigen-binding domain that specifically binds human CD3, and a second antigen binding domain that specifically binds human CD20, wherein the first antigen-binding domain binds to the same epitope on CD3 as any of the specific exemplary CD3-specific antigen-binding domains described herein, and/or wherein the second antigen-binding domain binds to the same epitope on CD20 as any of the specific exemplary CD20-specific antigen-binding domains described herein.

[0132] Likewise, the present invention also includes bispecific antigen-binding molecules comprising a first antigen-binding domain that specifically binds human CD3, and a second antigen binding domain that specifically binds human CD20, wherein the first antigen-binding domain competes for binding to CD3 with any of the specific exemplary CD3-specific antigen-binding domains described herein, and/or wherein the second antigen-binding domain competes for binding to CD20 with any of the specific exemplary CD20-specific antigen-binding domains described herein.

[0133] One can easily determine whether a particular antigen-binding molecule (*e.g.*, antibody) or antigen-binding domain thereof binds to the same epitope as, or competes for binding with, a reference antigen-binding molecule of the present invention by using routine methods known in the art. For example, to determine if a test antibody binds to the same epitope on CD3 (or CD20) as a reference bispecific antigen-binding molecule of the present invention, the reference bispecific molecule is first allowed to bind to a CD3 protein (or CD20 protein). Next, the ability of a test antibody to bind to the CD3 (or CD20) molecule is assessed. If the test antibody is able to bind to CD3 (or CD20) following saturation binding with the reference bispecific antigen-binding molecule, it can be concluded that the test antibody binds to a different epitope of CD3 (or CD20) than the reference bispecific antigen-binding molecule. On the other hand, if the test antibody is not able to bind to the CD3 (or CD20) molecule following saturation binding with the reference bispecific antigen-binding molecule, then the test antibody may bind to the same epitope of CD3 (or CD20) as the epitope bound by the reference bispecific antigen-binding molecule of the invention. Additional routine experimentation (*e.g.*, peptide mutation and binding analyses) can then be carried out to confirm whether the observed lack of binding of the test antibody is in fact due to binding to the same epitope as the reference bispecific antigen-binding molecule or if steric blocking (or another phenomenon) is responsible for the lack of observed binding. Experiments of this sort can be performed using ELISA, RIA, Biacore, flow cytometry or any other quantitative or qualitative antibody-binding assay available in the art. In accordance with certain embodiments of the present invention, two antigen-binding proteins bind to the same (or overlapping) epitope if, *e.g.*, a 1-, 5-, 10-, 20- or 100-fold excess of one antigen-binding protein inhibits binding of the other by at least 50% but preferably 75%, 90% or even 99% as measured in a competitive binding assay (see, e.g., Junghans et al., Cancer Res. 1990:50:1495-1502). Alternatively, two antigen-binding proteins are deemed to bind to the same epitope if essentially all amino acid mutations in the antigen that reduce or eliminate binding of one antigen-binding protein reduce or eliminate binding of the other. Two antigen-binding proteins are deemed to have "overlapping epitopes" if only a subset of the amino acid mutations that reduce or eliminate binding of one antigen-binding protein reduce or eliminate binding of the other.

[0134] To determine if an antibody or antigen-binding domain thereof competes for binding with a reference antigen-binding molecule, the above-described binding methodology is performed in two orientations: In a first orientation, the reference antigen-binding molecule is allowed to bind to a CD3 protein (or CD20 protein) under saturating conditions followed by assessment of binding of the test antibody to the CD3 (or CD20) molecule. In a second orientation, the test antibody is allowed to bind to a CD3 (or CD20) molecule under saturating conditions followed by assessment of binding of the reference antigen-binding molecule to the CD3 (or CD20) molecule. If, in both orientations, only the first (saturating) antigen-binding molecule is capable of binding to the CD3 (or CD20) molecule, then it is concluded that the test antibody and the reference antigen-binding molecule compete for binding to CD3 (or CD20). As will be appreciated by a person of ordinary skill in the art, an antibody that competes for binding with a reference antigen-binding molecule may not necessarily bind to the same epitope as the reference antibody, but may sterically block binding of the reference antibody by binding an overlapping or adjacent epitope.

Preparation of Antigen-Binding Domains and Construction of Bispecific Molecules

[0135] Antigen-binding domains specific for particular antigens can be prepared by any antibody generating technology known in the art. Once obtained, two different antigen-binding domains, specific for two different antigens (*e.g.*, CD3 and CD20), can be appropriately arranged relative to one another to produce a bispecific antigen-binding molecule of the present invention using routine methods. (A discussion of exemplary bispecific antibody formats that can be used to construct the bispecific antigen-binding molecules of the present invention is provided elsewhere herein). In certain embodiments, one or more of the individual components (*e.g.*, heavy and light chains) of the multispecific antigen-binding molecules of the invention are derived from chimeric, humanized or fully human antibodies. Methods for making such antibodies are well known in the art. For example, one or more of the heavy and/or light chains of the bispecific antigen-binding molecules of the present invention can be prepared using VELOCIMMUNE™ technology. Using VELOCIMMUNE™ technology (or any other human antibody generating technology), high affinity chimeric antibodies to a particular antigen (*e.g.*, CD3 or CD20) are initially isolated having a human variable region and a mouse constant region. The antibodies are characterized and selected for desirable characteristics, including affinity, selectivity, epitope, etc. The mouse constant regions are replaced with a desired human constant region to generate fully human heavy and/or light chains that can be incorporated into the bispecific antigen-binding molecules of the present invention.

[0136] Genetically engineered animals may be used to make human bispecific antigen-binding molecules. For example, a genetically modified mouse can be used which is incapable of rearranging and expressing an endogenous mouse immunoglobulin light chain variable sequence, wherein the mouse expresses only one or two human light chain variable domains encoded by human immunoglobulin sequences operably linked to the mouse kappa constant gene at the endogenous mouse kappa locus. Such genetically modified mice can be used to produce fully human bispecific antigen-binding molecules comprising two different heavy chains that associate with an identical light chain that comprises a variable domain derived from one of two different human light chain variable region gene segments. (*See*, *e.g.*, US 2011/0195454 for a detailed discussion of such engineered mice and the use thereof to produce bispecific antigen-binding molecules).

Bioequivalents

[0137] The present invention encompasses antigen-binding molecules having amino acid sequences that vary from those of the exemplary molecules disclosed herein but that retain the ability to bind CD3 and/or CD20. Such variant molecules may comprise one or more additions, deletions, or substitutions of amino acids when compared to parent sequence, but exhibit biological activity that is essentially equivalent to that of the described bispecific antigen-binding molecules.

[0138] The present invention includes antigen-binding molecules that are bioequivalent to any of the exemplary antigen-binding molecules set forth herein. Two antigen-binding proteins, or antibodies, are considered bioequivalent if, for example, they are pharmaceutical equivalents or pharmaceutical alternatives whose rate and extent of absorption do not show a significant difference when administered at the same molar dose under similar experimental conditions, either single does or multiple dose. Some antigen-binding proteins will be considered equivalents or pharmaceutical alternatives if they are equivalent in the extent of their absorption but not in their rate of absorption and yet may be considered bioequivalent because such differences in the rate of absorption are intentional and are reflected in the labeling, are not essential to the attainment of effective body drug concentrations on, e.g., chronic use, and are considered medically insignificant for the particular drug product studied.

[0139] In one embodiment, two antigen-binding proteins are bioequivalent if there are no clinically meaningful differences in their safety, purity, and potency.

[0140] In one embodiment, two antigen-binding proteins are bioequivalent if a patient can be switched one or more times between the reference product and the biological product without an expected increase in the risk of adverse effects, including a clinically significant change in immunogenicity, or diminished effectiveness, as compared to continued therapy without such switching.

[0141] In one embodiment, two antigen-binding proteins are bioequivalent if they both act by a common mechanism or mechanisms of action for the condition or conditions of use, to the extent that such mechanisms are known.

[0142] Bioequivalence may be demonstrated by in vivo and in vitro methods. Bioequivalence measures include, e.g., (a) an in vivo test in humans or other mammals, in which the concentration of the antibody or its metabolites is measured in blood, plasma, serum, or other biological fluid as a function of time; (b) an in vitro test that has been correlated with and is reasonably predictive of human in vivo bioavailability data; (c) an in vivo test in humans or other mammals in which the appropriate acute pharmacological effect of the antibody (or its target) is measured as a function of time; and (d) in a well-controlled clinical trial that establishes safety, efficacy, or bioavailability or bioequivalence of an antigen-binding protein.

[0143] Bioequivalent variants of the exemplary bispecific antigen-binding molecules set forth herein may be constructed by, for example, making various substitutions of residues or sequences or deleting terminal or internal residues or sequences not needed for biological activity. For example, cysteine residues not essential for biological activity can be deleted or replaced with other amino acids to prevent formation of unnecessary or incorrect intramolecular disulfide bridges upon renaturation. In other contexts, bioequivalent antigen-binding proteins may include variants of the exemplary bispecific antigen-binding molecules set forth herein comprising amino acid changes which modify the glycosylation characteristics of the molecules, *e.g.*, mutations which eliminate or remove glycosylation.

Species Selectivity and Species Cross-Reactivity

[0144] According to certain embodiments of the invention, antigen-binding molecules are provided which bind to human CD3 but not to CD3 from other species. Also provided are antigen-binding molecules which bind to human CD20 but not to CD20 from other species. The present invention also includes antigen-binding molecules that bind to human CD3 and to CD3 from one or more non-human species; and/or antigen-binding molecules that bind to human CD20 and to CD20 from one or more non-human species.

[0145] According to certain exemplary embodiments of the invention, antigen-binding molecules are provided which bind to human CD3 and/or human CD20 and may bind or not bind, as the case may be, to one or more of mouse, rat, guinea pig, hamster, gerbil, pig, cat, dog, rabbit, goat, sheep, cow, horse, camel, cynomolgus, marmoset, rhesus or chimpanzee CD3 and/or CD20. For example, in a particular exemplary embodiment of the present invention bispecific antigen-binding molecules are provided comprising a first antigen-binding domain that binds human CD3 and cynomologous CD3, and a second antigen-binding domain that specifically binds human CD20.

Immunoconjugates

[0146] The present invention encompasses antigen-binding molecules conjugated to a therapeutic moiety ("immunoconjugate"), such as a cytotoxin, a chemotherapeutic drug, an immunosuppressant or a radioisotope. Cytotoxic agents include any agent that is detrimental to cells. Examples of suitable cytotoxic agents and chemotherapeutic agents for forming immunoconjugates are known in the art, (see for example, WO 05/103081).

Therapeutic Formulation and Administration

[0147] The present invention provides pharmaceutical compositions comprising the antigen-binding molecules of the present invention. The pharmaceutical compositions of the invention are formulated with suitable carriers, excipients, and other agents that provide improved transfer, delivery, tolerance, and the like. A multitude of appropriate formulations can be found in the formulary known to all pharmaceutical chemists: Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, PA. These formulations include, for example, powders, pastes, ointments, jellies, waxes, oils, lipids, lipid (cationic or anionic) containing vesicles (such as LIPOFECTIN™, Life Technologies, Carlsbad, CA), DNA conjugates, anhydrous absorption pastes, oil-in-water and water-in-oil emulsions, emulsions carbowax (polyethylene glycols of various molecular weights), semi-solid gels, and semi-solid mixtures containing carbowax. See also Powell et al. "Compendium of excipients for parenteral formulations" PDA (1998) J Pharm Sci Technol 52:238-311.

[0148] The dose of antigen-binding molecule administered to a patient may vary depending upon the age and the size of the patient, target disease, conditions, route of administration, and the like. The preferred dose is typically calculated according to body weight or body surface area. When a bispecific antigen-binding molecule of the present invention is used for therapeutic purposes in an adult patient, it may be advantageous to intravenously administer the bispecific antigen-binding molecule of the present invention normally at a single dose of about 0.01 to about 20 mg/kg body weight, more preferably about 0.02 to about 7, about 0.03 to about 5, or about 0.05 to about 3 mg/kg body weight. Depending on the severity of the condition, the frequency and the duration of the treatment can be adjusted. Effective dosages and schedules for administering a bispecific antigen-binding molecule may be determined empirically; for example, patient progress can be monitored by periodic assessment, and the dose adjusted accordingly. Moreover, interspecies scaling of dosages can be performed using well-known methods in the art (*e.g.*, Mordenti *et al.*, 1991, *Pharmaceut. Res. 8*:1351).

[0149] Various delivery systems are known and can be used to administer the pharmaceutical composition of the invention, *e.g.*, encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the mutant viruses, receptor mediated endocytosis (see, e.g., Wu et al., 1987, J. Biol. Chem. 262:4429-4432). Methods of introduction include, but are not limited to, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The composition may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local.

[0150] A pharmaceutical composition of the present invention can be delivered subcutaneously or intravenously with a standard needle and syringe. In addition, with respect to subcutaneous delivery, a pen delivery device readily has applications in delivering a pharmaceutical composition of the present invention. Such a pen delivery device can be reusable or disposable. A reusable pen delivery device generally utilizes a replaceable cartridge that contains a pharmaceutical composition. Once all of the pharmaceutical composition within the cartridge has been administered and the cartridge is empty, the empty cartridge can readily be discarded and replaced with a new cartridge that contains the pharmaceutical composition. The pen delivery device can then be reused. In a disposable pen delivery device, there is no replaceable cartridge. Rather, the disposable pen delivery device comes prefilled with the pharmaceutical composition held in a reservoir within the device. Once the reservoir is emptied of the pharmaceutical composition, the entire device is discarded.

[0151] Numerous reusable pen and autoinjector delivery devices have applications in the subcutaneous delivery of a pharmaceutical composition of the present invention. Examples include, but are not limited to AUTOPEN™ (Owen Mumford, Inc., Woodstock, UK), DISETRONIC™ pen (Disetronic Medical Systems, Bergdorf, Switzerland), HUMALOG MIX 75/25™ pen, HUMALOG™ pen, HUMALIN 70/30™ pen (Eli Lilly and Co., Indianapolis, IN), NOVOPEN™ I, II and III (Novo Nordisk, Copenhagen, Denmark), NOVOPEN JUNIOR™ (Novo Nordisk, Copenhagen, Denmark), BD™ pen (Becton Dickinson, Franklin Lakes, NJ), OPTIPEN™, OPTIPEN PRO™, OPTIPEN STARLET™, and OPTICLIK™ (sanofi-aventis, Frankfurt, Germany), to name only a few. Examples of disposable pen delivery devices having applications in subcutaneous delivery of a pharmaceutical composition of the present invention include, but are not limited to the SOLOSTAR™ pen (sanofi-aventis), the FLEXPEN™ (Novo Nordisk), and the KWIKPEN™ (Eli Lilly), the SURECLICK™ Autoinjector (Amgen, Thousand Oaks, CA), the PENLET™ (Haselmeier, Stuttgart, Germany), the EPIPEN (Dey, L.P.), and the HUMIRA™ Pen (Abbott Labs, Abbott Park IL), to name only a few.

[0152] In certain situations, the pharmaceutical composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, supra; Sefton, 1987, CRC Crit. Ref. Biomed. Eng. 14:201). In another embodiment, polymeric materials can be used; see, Medical Applications of Controlled Release, Langer and Wise (eds.), 1974, CRC Pres., Boca Raton, Florida. In yet another embodiment, a controlled release system can be placed in proximity of the composition's target, thus requiring only a fraction of the systemic dose (see, *e.g.*, Goodson, 1984, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer, 1990, Science 249:1527-1533.

[0153] The injectable preparations may include dosage forms for intravenous, subcutaneous, intracutaneous and intramuscular injections, drip infusions, etc. These injectable preparations may be prepared by methods publicly known. For example, the injectable preparations may be prepared, *e.g.*, by dissolving, suspending or emulsifying the antibody or its salt described above in a sterile aqueous medium or an oily medium conventionally used for injections. As the aqueous medium for injections, there are, for example, physiological saline, an isotonic solution containing glucose and other auxiliary agents, etc., which may be used in combination with an appropriate solubilizing agent such as an alcohol (e.g., ethanol), a polyalcohol (e.g., propylene glycol, polyethylene glycol), a nonionic surfactant [e.g., polysorbate 80, HCO-50 (polyoxyethylene (50 mol) adduct of hydrogenated castor oil)], etc. As the oily medium, there are employed, e.g., sesame oil, soybean oil, etc., which may be used in combination with a solubilizing agent such as benzyl benzoate, benzyl alcohol, etc. The injection thus prepared is preferably filled in an appropriate ampoule.

[0154] Advantageously, the pharmaceutical compositions for oral or parenteral use described above are prepared into dosage forms in a unit dose suited to fit a dose of the active ingredients. Such dosage forms in a unit dose include, for example, tablets, pills, capsules, injections (ampoules), suppositories, etc. The amount of the aforesaid antibody contained is generally about 5 to about 500 mg per dosage form in a unit dose; especially in the form of injection, it is preferred that the aforesaid antibody is contained in about 5 to about 100 mg and in about 10 to about 250 mg for the other dosage forms.

Therapeutic Uses of the Antigen-Binding Molecules

[0155] The present invention includes methods comprising administering to a subject in need thereof a therapeutic composition comprising an anti-CD3 antibody or a bispecific antigen-binding molecule that specifically binds CD3 and a target antigen (*e.g.*, CD20). The therapeutic composition can comprise any of the antibodies or bispecific antigen-binding molecules as disclosed herein and a pharmaceutically acceptable carrier or diluent. As used herein, the expression "a subject in need thereof" means a human or non-human animal that exhibits one or more symptoms or indicia of cancer (*e.g.*, a subject expressing a tumor or suffering from any of the cancers mentioned herein below), or who otherwise would benefit from an inhibition or reduction in CD20 activity or a depletion of CD20+ B cells.

[0156] The antibodies and bispecific antigen-binding molecules of the invention (and therapeutic compositions comprising the same) are useful, *inter alia*, for treating any disease or disorder in which stimulation, activation and/or targeting of an immune response would be beneficial. In particular, the anti-CD3/anti-CD20 bispecific antigen-binding molecules of the present invention may be used for the treatment, prevention and/or amelioration of any disease or disorder associated with or mediated by CD20 expression or activity or the proliferation of CD20+ B cells. The mechanism of action by which the therapeutic methods of the invention are achieved include killing of the cells expressing CD20 in the presence of effector cells, for example, by CDC, apoptosis, ADCC, phagocytosis, or by a combination of two or more of these mechanisms. Cells expressing CD20 which can be inhibited or killed using the bispecific antigen-binding molecules of the invention include, for example, tumorigenic B cells.

[0157] The antigen-binding molecules of the present invention may be used to treat, *e.g.*, primary and/or metastatic tumors arising in the brain and meninges, oropharynx, lung and bronchial tree, gastrointestinal tract, male and female reproductive tract, muscle, bone, skin and appendages, connective tissue, spleen, immune system, blood forming cells and bone marrow, liver and urinary tract, and special sensory organs such as the eye. In certain embodiments, the bispecific antigen-binding molecules of the invention are used to treat one or more of the following cancers: renal cell carcinoma, pancreatic carcinoma, breast cancer, head and neck cancer, prostate cancer, malignant gliomas, osteosarcoma, colorectal cancer, gastric cancer (*e.g.*, gastric cancer with MET amplification), malignant mesothelioma, multiple myeloma, ovarian cancer, small cell lung cancer, non-small cell lung cancer, synovial sarcoma, thyroid cancer, or melanoma. According to certain exemplary embodiments, the bispecific antigen-binding molecules of the present invention are used to treat a B cell cancer (*e.g.*, Hodgkin's lymphoma, non-Hodgkin's lymphoma [NHL], precursor B cell lymphoblastic leukemia/lymphoma, mature B cell neoplasms, B cell chronic lymphocytic leukemia/small lymphocytic lymphoma, B cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, mantle cell lymphoma, follicular lymphoma, cutaneous follicle center lymphoma, marginal zone B cell lymphoma, hairy cell leukemia, diffuse large B cell lymphoma, Burkitt's lymphoma, plasmacytoma, plasma cell myeloma, post-transplant lymphoproliferative disorder, Waldenstrom's macroglobulinemia, and anaplastic large-cell lymphoma).

[0158] According to certain embodiments of the present invention, the antigen-binding molecules are useful for treating a patient afflicted with a B-cell lymphoma (*e.g.*, NHL) that is resistant to, or incompletely responsive to anti-CD20 therapy alone (*e.g.*, resistant to rituximab therapy). According to other related embodiments of the invention, methods are provided comprising administering an anti-CD3/anti-CD20 bispecific antigen-binding molecule as disclosed herein to a patient who is afflicted with a B-cell lymphoma (*e.g.*, NHL) that is refractory to anti-CD20 therapy (*e.g.*, a patient with a rituximab-refractory tumor or with relapsed or refractory B-cell lymphoma). Analytic/diagnostic methods known in the art, such as tumor scanning, etc., may be used to ascertain whether a patient harbors as tumor that is resistant to, incompletely responsive to, or refractory to anti-CD20 therapy alone.

[0159] The present invention also includes methods for treating residual cancer in a subject. As used herein, the term "residual cancer" means the existence or persistence of one or more cancerous cells in a subject following treatment with an anti-cancer therapy.

[0160] According to certain aspects, the present invention provides methods for treating a disease or disorder associated with CD20 expression (*e.g.*, B cell lymphoma) comprising administering one or more of the bispecific antigen-binding molecules described elsewhere herein to a subject after the subject has received anti-CD20 mono-therapy (*e.g.*, after administration of a pharmaceutical composition comprising an anti-CD20 antibody such as rituximab). For example, the present invention includes methods for treating B cell lymphoma comprising administering an anti-CD3/anti-CD20 bispecific antigen-binding molecule to a patient 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks or 4 weeks, 2 months, 4 months, 6 months, 8 months, 1 year, or more after the subject has received anti-CD20 mono-therapy (*e.g.*, rituximab treatment or an equivalent treatment thereof). In other aspects, a bispecific antigen-binding molecule of the invention (an anti-CD3/anti-CD20 bispecific antigen-binding molecule) comprising an IgG4 Fc domain is initially administered to a subject at one or more time points (*e.g.*, to provide robust initial depletion of B cells), followed by administration of an equivalent bispecific antigen-binding molecule comprising a different IgG domain, such as an IgG1 Fc domain, at subsequent time points.

Combination Therapies and Formulations

[0161] The present invention provides methods which comprise administering a pharmaceutical composition comprising any of the exemplary antibodies and bispecific antigen-binding molecules described herein in combination with one or more additional therapeutic agents. Exemplary additional therapeutic agents that may be combined with or administered in combination with an antigen-binding molecule of the present invention include, *e.g.*, an EGFR antagonist (*e.g.*, an anti-EGFR antibody [*e.g.*, cetuximab or panitumumab] or small molecule inhibitor of EGFR [*e.g.*, gefitinib or erlotinib]), an antagonist of another EGFR family member such as Her2/ErbB2, ErbB3 or ErbB4 (*e.g.*, anti-ErbB2, anti-ErbB3 or anti-ErbB4 antibody or small molecule inhibitor of ErbB2, ErbB3 or ErbB4 activity), an antagonist of EGFRvIII (*e.g.*, an antibody that specifically binds EGFRvIII), a cMET anagonist (*e.g.*, an anti-cMET antibody), an IGF1R antagonist (*e.g.*, an anti-IGF1R antibody), a B-raf inhibitor (*e.g.*, vemurafenib, sorafenib, GDC-0879, PLX-4720), a PDGFR-α inhibitor (*e.g.*, an anti-PDGFR-α antibody), a PDGFR-β inhibitor (*e.g.*, an anti-PDGFR-β antibody), a VEGF antagonist (*e.g.*, a VEGF-Trap, *see*, *e.g.*, US 7,087,411 (also referred to herein as a "VEGF-inhibiting fusion protein"), anti-VEGF antibody (*e.g.*, bevacizumab), a small molecule kinase inhibitor of VEGF receptor (*e.g.*, sunitinib, sorafenib or pazopanib)), a DLL4 antagonist (*e.g.*, an anti-DLL4 antibody disclosed in US 2009/0142354 such as REGN421), an Ang2 antagonist (*e.g.*, an anti-Ang2 antibody disclosed in US 2011/0027286 such as H1H685P), a FOLH1 antagonist (*e.g.*, an anti-FOLH1 antibody), a PRLR antagonist (*e.g.*, an anti-PRLR antibody), a STEAP1 or STEAP2 antagonist (*e.g.*, an anti-STEAP1 antibody or an anti-STEAP2 antibody), a TMPRSS2 antagonist (*e.g.*, an anti-TMPRSS2 antibody), a MSLN antagonist (*e.g.*, an anti-MSLN antibody), a CA9 antagonist (*e.g.*, an anti-CA9 antibody), a uroplakin antagonist (*e.g.*, an anti-uroplakin antibody), a monovalent CD20 antagonist (*e.g.*, a monovalent anti-CD20 antibody such as rituximab), etc. Other agents that may be beneficially administered in combination with the antigen-binding molecules of the invention include cytokine inhibitors, including small-molecule cytokine inhibitors and antibodies that bind to cytokines such as IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-11, IL-12, IL-13, IL-17, IL-18, or to their respective receptors. The pharmaceutical compositions of the present invention (*e.g.*, pharmaceutical compositions comprising an anti-CD3/anti-CD20 bispecific antigen-binding molecule as disclosed herein) may also be administered as part of a therapeutic regimen comprising one or more therapeutic combinations selected from "ICE": ifosfamide (*e.g.*, Ifex®), carboplatin (*e.g.*, Paraplatin®), etoposide (*e.g.*, Etopophos®, Toposar®, VePesid®, VP-16); "DHAP": dexamethasone (*e.g.*, Decadron®), cytarabine (*e.g.*, Cytosar-U®, cytosine arabinoside, ara-C), cisplatin (*e.g.*, Platinol®-AQ); and "ESHAP": etoposide (*e.g.*, Etopophos®, Toposar®, VePesid®, VP-16), methylprednisolone (*e.g.*, Medrol®), high-dose cytarabine, cisplatin (*e.g.*, Platinol®-AQ).

[0162] The present invention also includes therapeutic combinations comprising any of the antigen-binding molecules mentioned herein and an inhibitor of one or more of VEGF, Ang2, DLL4, EGFR, ErbB2, ErbB3, ErbB4, EGFRvIII, cMet, IGF1R, B-raf, PDGFR-α, PDGFR-β, FOLH1, PRLR, STEAP1, STEAP2, TMPRSS2, MSLN, CA9, uroplakin, or any of the aforementioned cytokines, wherein the inhibitor is an aptamer, an antisense molecule, a ribozyme, an siRNA, a peptibody, a nanobody or an antibody fragment (*e.g.*, Fab fragment; $F(ab')_2$ fragment; Fd fragment; Fv fragment; scFv; dAb fragment; or other engineered molecules, such as diabodies, triabodies, tetrabodies, minibodies and minimal recognition units). The antigen-binding molecules of the invention may also be administered and/or co-formulated in combination with antivirals, antibiotics, analgesics, corticosteroids and/or NSAIDs. The antigen-binding molecules of the invention may also be administered as part of a treatment regimen that also includes radiation treatment and/or conventional chemotherapy.

[0163] The additional therapeutically active component(s) may be administered just prior to, concurrent with, or shortly after the administration of an antigen-binding molecule of the present invention; (for purposes of the present disclosure, such administration regimens are considered the administration of an antigen-binding molecule "in combination with" an additional therapeutically active component).

[0164] The present invention includes pharmaceutical compositions in which an antigen-binding molecule of the present invention is co-formulated with one or more of the additional therapeutically active component(s) as described elsewhere herein.

Administration Regimens

[0165] According to certain embodiments of the present invention, multiple doses of an antigen-binding molecule (*e.g.*, an anti-CD3 antibody or a bispecific antigen-binding molecule that specifically binds CD20 and CD3) may be administered to a subject over a defined time course. The methods according to this aspect of the invention comprise sequentially administering to a subject multiple doses of an antigen-binding molecule of the invention. As used herein, "sequentially administering" means that each dose of an antigen-binding molecule is administered to the subject at a different point in time, *e.g.*, on different days separated by a predetermined interval (*e.g.*, hours, days, weeks or months). The present invention includes methods which comprise sequentially administering to the patient a single initial dose of an antigen-binding molecule, followed by one or more secondary doses of the antigen-binding molecule, and optionally followed by one or more tertiary doses of the antigen-binding molecule.

[0166] The terms "initial dose," "secondary doses," and "tertiary doses," refer to the temporal sequence of administration of the antigen-binding molecule of the invention. Thus, the "initial dose" is the dose which is administered at the beginning of the treatment regimen (also referred to as the "baseline dose"); the "secondary doses" are the doses which are administered after the initial dose; and the "tertiary doses" are the doses which are administered after the secondary doses. The initial, secondary, and tertiary doses may all contain the same amount of the antigen-binding molecule, but generally may differ from one another in terms of frequency of administration. In certain embodiments, however, the amount of an antigen-binding molecule contained in the initial, secondary and/or tertiary doses varies from one another (*e.g.*, adjusted up or down as appropriate) during the course of treatment. In certain embodiments, two or more (*e.g.*, 2, 3, 4, or 5) doses are administered at the beginning of the treatment regimen as "loading doses" followed by subsequent doses that are administered on a less frequent basis (*e.g.*, "maintenance doses").

[0167] In one exemplary embodiment of the present invention, each secondary and/or tertiary dose is administered 1 to 26 (*e.g.*, 1, 1½, 2, 2½, 3, 3½, 4, 4½, 5, 5½, 6, 6½, 7, 7½, 8, 8½, 9, 9½, 10, 10½, 11, 11½, 12, 12½, 13, 13½, 14, 14½, 15, 15½, 16, 16½, 17, 17½, 18, 18½, 19, 19½, 20, 20½, 21, 21½, 22, 22½, 23, 23½, 24, 24½, 25, 25½, 26, 26½, or more) weeks after the immediately preceding dose. The phrase "the immediately preceding dose," as used herein, means, in a sequence of multiple administrations, the dose of antigen-binding molecule which is administered to a patient prior to the administration of the very next dose in the sequence with no intervening doses.

[0168] The methods according to this aspect of the invention may comprise administering to a patient any number of secondary and/or tertiary doses of an antigen-binding molecule (*e.g.*, an anti-CD3 antibody or a bispecific antigen-binding molecule that specifically binds CD20 and CD3). For example, in certain embodiments, only a single secondary dose is administered to the patient. In other embodiments, two or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, or more) secondary doses are administered to the patient. Likewise, in certain embodiments, only a single tertiary dose is administered to the patient. In other embodiments, two or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, or more) tertiary doses are administered to the patient.

[0169] In embodiments involving multiple secondary doses, each secondary dose may be administered at the same frequency as the other secondary doses. For example, each secondary dose may be administered to the patient 1 to 2 weeks after the immediately preceding dose. Similarly, in embodiments involving multiple tertiary doses, each tertiary dose may be administered at the same frequency as the other tertiary doses. For example, each tertiary dose may be administered to the patient 2 to 4 weeks after the immediately preceding dose. Alternatively, the frequency at which the secondary and/or tertiary doses are administered to a patient can vary over the course of the treatment regimen. The frequency of administration may also be adjusted during the course of treatment by a physician depending on the needs of the individual patient following clinical examination.

Diagnostic Uses of the Antibodies

[0170] The anti-CD3 antibodies of the present invention may also be used to detect and/or measure CD3, or CD3-expressing cells in a sample, *e.g.*, for diagnostic purposes. For example, an anti-CD3 antibody, or fragment thereof, may be used to diagnose a condition or disease characterized by aberrant expression (*e.g.*, over-expression, under-expression, lack of expression, etc.) of CD3. Exemplary diagnostic assays for CD3 may comprise, *e.g.*, contacting a sample, obtained from a patient, with an anti-CD3 antibody of the invention, wherein the anti-CD3 antibody is labeled with a detectable label or reporter molecule. Alternatively, an unlabeled anti-CD3 antibody can be used in diagnostic applications in combination with a secondary antibody which is itself detectably labeled. The detectable label or reporter molecule can be a radioisotope, such as ^{3}H, ^{14}C, ^{32}P, ^{35}S, or ^{125}I; a fluorescent or chemiluminescent moiety such as fluorescein isothiocyanate, or rhodamine; or an enzyme such as alkaline phosphatase, beta-galactosidase, horseradish peroxidase, or luciferase. Specific exemplary assays that can be used to detect or measure CD3 in a sample include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence-activated cell sorting (FACS).
Samples that can be used in CD3 diagnostic assays according to the present invention include any tissue or fluid sample obtainable from a patient which contains detectable quantities of CD3 protein, or fragments thereof, under normal or pathological conditions. Generally, levels of CD3 in a particular sample obtained from a healthy patient (*e.g.*, a patient not afflicted with a disease or condition associated with abnormal CD3 levels or activity) will be measured to initially establish a baseline, or standard, level of CD3. This baseline level of CD3 can then be compared against the levels of CD3 measured in samples obtained from individuals suspected of having a CD3 related disease or condition.

EXAMPLES

[0171] The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the methods and compositions of the invention, and are not intended to limit the scope of what the inventors regard as their invention. Efforts have been made to ensure accuracy with respect to numbers used (e.g., amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, molecular weight is average molecular weight, temperature is in degrees Centigrade, and pressure is at or near atmospheric.

Example 1. Generation of Anti-CD3 Antibodies

[0172] Anti-CD3 antibodies were obtained by immunizing a VELOCIMMUNE® mouse (*i.e.*, an engineered mouse comprising DNA encoding human Immunoglobulin heavy and kappa light chain variable regions) with cells expressing CD3 or with DNA encoding CD3. The antibody immune response was monitored by a CD3-specific immunoassay. When a desired immune response was achieved splenocytes were harvested and fused with mouse myeloma cells to preserve their viability and form hybridoma cell lines. The hybridoma cell lines were screened and selected to identify cell lines that produce CD3-specific antibodies. Using this technique several anti-CD3 chimeric antibodies (*i.e.*, antibodies possessing human variable domains and mouse constant domains) were obtained. In addition, several fully human anti-CD3 antibodies were isolated directly from antigen-positive B cells without fusion to myeloma cells, as described in US 2007/0280945A1.

[0173] Certain biological properties of the exemplary anti-CD3 antibodies generated in accordance with the methods of this Example are described in detail in the Examples set forth below.

Example 2. Heavy and Light Chain Variable Region Amino Acid and Nucleic Acid Sequences

[0174] Table 1 sets forth the amino acid sequence identifiers of the heavy and light chain variable regions and CDRs of selected anti-CD3 antibodies of the invention. The corresponding nucleic acid sequence identifiers are set forth in Table 2.

Table 1: Amino Acid Sequence Identifiers

	SEQ ID NOs:							
Antibody Designation	**HCVR**	**HCDR1**	**HCDR2**	**HCDR3**	**LCVR**	**LCDR1**	**LCDR2**	**LCDR3**
H1H2712N	2	4	6	8	10	12	14	16
H1M2692N	18	20	22	24	26	28	30	32
H1M3542N	34	36	38	40	42	44	46	48
H1M3544N	50	52	54	56	58	60	62	64
H1M3549N	66	68	70	72	74	76	78	80
H1M3613N	82	84	86	88	90	92	94	96
H2M2689N	98	100	102	104	106	108	110	112
H2M2690N	114	116	118	120	122	124	126	128
H2M2691N	130	132	134	136	138	140	142	144
H2M2704N	146	148	150	152	154	156	158	160
H2M2705N	162	164	166	168	170	172	174	176
H2M2706N	178	180	182	184	186	188	190	192

H2M2707N	194	196	198	200	202	204	206	208
H2M2708N	210	212	214	216	218	220	222	224
H2M2709N	226	228	230	232	234	236	238	240
H2M2710N	242	244	246	248	250	252	254	256
H2M2711N	258	260	262	264	266	268	270	272
H2M2774N	274	276	278	280	282	284	286	288
H2M2775N	290	292	294	296	298	300	302	304
H2M2776N	306	308	310	312	314	316	318	320
H2M2777N	322	324	326	328	330	332	334	336
H2M2778N	338	340	342	344	346	348	350	352
H2M2779N	354	356	358	360	362	364	366	368
H2M2789N	370	372	374	376	378	380	382	384
H2M2862N	386	388	390	392	394	396	398	400
H2M2885N	402	404	406	408	410	412	414	416
H2M2886N	418	420	422	424	426	428	430	432
H2M3540N	434	436	438	440	442	444	446	448
H2M3541N	450	452	454	456	458	460	462	464
H2M3543N	466	468	470	472	474	476	478	480
H2M3547N	482	484	486	488	490	492	494	496
H2M3548N	498	500	502	504	506	508	510	512
H2M3563N	514	516	518	520	522	524	526	528
H1H5751P	530	532	534	536	538	540	542	544
H1H5752P	546	548	550	552	554	556	558	560
H1H5753B	562	564	566	568	570	572	574	576
H1H5754B	578	580	582	584	586	588	590	592
H1H5755B	594	596	598	600	602	604	606	608
H1H5756B	610	612	614	616	618	620	622	624
H1H5757B	626	628	630	632	634	636	638	640
H1H5758B	642	644	646	648	650	652	654	656
H1H5761P	658	660	662	664	666	668	670	672
H1H5763P	674	676	678	680	682	684	686	688
H1H5764P	690	692	694	696	698	700	702	704
H1H5769P	706	708	710	712	714	716	718	720
H1H5771P	722	724	726	728	730	732	734	736
H1H5772P	738	740	742	744	746	748	750	752
H1H5777P	754	756	758	460	762	764	766	768
H1H5778P	770	772	774	776	778	780	782	784
H1H5780P	786	788	790	792	794	796	798	800
H1H5781P	802	804	806	808	810	812	814	816
H1H5782P	818	820	822	824	826	828	830	832
H1H5785B	834	836	838	840	842	844	846	848
H1H5786B	850	852	854	856	858	860	862	864
H1H5788P	866	868	870	872	874	876	878	880
H1H5790B	882	884	886	888	890	892	894	896
H1H5791B	898	900	902	904	906	908	910	912

H1H5792B	914	916	918	920	922	924	926	928
H1H5793B	930	932	934	936	938	940	942	944
H1H5795B	946	948	950	952	954	956	958	960
H1H5796B	962	964	966	968	970	972	974	976
H1H5797B	978	980	982	984	986	988	990	992
H1H5798B	994	996	998	1000	1002	1004	1006	1008
H1H5799P	1010	1012	1014	1016	1018	1020	1022	1024
H1H5801B	1026	1028	1030	1032	1034	1036	1038	1040
H1H7194B	1042	1044	1046	1048	1234	1236	1238	1240
H1H7195B	1050	1052	1054	1056	1234	1236	1238	1240
H1H7196B	1058	1060	1062	1064	1234	1236	1238	1240
H1H7198B	1066	1068	1070	1072	1234	1236	1238	1240
H1H7203B	1074	1076	1078	1080	1234	1236	1238	1240
H1H7204B	1082	1084	1086	1088	1234	1236	1238	1240
H1H7208B	1090	1092	1094	1096	1234	1236	1238	1240
H1H7211B	1098	1100	1102	1104	1234	1236	1238	1240
H1H7221B	1106	1108	1110	1112	1234	1236	1238	1240
H1H7223B	1114	1116	1118	1120	1234	1236	1238	1240
H1H7226B	1122	1124	1126	1128	1234	1236	1238	1240
H1H7232B	1130	1132	1134	1136	1234	1236	1238	1240
H1H7233B	1138	1140	1142	1144	1234	1236	1238	1240
H1H7241B	1146	1148	1150	1152	1234	1236	1238	1240
H1H7242B	1154	1156	1158	1160	1234	1236	1238	1240
H1H7250B	1162	1164	1166	1168	1234	1236	1238	1240
H1H7251B	1170	1172	1174	1176	1234	1236	1238	1240
H1H7254B	1178	1180	1182	1184	1234	1236	1238	1240
H1H7258B	1186	1188	1190	1192	1234	1236	1238	1240
H1H7269B	1194	1196	1198	1200	1234	1236	1238	1240
H1H7279B	1202	1204	1206	1208	1234	1236	1238	1240
H1xH7221G	1210	1212	1214	1216	1234	1236	1238	1240
H1xH7221G3	1218	1220	1222	1224	1234	1236	1238	1240
H1xH7221G5	1226	1228	1230	1232	1234	1236	1238	1240

Table 2: Nucleic Acid Sequence Identifiers

	SEQ ID NOs:							
Antibody Designation	**HCVR**	**HCDR1**	**HCDR2**	**HCDR3**	**LCVR**	**LCDR1**	**LCDR2**	**LCDR3**
H1H2712N	1	3	5	7	9	11	13	15
H1M2692N	17	19	21	23	25	27	29	31
H1M3542N	33	35	37	39	41	43	45	47
H1M3544N	49	51	53	55	57	59	61	63
H1M3549N	65	67	69	71	73	75	77	79
H1M3613N	81	83	85	87	89	91	93	95
H2M2689N	97	99	101	103	105	107	109	111
H2M2690N	113	115	117	119	121	123	125	127
H2M2691N	129	131	133	135	137	139	141	143
H2M2704N	145	147	149	151	153	155	157	159
H2M2705N	161	163	165	167	169	171	173	175
H2M2706N	177	179	181	183	185	187	189	191

H2M2707N	193	195	197	199	201	203	205	207
H2M2708N	209	211	213	215	217	219	221	223
H2M2709N	225	227	229	231	233	235	237	239
H2M2710N	241	243	245	247	249	251	253	255
H2M2711N	257	259	261	263	265	267	269	271
H2M2774N	273	275	277	279	281	283	285	287
H2M2775N	289	291	293	295	297	299	301	303
H2M2776N	305	307	309	311	313	315	317	319
H2M2777N	321	323	325	327	329	331	333	335
H2M2778N	337	339	341	343	345	347	349	351
H2M2779N	353	355	357	359	361	363	365	367
H2M2789N	369	371	373	375	377	379	381	383
H2M2862N	385	387	389	391	393	395	397	399
H2M2885N	401	403	405	407	409	411	413	415
H2M2886N	417	419	421	423	425	427	429	431
H2M3540N	433	435	437	439	441	443	445	447
H2M3541N	449	451	453	455	457	459	461	463
H2M3543N	465	467	469	471	473	475	477	479
H2M3547N	481	483	485	487	489	491	493	495
H2M3548N	497	499	501	503	505	507	509	511
H2M3563N	513	515	517	519	521	523	525	527
H1H5751P	529	531	533	535	537	539	541	543
H1H5752P	545	547	549	551	553	555	557	559
H1H5753B	561	563	565	567	569	571	573	575
H1H5754B	577	579	581	583	585	587	589	591
H1H5755B	593	595	597	599	601	603	605	607
H1H5756B	609	611	613	615	617	619	621	623
H1H5757B	625	627	629	631	633	635	637	639
H1H5758B	641	643	645	647	649	651	653	655
H1H5761P	657	659	661	663	665	667	669	671
H1H5763P	673	675	677	679	681	683	685	687
H1H5764P	689	691	693	695	697	699	701	703
H1H5769P	705	707	709	711	713	715	717	719
H1H5771P	721	723	725	727	729	731	733	735
H1H5772P	737	739	741	743	745	747	749	751
H1H5777P	753	755	757	759	761	763	765	767
H1H5778P	769	771	773	775	777	779	781	783
H1H5780P	785	787	789	791	793	795	797	799
H1H5781P	801	803	805	807	809	811	813	815
H1H5782P	817	819	821	823	825	827	829	831
H1H5785B	833	835	837	839	841	843	845	847
H1H5786B	849	851	853	855	857	859	861	863
H1H5788P	865	867	869	871	873	875	877	879
H1H5790B	881	883	885	887	889	891	893	895
H1H5791B	897	899	901	903	905	907	909	911
H1H5792B	913	915	917	919	921	923	925	927
H1H5793B	929	931	933	935	937	939	941	943
H1H5795B	945	947	949	951	953	955	957	959
H1H5796B	961	963	965	967	969	971	973	975
H1H5797B	977	979	981	983	985	987	989	991
H1H5798B	993	995	997	999	1001	1003	1005	1007
H1H5799P	1009	1011	1013	1015	1017	1019	1021	1023
H1H5801B	1025	1027	1029	1031	1033	1035	1037	1039
H1H7194B	1041	1043	1045	1047	1233	1235	1237	1239
H1H7195B	1049	1051	1053	1055	1233	1235	1237	1239

H1H7196B	1057	1059	1061	1063	1233	1235	1237	1239
H1H7198B	1065	1067	1069	1071	1233	1235	1237	1239
H1H7203B	1073	1075	1077	1079	1233	1235	1237	1239
H1H7204B	1081	1083	1085	1087	1233	1235	1237	1239
H1H7208B	1089	1091	1093	1095	1233	1235	1237	1239
H1H7211B	1097	1099	1101	1103	1233	1235	1237	1239
H1H7221B	1105	1107	1109	1111	1233	1235	1237	1239
H1H7223B	1113	1115	1117	1119	1233	1235	1237	1239
H1H7226B	1121	1123	1125	1127	1233	1235	1237	1239
H1H7232B	1129	1131	1133	1135	1233	1235	1237	1239
H1H7233B	1137	1139	1141	1143	1233	1235	1237	1239
H1H7241B	1145	1147	1149	1151	1233	1235	1237	1239
H1H7242B	1153	1155	1157	1159	1233	1235	1237	1239
H1H7250B	1161	1163	1165	1167	1233	1235	1237	1239
H1H7251B	1169	1171	1173	1175	1233	1235	1237	1239
H1H7254B	1177	1179	1181	1183	1233	1235	1237	1239
H1H7258B	1185	1187	1189	1191	1233	1235	1237	1239
H1H7269B	1193	1195	1197	1199	1233	1235	1237	1239
H1H7279B	1201	1203	1205	1207	1233	1235	1237	1239
H1xH7221G	1209	1211	1213	1215	1233	1235	1237	1239
H1xH7221G3	1217	1219	1221	1223	1233	1235	1237	1239
H1xH7221G5	1225	1227	1229	1231	1233	1235	1237	1239

[0175] Antibodies are typically referred to herein according to the following nomenclature: Fc prefix (*e.g.* "H1H," "H1M," "H2M," etc.), followed by a numerical identifier (*e.g.* "2712," "2692," etc., as shown in Table 1), followed by a "P," "N," or "B" suffix. Thus, according to this nomenclature, an antibody may be referred to herein as, *e.g.*, "H1H2712N," "H1M2692N," "H2M2689N," etc. The H1H, H1M and H2M prefixes on the antibody designations used herein indicate the particular Fc region isotype of the antibody. For example, an "H1H" antibody has a human IgG1 Fc, an "H1M" antibody has a mouse IgG1 Fc, and an "H2M" antibody has a mouse IgG2 Fc, (all variable regions are fully human as denoted by the first 'H' in the antibody designation). As will be appreciated by a person of ordinary skill in the art, an antibody having a particular Fc isotype can be converted to an antibody with a different Fc isotype (*e.g.*, an antibody with a mouse IgG1 Fc can be converted to an antibody with a human IgG4, etc.), but in any event, the variable domains (including the CDRs) – which are indicated by the numerical identifiers shown in Table 1 – will remain the same, and the binding properties are expected to be identical or substantially similar regardless of the nature of the Fc domain.

Control Constructs Used in the Following Examples

[0176] Various control constructs (anti-CD3 antibodies) were included in the following experiments for comparative purposes: "OKT-3," a mouse monoclonal antibody against human T-cell surface antigens available from the American Type Culture Collection (ATCC) under catalog no. CRL-8001; and "SP34," a commercially available mouse monoclonal antibody obtained from Biolegend, San Diego, CA (Cat. No. 302914), reactive against the epsilon chain of the T3 complex on human T lymphocyte cells.

Example 3. Surface Plasmon Resonance Derived Binding Affinities and Kinetic Constants of Human Monoclonal Anti-CD3 Antibodies

[0177] Binding affinities and kinetic constants of human monoclonal anti-CD3 antibodies were determined by surface plasmon resonance at 25°C using either an antibody-capture format (Tables 3, 5 and 7) or an antigen-capture format (Tables 4, 6 and 8). Measurements were conducted on a T200 Biacore instrument.

[0178] In the antibody-capture format, the Biacore sensor surface was derivatized with a rabbit anti-mouse Fc for hybridoma capture (antibody prefix H1M or H2M) or a mouse anti-human Fc surface for human IgG formatted antibodies (antibody prefix H1H). Soluble heterodimeric CD3 protein (hCD3-epsilon/hCD3-delta; SEQ ID NOs:1370/1371) with either a human Fc tag (hFcΔAdp/hFc; SEQ ID NOs:1372/1373) or a mouse Fc tag (mFcΔAdp/mFc; SEQ ID NOs:1374/1375) was injected over the antibody captured surface and the binding response was recorded. Heterodimeric CD3 protein was purified using the method described in Davis *et al.* (US2010/0331527).

[0179] In the antigen-capture format, heterodimeric CD3 protein was captured using a rabbit anti-mouse Fc or mouse anti-human Fc and the respective antibodies were injected over the captured antigen.

[0180] Antibodies were analyzed in their conventional divalent format (Tables 3 to 6) or in a monovalent 1-arm configuration (Tables 7 and 8) in which the second Fab from the antibody was removed and only the Fc portion (CH2-CH3) was expressed.

[0181] Kinetic association (k_a) and dissociation (k_d) rate constants were determined by processing and fitting the data to a 1:1 binding model using Scrubber 2.0 curve fitting software. Binding dissociation equilibrium constants (K_D) and dissociative half-lives ($t_{1/2}$) were calculated from the kinetic rate constants as: K_D (M) = k_d / k_a; and $t_{1/2}$ (min) = (ln2/(60*k_d). NT = not tested; NB = no binding observed.

Table 3: Biacore Binding Affinities of Hybridoma mAbs (H1M and H2M)

Binding at 25ºC / Antibody-Capture Format				
Antibody	**ka (Ms^{-1})**	**kd (s^{-1})**	**K_D (Molar)**	**T½ (min)**
H2M2689N	7.73E+05	3.23E-03	4.18E-09	4
H2M2690N	9.70E+03	2.02E-04	2.09E-08	57
H2M2691N	1.03E+04	2.07E-04	2.01E-08	56
H1M2692N	8.05E+03	4.34E-04	5.39E-08	27
H2M2704N	3.46E+04	6.92E-04	2.00E-08	17
H2M2705N	6.62E+04	9.10E-04	1.37E-08	13
H2M2706N	3.29E+04	4.44E-03	1.35E-07	3
H2M2707N	2.95E+04	1.87E-03	6.35E-08	6
H2M2708N	6.94E+04	6.12E-04	8.82E-09	19

H2M2709N	NT	NT	NT	NT
H2M2710N	6.72E+04	7.53E-04	1.12E-08	15
H2M2711N	6.72E+04	7.67E-04	1.14E-08	15
H1M2712N	9.32E+03	2.19E-04	2.35E-08	53
H2M2774N	7.79E+04	9.18E-04	1.18E-08	13
H2M2775N	6.97E+04	6.26E-04	8.98E-09	18
H2M2776N	6.29E+04	6.39E-04	1.02E-08	18
H2M2777N	3.70E+04	1.63E-03	4.39E-08	7
H2M2778N	2.13E+04	1.89E-04	8.90E-09	61
H2M2779N	2.18E+04	2.28E-04	1.05E-08	51
H2M2789N	NT	NT	NT	NT
H2M2862N	3.72E+04	3.00E-03	8.07E-08	4
H2M2885N	6.82E+04	6.51E-04	9.54E-09	18
H2M2886N	7.29E+04	6.53E-04	8.96E-09	18
H2M3540N	3.77E+04	6.11E-04	1.62E-08	19
H2M3541N	7.10E+03	1.35E-03	1.89E-07	9
H1M3542N	2.37E+04	5.08E-04	2.14E-08	23
H2M3543N	7.53E+03	2.26E-04	3.00E-08	51
H1M3544N	9.69E+03	1.42E-04	1.46E-08	82
H2M3547N	2.18E+04	3.47E-04	1.59E-08	33
H2M3548N	3.87E+04	5.04E-03	1.30E-07	2
H1M3549N	1.18E+04	9.19E-04	7.76E-08	13
H2M3563N	3.24E+04	1.19E-04	3.66E-09	97
H1M3613N	1.93E+04	3.04E-04	1.57E-08	38

Table 4: Biacore Binding Affinities of Hybridoma mAbs (H1M and H2M)

Binding at 25ºC / Antigen-Capture Format				
Antibody	**ka (Ms^{-1})**	**kd (s^{-1})**	**K_D (Molar)**	**T½ (min)**
H2M2689N	1.71E+06	9.97E-05	5.83E-11	116
H2M2690N	7.51E+04	6.35E-06	7.99E-11	1820
H2M2691N	3.94E+04	9.98E-06	2.54E-10	1158
H1M2692N	4.19E+04	9.90E-06	2.38E-10	1167
H2M2704N	1.32E+06	2.48E-04	1.87E-10	47
H2M2705N	2.43E+06	3.41E-04	1.40E-10	34
H2M2706N	5.63E+05	3.06E-04	5.44E-10	38
H2M2707N	3.99E+05	2.85E-04	7.15E-10	41
H2M2708N	1.73E+06	2.27E-04	1.31E-10	51
H2M2709N	NT	NT	NT	NT
H2M2710N	1.59E+06	2.43E-04	1.53E-10	48

H2M2711N	1.59E+06	2.40E-04	1.51E-10	48
H1M2712N	4.75E+04	1.37E-05	2.95E-10	846
H2M2774N	2.49E+06	3.36E-04	1.35E-10	34
H2M2775N	1.56E+06	2.16E-04	1.38E-10	53
H2M2776N	1.58E+06	2.22E-04	1.40E-10	52
H2M2777N	5.80E+05	3.21E-04	5.54E-10	36
H2M2778N	1.50E+05	6.57E-06	4.68E-11	1758
H2M2779N	1.28E+05	1.23E-05	9.38E-11	941
H2M2789N	NT	NT	NT	NT
H2M2862N	5.91E+05	3.21E-04	5.41E-10	36
H2M2885N	1.37E+06	1.52E-04	1.11E-10	76
H2M2886N	1.42E+06	1.36E-04	9.56E-11	85
H2M3540N	2.55E+06	5.87E-04	2.31E-10	20
H2M3541N	8.40E+04	1.16E-03	1.38E-08	10
H1M3542N	4.37E+05	2.00E-04	4.57E-10	58
H2M3543N	1.22E+05	7.96E-05	6.53E-10	145
H1M3544N	5.74E+04	5.98E-05	1.04E-09	193
H2M3547N	4.70E-05	1.00E-05	2.15E-11	1155
H2M3548N	NT	NT	NT	NT
H1M3549N	2.81E+05	2.89E-04	1.03E-09	40
H2M3563N	6.16E+05	4.77E-05	7.73E-11	242
H1M3613N	2.20E+05	9.60E-05	4.35E-10	120

Table 5: Biacore Binding Affinities of Human Fc mAbs (H1H)

Binding at 25ºC / Antibody-Capture Format				
Antibody	**ka (Ms^{-1})**	**kd (s^{-1})**	**K_D (Molar)**	**T½ (min)**
H1H2690N	NT	NT	NT	NT
H1H2712N	3.06E+03	2.70E-04	8.82E-08	43
H1H5751P	4.01E+03	5.18E-04	1.29E-07	22
H1H5752P	NB	NB	NB	NB
H1H5753B	NT	NT	NT	NT
H1H5755B	8.21E+03	4.72E-04	5.75E-08	24
H1H5756B	8.15E+03	2.66E-04	3.26E-08	43
H1H5757B	6.63E+03	7.85E-04	1.18E-07	15
H1H5758B	5.02E+03	1.17E-03	2.33E-07	10
H1H5761P	4.72E+03	2.44E-02	5.16E-06	0
H1H5763P	1.85E+04	5.40E-02	2.92E-06	0
H1H5764P	4.16E+03	1.59E-02	3.82E-06	1
H1H5769P	7.80E+03	9.41E-04	1.21E-07	12

H1H5771P	3.00E+04	6.26E-04	2.09E-08	18
H1H5772S	1.56E+04	1.55E-03	9.96E-08	7
H1H5777P	1.35E+04	3.02E-03	2.24E-07	4
H1H5778P	5.52E+03	1.54E-04	2.78E-08	75
H1H5780P	1.31E+04	3.99E-04	3.04E-08	29
H1H5781P	8.61E+03	4.97E-04	5.77E-08	23
H1H5782P	NB	NB	NB	NB
H1H5785B	NT	NT	NT	NT
H1H5786B	1.26E+04	1.08E-03	8.54E-08	11
H1H5788P	2.88E+03	2.91E-04	1.01E-07	40
H1H5790B	1.82E+04	5.17E-04	2.83E-08	22
H1H5791B	1.09E+04	7.90E-04	7.25E-08	15
H1H5792B	NT	NT	NT	NT
H1H5793B	8.54E+03	3.82E-04	4.47E-08	30
H1H5795B	1.73E+04	5.76E-04	3.33E-08	20
H1H5796B	1.47E+04	8.91E-04	6.05E-08	13
H1H5797B	NT	NT	NT	NT
H1H5798B	NT	NT	NT	NT
H1H5799P	1.36E+04	7.88E-03	5.79E-07	1
H1H5801B	6.57E+03	1.62E-03	2.46E-07	7
OKT3	2.10E+06	2.00E+00	1.00E-06	0.35 sec

Table 6: Biacore Binding Affinities of Human Fc mAbs (H1H)

Binding at 25ºC / Antigen-Capture Format				
Antibody	**ka (Ms^{-1})**	**kd (s^{-1})**	**K_D (Molar)**	**T½ (min)**
H1H2690N	NT	NT	NT	NT
H1H2712N	8.93E+04	8.68E-05	9.71E-10	133
H1H5751P	7.24E+04	2.47E-04	3.42E-09	47
H1H5752P	NB	NB	NB	NB
H1H5753B	NT	NT	NT	NT
H1H5755B	2.15E+05	2.01E-04	9.36E-10	57
H1H5756B	1.44E+05	1.11E-04	7.67E-10	105
H1H5757B	1.80E+05	2.95E-04	1.64E-09	39
H1H5758B	1.42E+05	5.62E-04	3.97E-09	21
H1H5761P	2.11E+05	1.13E-02	5.34E-08	1
H1H5763P	1.84E+05	1.70E-02	9.24E-08	1
H1H5764P	3.50E+05	7.36E-03	2.10E-08	2
H1H5769P	1.19E+05	5.23E-04	4.41E-09	22
H1H5771P	9.23E+05	3.42E-04	3.71E-10	34
H1H5772S	5.19E+05	8.69E-04	1.67E-09	13
H1H5777P	4.83E+05	1.70E-03	3.52E-09	7
H1H5778P	3.99E+05	3.42E-05	8.56E-11	338

H1H5780P	4.78E+05	1.71E-04	3.58E-10	68
H1H5781P	1.40E+05	2.68E-04	1.92E-09	43
H1H5782P	NB	NB	NB	NB
H1H5785B	NT	NT	NT	NT
H1H5786B	3.00E+06	4.24E-04	1.41E-10	27
H1H5788P	7.06E+04	1.64E-04	2.33E-09	70
H1H5790B	9.25E+05	2.36E-04	2.54E-10	49
H1H5791B	7.86E+05	3.40E-04	4.33E-10	34
H1H5792B	NT	NT	NT	NT
H1H5793B	4.78E+05	1.59E-04	3.33E-10	73
H1H5795B	1.58E+06	2.29E-04	1.45E-10	50
H1H5796B	1.05E+05	2.44E-04	2.32E-09	47
H1H5797B	NT	NT	NT	NT
H1H5798B	NT	NT	NT	NT
H1H5799P	7.18E+05	5.64E-03	7.85E-09	2
H1H5801B	3.31E+05	1.12E-03	3.38E-09	10
OKT3	3.94E+06	2.18E-02	5.53E-09	0.5

Table 7: Biacore Binding Affinities of monovalent 1-arm mAbs

Binding at 25°C / Antibody-Capture Format				
Antibody	**ka (Ms^{-1})**	**kd (s^{-1})**	**K_D (Molar)**	**T½ (min)**
H1H7194P	1.16E+04	1.51E-04	1.30E-08	76
H1H7195P	3.13E+04	9.89E-05	3.16E-09	117
H1H7196P	1.07E+04	4.43E-04	4.13E-08	26
H1H7198P	2.63E+04	1.58E-04	6.02E-09	73
H1H7203P	1.46E+04	2.67E-04	1.83E-08	43
H1H7204P	1.43E+04	3.62E-04	2.53E-08	32
H1H7208P	NT	NT	NT	NT
H1H7211P	1.41E+04	1.59E-04	1.13E-08	73
H1H7221P	1.07E+04	2.92E-04	2.75E-08	40
H1H7223P	1.60E+04	3.07E-04	1.92E-08	38
H1H7226P	1.30E+04	3.55E-04	2.72E-08	33
H1H7232P	8.03E+03	1.77E-03	2.20E-07	7
H1H7233P	1.11E+04	2.69E-04	2.42E-08	43
H1H7241P	1.34E+04	2.95E-04	2.20E-08	39
H1H7242P	2.15E+04	6.64E-04	3.09E-08	17
H1H7250P	2.34E+04	2.47E-04	1.05E-08	47
H1H7251P	2.56E+04	1.07E-03	4.17E-08	11
H1H7254P	2.60E+04	3.88E-04	1.49E-08	30
H1H7258P	1.26E+04	3.02E-04	2.40E-08	38
H1H7269P	2.57E+04	6.24E-03	2.43E-07	2
H1H7279P	NB	NB	NB	NB
H1xH7221G	NT	NT	NT	NT
H1xH7221G3	NB	NB	NB	NB
H1xH7221G5	NB	NB	NB	NB

Table 8: Biacore Binding Affinities of monovalent 1-arm mAbs

Binding at 25°C / Antigen-Capture Format				
Antibody	**ka (Ms^{-1})**	**kd (s^{-1})**	**K_D (Molar)**	**T½ (min)**
H1H7194P	3.50E+05	8.43E-05	2.41E-10	137
H1H7195P	5.66E+05	7.14E-05	1.26E-10	162
H1H7196P	1.85E+05	4.61E-04	2.49E-09	25
H1H7198P	6.28E+05	7.07E-05	1.12E-10	163
H1H7203P	4.79E+05	2.38E-04	4.98E-10	48
H1H7204P	1.73E+05	3.65E-04	2.12E-09	32
H1H7208P	NT	NT	NT	NT
H1H7211P	3.45E+05	9.61E-05	2.79E-10	120
H1H7221P	1.36E+05	2.39E-04	1.75E-09	48
H1H7223P	1.87E+05	2.86E-04	1.53E-09	40
H1H7226P	4.18E+05	2.36E-04	5.65E-10	49
H1H7232P	1.49E+05	1.49E-03	1.00E-08	8
H1H7233P	1.61E+05	2.04E-04	1.27E-09	57
H1H7241P	1.87E+05	2.36E-04	1.26E-09	49
H1H7242P	3.83E+05	1.01E-03	2.63E-09	11
H1H7250P	2.31E+05	1.89E-04	8.20E-10	61
H1H7251P	4.47E+05	1.19E-03	2.67E-09	10
H1H7254P	4.33E+05	3.30E-04	7.62E-10	35
H1H7258P	1.33E+05	2.90E-04	2.18E-09	40
H1H7269P	2.77E+05	6.89E-03	2.49E-08	2
H1H7279P	NB	NB	NB	NB
H1xH7221G	NT	NT	NT	NT
H1xH7221G3	NB	NB	NB	NB
H1xH7221G5	NB	NB	NB	NB

[0182] As shown in Tables 3-8, Several anti-CD3 antibodies of the present invention bind CD3, in either antibody-capture or antigen-capture formats, with high affinity.

Example 4. Anti-CD3 Antibodies Bind and Proliferate Human T-Cells

[0183] Anti-CD3 antibodies of the present invention were tested for their ability to bind to human T-cells and induce their proliferation. Binding was assessed using Jurkat cells (a CD3+ human T-cell line), while proliferation of Peripheral Blood Mononuclear Cells (PBMC) was assessed using ATP catalyzed quantification (CellTiter Glo®). Anti-CD3 antibody OKT3 acted as a positive control and irrelevant isotype matched antibodies served as negative controls.

[0184] FACS data was acquired using the following protocol: Cells at $2x10^5$ per well were incubated with serially diluted antibodies for 30 min on ice. Post incubation, cells were washed and secondary antibody was added and incubated for an additional 30 minutes. After incubation, cells were washed, re-suspended in cold PBS containing 1% BSA and analyzed by flow cytometry with viable Jurkat cells gated by side and forward scatters. The EC_{50}s for cell binding titration were determined using Prism software with values calculated using a 4-

parameter non-linear regression analysis.

[0185] Proliferation data was acquired using the following protocol: Human PBMC ($5x10^4$ / well) were incubated with a 3-fold serial dilution of anti-CD3 and a fixed concentration of a commercial anti-CD28 antibody (200ng/ml) in 96 well plates for 72 h at 37°C. Following incubation, CellTiter Glo® was added and luminescence was measured using a VICTOR X5 multi-label plate reader (PerkinElmer). The EC_{50} of cell viability (ATP catalyzed quantification) was calculated using a 4-parameter non-linear regression analysis in GraphPad Prism.

[0186] Results of the binding and proliferation experiments are summarized in Tables 9-11.

Table 9: Hybridoma Anti-CD3 mAbs Bind & Proliferate Human T-Cells

Antibody	EC50 [M] FACS JURKAT	EC50 [M] hPBMC Proliferation
H2M2689N	NB	0.00E+00
H2M2690N	4.37E-09	5.37E-12
H2M2691N	6.77E-09	3.43E-11
H1M2692N	5.99E-09	1.42E-10
H2M2704N	8.45E-10	2.93E-12
H2M2705N	2.96E-10	1.76E-11
H2M2706N	2.37E-09	3.86E-12
H2M2707N	1.24E-07	1.92E-12
H2M2708N	6.58E-10	2.69E-08
H2M2709N	7.11E-10	2.48E-11
H2M2710N	7.10E-10	2.11E-10
H2M2711N	1.16E-09	6.48E-10
H1M2712N	2.19E-08	1.28E-10
H2M2774N	3.52E-10	4.92E-10
H2M2775N	1.32E-09	1.09E-09
H2M2776N	4.91E-10	2.84E-11
H2M2777N	2.16E-09	2.51E-11
H2M2778N	3.62E-09	0.00E+00
H2M2779N	NT	0.00E+00
H2M2789N	NT	2.85E-08
H2M2862N	7.68E-09	6.72E-13
H2M2885N	2.09E-09	2.49E-12
H2M2886N	3.97E-09	2.69E-12
H2M3540N	3.99E-09	3.16E-12
H2M3541N	3.70E-09	6.40E-12
H1M3542N	2.01E-09	0.00E+00
H2M3543N	5.63E-09	6.12E-12
H1M3544N	2.32E-08	0.00E+00
H2M3547N	2.71E-09	5.02E-12
H2M3548N	1.10E-09	1.89E-12
H1M3549N	2.30E-09	0.00E+00
H2M3563N	1.07E-09	7.74E-12
H1M3613N	1.03E-08	0.00E+00

Isotype Ctrl	NB	0.00E+00

NB: No Binding; NT: Not Tested

Table 10: Human Fc Anti-CD3 mAbs Bind & Proliferate Human T-Cells

Antibody	EC50 [M] FACS JURKAT	EC50 [M] hPBMC Proliferation
H1H5751P	2.12E-09	9.29E-12
H1H5752P	3.43E-10	1.09E-12
H1H5753B	NB	9.14E-11
H1H5755B	1.23E-09	4.24E-12
H1H5756B	NB	0.00E+00
H1H5757B	3.38E-09	4.86E-12
H1H5758B	1.90E-09	2.13E-12
H1H5761P	2.10E-09	3.62E-13
H1H5763P	2.76E-09	3.11E-13
H1H5764P	8.80E-10	3.27E-13
H1H5769P	4.10E-09	6.17E-12
H1H5771P	NT	6.35E-12
H1H5772S	6.64E-10	4.42E-12
H1H5777P	5.71E-10	3.04E-12
H1H5778P	6.85E-10	5.04E-12
H1H5780P	7.62E-10	3.44E-12
H1H5781P	1.23E-09	6.08E-12
H1H5782P	NB	5.17E-12
H1H5785B	NB	0.00E+00
H1H5786B	1.10E-09	1.79E-12
H1H5788P	3.53E-09	4.62E-12
H1H5790B	3.55E-09	2.71E-12
H1H5791B	3.77E-09	1.75E-12
H1H5792B	5.87E-09	6.47E-12
H1H5793B	4.62E-09	3.28E-12
H1H5795B	2.04E-09	3.09E-12
H1H5796B	9.82E-09	4.37E-12
H1H5797B	3.96E-08	1.07E-11
H1H5798B	5.57E-09	2.59E-12
H1H5799P	NT	1.63E-13
H1H5801B	1.55E-08	1.09E-12
OKT3	1.96E-10	3.30E-13
Isotype Ctrl	NB	0.00E+00

NB: No Binding; NT: Not Tested

Table 11: Monovalent 1-arm Anti-CD3 mAbs Bind & Proliferate Human T-Cells

Antibody	EC50 [M] FACS JURKAT	EC50 [M] hPBMC Proliferation
H1H7194P	1.50E-09	2.37E-12
H1H7195P	3.42E-10	2.42E-12
H1H7196P	3.44E-08	1.27E-12

H1H7198P	7.26E-10	2.55E-12
H1H7203P	3.24E-09	1.64E-12
H1H7204P	2.29E-09	1.51E-12
H1H7208P	5.19E-08	1.46E-12
H1H7211P	7.01E-10	2.75E-12
H1H7221P	1.40E-09	2.60E-12
H1H7223P	9.37E-10	1.07E-12
H1H7226P	7.95E-10	9.52E-13
H1H7232P	1.50E-09	1.03E-12
H1H7233P	7.15E-10	7.34E-13
H1H7241P	1.01E-09	1.05E-12
H1H7242P	1.83E-09	2.13E-12
H1H7250P	1.37E-09	2.43E-12
H1H7251P	1.45E-09	1.30E-12
H1H7254P	1.09E-09	2.80E-12
H1H7258P	1.07E-09	2.17E-12
H1H7269P	1.95E-09	1.15E-12
H1H7279P	NB	0.00E+00
Isotype Ctrl	NB	0.00E+00

NB: No Binding; NT: Not Tested

[0187] As shown in Tables 7-9, the vast majority of anti-CD3 antibodies of the invention bound human T-cells and induced T-cell proliferation.

Example 5. Anti-CD3 Antibodies Bind and Proliferate Monkey T-Cells

[0188] A subset of anti-CD3 antibodies of the invention was tested for the ability to bind to and induce proliferation of monkey T-cells.

[0189] FACS data was acquired using the following protocol: Cells at $2x10^5$ per well were incubated with serially diluted antibodies for 30 min on ice. Post incubation, cells were washed and secondary antibodies were added and incubated for an additional 30 minutes. After incubation, cells were washed, re-suspended in cold PBS containing 1% BSA and analyzed by flow cytometry. CD4+ monkey T cells were gated by side and forward scatters, and on the CD2+CD4+CD20- population. The EC_{50}s for cell binding titration were calculated using a 4-parameter non-linear regression analysis in GraphPad Prism.

[0190] Proliferation data was acquired using the following protocol: Freshly isolated cynomolgus monkey derived PBMC ($5x10^4$ / well) were incubated with a 3-fold serial dilution of anti-CD3 antibody and a fixed concentration of a commercial anti-CD28 antibody (500 ng/ml) antibody in 96 well plates for 72 h at 37°C. Following incubation, CellTiter Glo® was added and luminescence was measured using a VICTOR X5 multi-label plate reader (PerkinElmer). The EC_{50} of cell viability (ATP catalyzed quantification) was calculated using a 4-parameter non-linear regression analysis in GraphPad Prism.

[0191] Results of the binding and proliferation experiments are summarized in Tables 12 and 13.

Table 12: Anti-CD3 mAbs Bind & Proliferate monkey PBMCs

Antibody	EC50 [M] FACS PBMCs	EC50 [M] mfPBMC Proliferation
H1H2690N	5.66E-09	2.71E-12
H1H2712N	2.29E-09	2.72E-12
H2M3547N	1.12E-10	NT
H2M3563N	1.65E-10	NT
H1H5761P	NT	2.81E-09
H1H5763P	NT	0.00E+00
H1H5764P	NT	4.06E-10
H1H5769P	NT	8.33E-13
H1H5771P	NT	2.74E-12
H1H5772S	NT	1.47E-12
H1H5778P	NT	5.93E-13
H1H5780P	NT	3.13E-13
H1H5781P	NT	7.92E-13
H1H5788P	NT	2.01E-12
OKT3	NB	NT
SP34	7.03E-11	1.71E-12

NB: No Binding; NT: not tested

Table 13: Monovalent 1-arm Anti-CD3 mAbs Bind & Proliferate Monkey PBMCs

Antibody	EC50 [M] FACS PBMCs	EC50 [M] mfPBMC Proliferation
H1H7194P	NT	4.84E-12
H1H7195P	NT	1.36E-12
H1H7196P	NT	1.40E-08
H1H7198P	NT	2.29E-12
H1H7203P	NT	4.97E-13
H1H7204P	NT	1.26E-11
H1H7208P	NT	7.02E-12
H1H7211P	NT	2.81E-13
H1H7221P	NT	1.72E-12
H1H7223P	NT	6.75E-11
H1H7226P	NT	2.26E-11
H1H7232P	NT	4.90E-11
H1H7233P	NT	4.35E-12
H1H7241P	NT	2.05E-11
H1H7242P	NT	1.38E-11
H1H7250P	NT	7.27E-11
H1H7251P	NT	1.83E-11
H1H7254P	NT	8.88E-11
H1H7258P	NT	1.11E-11

NB: No Binding; NT: not tested

[0192] As shown in Tables 12 and 13, several anti-CD3 antibodies of the invention bound

CD2+CD4+ monkey T-cells and induced their proliferation. OKT3 did not drive monkey PBMC proliferation, while SP34 was active against monkey PBMCs.

Example 6. Anti-CD3 mAbs Support T-Cell-Mediated Killing of Tumor Cells

[0193] The ability of anti-CD3 antibodies to redirect T-cell mediated killing via Fc/FcR interactions was studied using a calcein based U937 killing assay. Briefly, human PBMC were isolated over Ficoll-Paque and activated over a course of several days with media containing human IL-2 (30 U/ml) and T-cell activation beads (anti-CD3/CD28). U937 cells were labeled with calcein, and then incubated with activated T-cells at a 10:1 effector: target ratio using 3-fold serial dilutions of antibodies over a course of 3 hours at 37°C. Following incubation, the plates were centrifuged and supernatants were transferred to a translucent black clear bottom plate for fluorescence analysis. EC_{50} values, defined as the molar concentration of CD3 antibody that induces 50% cytotoxicity, were calculated using a 4-parameter non-linear regression analysis in GraphPad Prism. Results using hybridoma antibodies, human Fc antibodies, and monovalent one-arm antibodies are shown in Tables 14, 15 and 16, respectively.

Table 14: Hybridoma Anti-CD3 mAbs Redirect T-Cell Killing to U937 Cells

Antibody	U937 Cytotoxicity Human T-cells [M]
H2M2689N	0.00E+00
H2M2690N	2.79E-11
H2M2691N	2.34E-11
H1M2692N	3.59E-10
H2M2704N	2.49E-12
H2M2705N	1.73E-12
H2M2706N	7.91E-12
H2M2707N	7.21E-12
H2M2708N	3.27E-12
H2M2709N	3.47E-12
H2M2710N	3.97E-12
H2M2711N	3.66E-12
H1M2712N	3.14E-10
H2M2774N	2.46E-12
H2M2775N	3.38E-12
H2M2776N	4.06E-12
H2M2777N	4.86E-12
H2M2778N	0.00E+00
H2M2779N	6.75E-10
H2M2789N	NT
H2M2862N	7.66E-12
H2M2885N	3.71E-12
H2M2886N	8.06E-12
H2M3540N	1.25E-11
H2M3541N	5.39E-11

H1M3542N	2.92E-11
H2M3543N	1.31E-11
H1M3544N	1.72E-10
H2M3547N	3.17E-11
H2M3548N	5.50E-12
H1M3549N	1.07E-10
H2M3563N	4.05E-11
H1M3613N	8.66E-10
Isotype Ctrl	0.00E+00

NT: Not Tested

Table 15: Human Fc formatted Anti-CD3 mAbs Redirect T-Cell Killing to U937 Cells

Antibody	U937 Cytotoxicity Human T-cells [M]
H1H5751P	1.30E-10
H1H5752P	1.85E-11
H1H5753B	3.79E-10
H1H5755B	5.16E-11
H1H5756B	7.69E-11
H1H5757B	9.65E-11
H1H5758B	8.86E-08
H1H5761P	2.00E-12
H1H5763P	NT
H1H5764P	NT
H1H5769P	5.65E-11
H1H5771P	NT
H1H5772S	6.89E-13
H1H5777P	4.87E-13
H1H5778P	3.41E-13
H1H5780P	4.03E-12
H1H5781P	1.83E-12
H1H5782P	5.18E-12
H1H5785B	4.43E-11
H1H5786B	6.10E-11
H1H5788P	1.54E-11
H1H5790B	8.71E-11
H1H5791B	8.01E-11
H1H5792B	1.40E-10
H1H5793B	8.85E-11
H1H5795B	6.74E-11
H1H5796B	5.03E-10
H1H5797B	5.76E-10
H1H5798B	1.81E-10
H1H5799P	NT
H1H5801B	9.23E-11
OKT3	2.35E-12
Isotype Ctrl	0.00E+00

NT: Not Tested

Table 16: Monovalent 1-arm Anti-CD3 mAbs Redirect T-Cell Killing to U937 Cells

Antibody	U937 Cytotoxicity Human T-cells [M]
H1H7194P	4.71E-12
H1H7195P	6.10E-12
H1H7196P	1.96E-11
H1H7198P	5.21E-12
H1H7203P	5.47E-12
H1H7204P	1.08E-11
H1H7208P	4.59E-11
H1H7211P	7.89E-12
H1H7221P	9.21E-12
H1H7223P	5.30E-12
H1H7226P	1.04E-11
H1H7232P	9.96E-12
H1H7233P	1.19E-11
H1H7241P	1.23E-11
H1H7242P	7.50E-12
H1H7250P	5.91E-12
H1H7251P	1.81E-12
H1H7254P	4.18E-12
H1H7258P	1.53E-11
H1H7269P	1.08E-11
H1H7279P	0.00E+00
Isotype Ctrl	0.00E+00

NT: Not Tested

As shown in Tables 14-16, most anti-CD3 antibodies, as well as OKT3, supported redirected T-cell mediated killing in this assay system. The observed killing, believed to be dependent on the antibody's Fc engagement with the Fc Receptor on U937 cells leading to clustering of CD3 on adjacent T-cells, was squelched by addition of non-specific human IgG (data not shown).

Example 7. Generation of Bispecific Antibodies that Bind CD3 and CD20

[0194] Bispecific antibodies comprising an anti-CD3-specific binding domain and an anti-CD20-specific binding domain were constructed using standard methodologies wherein a heavy chain and a light chain from an anti-CD3 antibody were combined with a heavy chain from an anti-CD20 antibody. The anti-CD3 antibodies used to construct the bispecific antibodies of this example were obtained by immunizing a VelocImmune® mouse with cells expressing CD3 or with DNA encoding CD3, or in the case of BS3/20-007 and -009, from a known anti-CD3 antibody (*i.e.*, the anti-CD3 antibody "L2K" as set forth in WO2004/106380). The anti-CD20 antibodies used to construct the bispecific antibodies of this example are as set forth in US 7,879,984.

[0195] The bispecific antibodies created in accordance with the present Example comprise two separate antigen-binding domains (*i.e.*, binding arms). The first antigen-binding domain comprises a heavy chain variable region derived from an anti-CD20 antibody ("CD20-VH"), paired with a light chain variable region derived from an anti-CD3 antibody ("CD3-VL"). The CD20-VH/CD3-VL pairing creates an antigen-binding domain that specifically recognizes CD20. The second antigen-binding domain comprises a heavy chain variable region derived from an anti-CD3 antibody ("CD3-VH"), paired with a light chain variable region derived from an anti-CD3 antibody ("CD3-VL"). The CD3-VH/CD3-VL pairing creates an antigen-binding domain that specifically recognizes CD3. The same CD20-VH was used in all bispecific antibodies created in this example and is designated "CD20-VH-A" (except for BS3/20-009, which used a different CD20-VH called "CD20-VH-B"). However, several different CD3-VH and CD3-VL components (designated "CD3-VH-A, CD3-VH-B, etc. and CD3-VL-A, CD3-VL-B, etc., derived from different anti-CD3 antibodies) were used in the different bispecific antibodies of the following Examples.

[0196] A summary of the component parts of the antigen-binding domains of the various bispecific antibodies made in accordance with this Example is set forth in Table 17.

Table 17

Bispecific Antibody Identifier	Anti-CD20 Antigen-Binding Domain		Anti-CD3 Antigen-Binding Domain	
	Heavy Chain Variable Region	Light Chain Variable Region	Heavy Chain Variable Region	Light Chain Variable Region
BS3/20-001	CD20-VH-A	CD3-VL-A	CD3-VH-A	CD3-VL-A
BS3/20-002	CD20-VH-A	CD3-VL-B	CD3-VH-B	CD3-VL-B
BS3/20-003	CD20-VH-A	CD3-VL-C	CD3-VH-C	CD3-VL-C
BS3/20-004	CD20-VH-A	CD3-VL-D	CD3-VH-D	CD3-VL-D
BS3/20-005	CD20-VH-A	CD3-VL-E	CD3-VH-E	CD3-VL-E
BS3/20-007	CD20-VH-A	CD3-VL-F[#]	CD3-VH-F[#]	CD3-VL-F[#]
BS3/20-009*	CD20-VH-B	CD3-VL-F[#]	CD3-VH-F[#]	CD3-VL-F[#]

[#] The heavy and light chain variable regions of CD3-VH-F and CD3-VL-F were derived from the anti-CD3 antibody designated "L2K" as set forth in WO2004/106380.

* The anti-CD20 arm of BS3/20-009, comprising the CD20-VH-B/CD3-VL-F pairing, is non-functional; *i.e.*, it does not bind CD20. However, the anti-CD3 arm (comprising the CD3-VH-F/CD3-VL-F pairing) specifically binds CD3. Thus, BS3/20-009 retains the same general "bispecific" structure of the other bispecific molecules generated in this example, but it only binds CD3.

[0197] Tables 18 and 19 set out the amino acid sequence identifiers for the various heavy chain variable regions (Table 18) and light chain variable regions (Table 19), and their corresponding CDRs, of the bispecific antibodies of this Example.

Table 18 (Heavy Chain Variable Region Amino Acid Sequences)

	SEQ ID NOs			
Heavy Chain Identifier	HCVR	HCDR1	HCDR2	HCDR3
CD20-VH-A	1242	1244	1246	1248
CD20-VH-B	1338	1340	1342	1344
CD3-VH-A	1250	1252	1254	1256

CD3-VH-B	1266	1268	1270	1272
CD3-VH-C	1282	1284	1286	1288
CD3-VH-D	1298	1300	1302	1304
CD3-VH-E	1314	1316	1318	1320
CD3-VH-F	1329	1330	1331	1332

Table 19 (Light Chain Variable Region Amino Acid Sequences)

	SEQ ID NOs			
Light Chain Identifier	**LCVR**	**LCDR1**	**LCDR2**	**LCDR3**
CD3-VL-A	1258	1260	1262	1264
CD3-VL-B	1274	1276	1278	1280
CD3-VL-C	1290	1292	1294	1296
CD3-VL-D	1306	1308	1310	1312
CD3-VL-E	1322	1324	1326	1328
CD3-VL-F	1333	1334	1335	1336

[0198] In addition, Tables 20 and 21 set out the sequence identifiers for the nucleotide sequences encoding the heavy chain variable regions (Table 20) and light chain variable regions (Table 21), and their corresponding CDRs, of the bispecific antibodies of this Example.

Table 20 (Nucleotide Sequences Encoding Heavy Chain Variable Region Sequences)

	SEQ ID NOs			
Heavy Chain Identifier	**HCVR**	**HCDR1**	**HCDR2**	**HCDR3**
CD20-VH-A	1241	1243	1245	1247
CD20-VH-B	1337	1339	1341	1343
CD3-VH-A	1249	1251	1253	1255
CD3-VH-B	1265	1267	1269	1271
CD3-VH-C	1281	1283	1285	1287
CD3-VH-D	1297	1299	1301	1303
CD3-VH-E	1313	1315	1317	1319

Table 21 (Nucleotide Sequences Encoding Light Chain Variable Region Sequences)

	SEQ ID NOs			
Light Chain Identifier	**LCVR**	**LCDR1**	**LCDR2**	**LCDR3**
CD3-VL-A	1257	1259	1261	1263
CD3-VL-B	1273	1275	1277	1279
CD3-VL-C	1289	1291	1293	1295
CD3-VL-D	1305	1307	1309	1311
CD3-VL-E	1321	1323	1325	1327

[0199] In addition to the bispecific antibodies described above, the following control antibodies were also used in certain of the experiments set out in the Examples that follow:

[0200] Control I: Monoclonal antibody "OKT-3" against human T-cell surface antigens as set forth in US 4,361,549 and available from hybridoma CRL-8001 (American Type Culture Collection, Manassas, VA).

[0201] Control II: Antibody "SP34" reactive against the epsilon chain of the T3 complex on human T lymphocyte cells, available from BD Pharmagen, Cat # 55052.

[0202] Control III: anti-CD20 therapeutic antibody, with heavy and light chain sequences of Rituxan (Rituximab) as disclosed in US 5,736,137.

[0203] Control IV: Monoclonal anti-CD20 antibody designated "3B9-10" as disclosed in US 7,879,984, and set forth herein as an antibody comprising the HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 1242/1346 and HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 amino acid sequences of SEQ ID NOs: 1244-1246-1248-1348-1350-1352.

[0204] Control V: Monoclonal anti-CD20 antibody designated "10F2-13" as disclosed in US 7,879,984, and set forth herein as an antibody comprising the HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 1354/1362 and HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 amino acid sequences of SEQ ID NOs: 1356-1358-1360-1364-1366-1368.

Example 8. CD20 x CD3 Bispecific Antibodies Selectively Bind Jurkat, Raji and Monkey T-Cells

[0205] CD20 x CD3 bispecific antibodies and Control constructs, as set forth in Example 1, were tested via FACS for their ability to bind to Jurkat (CD3+, CD20 - human T-cell line), Raji (CD3-, CD20+ Human B-cell line), or cynomolgus PBMCs ("mkT cells").

[0206] FACS data was acquired using the following protocol: Cells at $2x10^5$ per well were incubated with serially diluted antibodies for 30 min on ice. Post incubation, cells were washed and appropriate secondary (Jurkat, RAJI cells) or cocktail of secondary antibodies (for cyno PBMC) was added and incubated for an additional 30 minutes. After incubation, cells were washed, re-suspended in cold PBS containing 1% BSA and analyzed by flow cytometry on a BD FACS Canto II. Jurkat and Raji cells were gated by side and forward scatters, while cynomolgus T cells were also gated in a CD2+CD4+ population. The EC_{50}s for cell binding titration were determined using Prism software with values calculated using a 4-parameter non-linear regression analysis. Results are shown in Table 22.

Table 22. EC50 Binding Values (Molar) for CD3xCD20 Bispecific Antibodies

Antibody	FACS – Jurkat	FACS – RAJI	FACS – mkT cells
Control I (anti-CD3)	1.96E-10	NB	NB
Control II (anti-CD3)	(+)	NB	7.03E-11
Control IV (anti-CD20)	No Binding	(+)	NB
BS3/20-001	3.85E-08	5.99E-08	8.74E-06
BS3/20-002	5.62E-08	1.15E-08	NT
BS3/20-003	5.67E-08	9.24E-08	2.48E-08
BS3/20-004	4.89E-08	1.02E-08	NT
BS3/20-005	1.95E-09	8.17E-08	NT

(+) EC_{50} values not determined, but binding observed; NB no binding; NT not tested

[0207] As shown in Table 22, the panel of tested antibodies showed a range of binding affinities on the various cell lines, depending on their specificities. Bispecific antibodies (BS3/20-001, -002, -003, -004 and -005) showed the ability to bind both human target lines. A subset of antibodies also showed the ability to bind to cynomolgus cells (Control II, BS3/20-001 and BS3/20-003). Anti-CD3 Control I (OKT3), anti-CD3 Control II (SP34), and anti-CD20 Control IV bound to Jurkat, cynomolgus T cells, and RAJI, respectively.

Example 9. CD20 x CD3 Bispecific Antibodies Induce PBMC Proliferation *in vitro*

[0208] The ability of selected CD20 x CD3 bispecific antibodies and Control constructs to stimulate Peripheral Blood Mononuclear Cells (PBMC) and induce proliferation was assessed using ATP catalyzed quantification (CellTiter Glo®). The activation of PBMCs results in the release of cytokines, which drive cellular proliferation.

[0209] Proliferation data was acquired using the following protocol: Human or cynomolgus monkey derived PBMC ($5x10^5$/ well) were incubated with a 3-fold serial dilution of anti-CD3xCD20 or Control antibody in 96 well plates for 72 h at 37°C. Following incubation, CellTiter Glo® was added and luminescence was measured using a VICTOR X5 multi-label plate reader (PerkinElmer). The EC_{50} of cell viability (ATP catalyzed quantification) was determined using Prism software. Values were calculated using a 4-parameter non-linear regression analysis and are shown in Table 23.

Table 23. EC_{50}s for human and cynomolgus PBMC proliferation induced by anti-CD20 x CD3 bispecific antibodies

Antibody	Human PBMC Proliferation EC_{50} [M]	Cyno PBMC Proliferation EC_{50} [M]
Control I	3.30E-13	NA
Control II	8.93E-12	1.71E-12
BS3/20-001	1.08E-11*	4.02E-11*
BS3/20-002	8.59E-12*	2.60E-11*
BS3/20-003	9.55E-12*	2.78E-11*
BS3/20-004	1.45E-12*	NT
BS3/20-005	1.05E-12*	NT

(*) Data are median values of 3 or more independent assays. Data without a (*) are representative/average values of 1 or 2 independent assays. NA = no activity; NT = not tested.

[0210] As shown in Table 23, all CD20 x CD3 bispecific antibodies of the invention were activators of human or cynomolgus PBMCs. In general, anti-CD3 mono specific bivalent parental antibodies (Contros I and II) were 2-10 fold more potent than the bispecific counterparts. Control I (OKT3) did not drive monkey PBMC proliferation, while Control II (SP34) was active against both human and monkey PBMCs.

Example 10. CD20 x CD3 Bispecific Antibodies Activate T-cells and Induce IFN-gamma Release and CD25 Upregulation in Human Whole Blood

[0211] Selected CD20 x CD3 bispecific antibodies were tested for their ability to activate T-cells in human whole blood. The extent of T-cell activation was determined by measuring interferon-gamma (IFNγ) secretion as well as the upregulation of CD25 on CD8+ T cells.

[0212] Interferon-gamma (IFNγ) secretion was quantified by combining heparinized whole blood with 5-fold serial dilutions of bispecific antibodies in 96-well plates. After 20 hours, the plates were centrifuged for 5 minutes and plasma was removed for ELISA analysis to determine IFNγ levels. Extrapolated IFNγ concentrations were plotted versus antibody concentration, and EC_{50} values were calculated using a 4-parameter non-linear regression analysis using Prism software.

[0213] For analysis of CD25 expression on CD8+ T-cells, following incubation with antibodies and removal of plasma, 150 μl of blood was transferred to a deep well plate and lysed for 15 minutes with 1.5 mL RBC lysis buffer. Cells were washed twice, blocked for 10 minutes at room temperature with hFcR blocking reagent, and then incubated for 30 min at 4°C with antibodies conjugated directly to CD2, CD19, CD4, CD8, and CD25. Next, cells were washed twice before analysis with a FACSCanto cytometer and FlowJo software.

[0214] The percentage of CD2+CD8+ T cells expressing the activation marker CD25 was plotted versus antibody concentration, and EC_{50} values were calculated using a 4-parameter non-linear regression analysis using Prism software. Results are shown in Table 24.

Table 24: EC_{50} values of Bispecific antibody mediated upregulation of CD25 and IFNγ production in whole blood

Bispecific Antibody	EC_{50} of CD25 Upregulation [M]	EC_{50} of IFNγ Production [M]	Max IFNγ (pg/mL)
BS3/20-001	1.3E-10	3.9E-10	1815
BS3/20-003	1.7E-10	5.7E-10	1693
BS3/20-004	2.9E-10	2.3E-09	5810

Median values of at least 3 independent experiments (except IFN-gamma expression of BS3/20-003, which is n=2)

[0215] As shown in Table 24, the CD20 x CD3 bispecific antibodies mediated the upregulation of CD25 on CD8+ T cells in whole blood with EC_{50} values ranging from 130-290 pM with corresponding EC_{50} values for IFNγ that were slightly higher ranging from 390 pM to 2 nM. BS3/20-004 was less slightly less potent then BS3/20-001 and BS3/20-003 in mediating CD25 upregulation and IFNγ production as determined by EC_{50}, however BS3/20-004 could induce greater levels of IFNγ in whole blood cultures.

Example 11. CD20 x CD3 Bispecific Antibodies Induce T-cell Mediated Cytotoxicity on Rituximab Resistant Cell Lines

[0216] The ability of selected CD20 x CD3 bispecific antibodies and Control constructs to mediate complement-dependent cytotoxicity (CDC) and T-cell mediated cytotoxicity was evaluated using parental Raji cells and Raji SCID lines. The later (Raji SCID lines) were derived from individual anti-CD20 resistant tumors isolated from immunodeficient mice injected subcutaneously with Raji cells following treatment with the anti-CD20 mAb Rituximab. Four lines (Raji SCID 1-4) were used in this Example.

[0217] The expression of CD20 and the complement inhibitory molecules CD55 and CD59 on Raji cell lines was determined by FACS. Briefly, $1x10^6$ cells were incubated in individual tubes for 30 minutes with antibodies directly conjugated to CD20, CD55 and CD59. Cells were washed twice before FACS acquisition by a FACSCanto cytometer and analysis with FlowJo software.

[0218] To determine the ability of anti-CD20 and anti-CD3xCD20 antibodies to mediate T-cell directed killing of Raji cell lines, calcein labeled Raji cells were incubated for 2 hours at 37°C with pre-activated T cells (ficoll-isolated human PBMC activated with rhIL-2 (30U/mL) and anti-CD3/CD28 activation beads) and 3-fold serial dilutions of antibodies starting at 2 nM. Following incubation, plates were centrifuged and supernatants were transferred to a translucent black clear bottom plate for 530nm fluorescence detection at 485nm emission. Percent cytotoxicity was determined based on spontaneous (target cells alone) and maximum release (target cells lysed with detergent) values. EC_{50} values were calculated using a 4-parameter non-linear regression analysis using Prism software.

[0219] To determine the activity of the antibodies to mediate CDC, Raji cell lines were incubated with 5% normal human serum complement and 3-fold serial dilutions of antibodies starting at 100 nM. After incubation for 4.5 hours at 37C, cell death was determined using CellTiter Glo®. Percent cytotoxicity was determined based on spontaneous (target cells alone) and maximum release (target cells lysed with detergent) values. EC_{50} values were calculated using a 4-parameter non-linear regression analysis using Prism software.

[0220] Results are shown in Table 25.

Table 25. EC50 values for antibody mediated CDC and T-cell mediated cytotoxicity

			CDC			T-Cell Mediated Cytotoxicity	
Cell Line	**CD20 MFI**	**% CD55/ CD59+**	**BS3/20-007**	**Control IV (anti-CD20)**	**Control III (anti-CD20)**	**BS3/20-007**	**Control IV (anti-CD20)**
Raji	1709	8.81	2.62E-09	2.47E-10	9.66E-11	1.66E-12	No Activity
Raji SCID1	570	80.7	1.01E-07	5.19E-08	8.56E-08	1.11E-12	No Activity
Raji SCID2	1373	9.1	8.83E-09	2.29E-10	5.87E-11	6.52E-13	No Activity
Raji SCID3	1151	97.3	3.77E-08	5.71E-09	2.55E-08	2.93E-13	No Activity
Raji SCID4	1717	64.6	1.40E-07	1.14E-09	5.29E-09	1.53E-12	No Activity

[0221] Compared to parental Raji cells, 2 of 4 Raji SCID lines showed reduced expression of CD20 (Table 25; lines Raji SCID 1 and 3), with significantly higher percentage of cells expressing the complement inhibitory molecules CD55 and CD59. The sensitivity of the Raji SCID cells to CDC mediated by either anti-CD20 or anti-CD20 x CD3 antibodies was dependent on the percentage of CD55/CD59 expressing cells, but not on the levels of CD20, such that increased expression of CD55/CD59 on target cells inhibited CDC.

[0222] The anti-CD20 antibodies (Control IV & Control III [Rituximab]) were more potent than the anti-CD20 x CD3 (BS3/20-007) in mediating CDC, as the bispecific is monovalent for CD20.

However, in contrast to CDC, T-cell mediated cytotoxicity was not dependent on CD20 or CD55/CD59 levels, as all cell lines were equally susceptible to cell death by activated T-cells in the presence of anti-CD20 x CD3 bispecific antibody. Additionally, the bispecific antibody was 100-1000 fold more potent in mediating T-cell dependent killing of Raji cells than the anti-CD20 antibody in the CDC assay.

Example 12. CD25 Upregulation on CD8+ T-cells is Dependent on CD20 Concentration when in the Presence of CD20 x CD3 Bispecific Antibodies

[0223] To evaluate if higher concentrations of target cell (CD20+ lymphomas) would lead to an increased potency of CD20 x CD3 bispecific antibodies, human peripheral blood mononuclear cells (PBMCs) were co-cultured in the presence of a Burkitt's lymphoma-derived cell line, *i.e.*, Raji.

[0224] CD25 upregulation on CD8+ T-cells was determined using the following protocol: Human PBMCs ($5x10^5$/mL), isolated via centrifugation of mononuclear-cell enriched leukapharesis-derived blood over Ficoll, were incubated in the presence ($1x10^5$/mL) or absence of Raji cells, at 37°C in 96-well flat bottom plates with 5-fold serial dilutions of the bispecific antibodies. After 48 hours, cells were washed 2x, blocked for 10 minutes at room temperature with hFcR blocking reagent, and then incubated for 30 minutes at 4°C with directly conjugated antibodies to CD2, CD19, CD4, CD8, and CD25. After staining, cells were washed twice before FACS acquisition by a FACSCanto cytometer and analysis with FlowJo software. The percentage of activated CD2+CD8+ T cells expressing CD25 was plotted versus antibody concentration, and EC_{50} values were calculated using a 4-parameter non-linear regression analysis using Prism software. Results are shown in Table 26.

Table 26. CD25 upregulation on CD8+ T-cells following incubation of human PBMC with CD20 x CD3 bispecific antibodies plus or minus Raji cells

	PBMC		PBMC + Raji	
Antibody	**EC_{50} (M)**	**Max % CD25+**	**EC_{50} (M)**	**Max % CD25+**
BS3/20-001	1.12E-10	14.2	1.35E-12	92.2
BS3/20-003	3.65E-10	21.1	3.38E-13	94.4

[0225] As shown in Table 26, activated T-cells when cultured in the presence of Raji (target) cells showed an upregulation of CD25, and a subsequent 100-fold decrease in their EC_{50} values.

Example 13. CD20 x CD3 Bispecific Antibodies Induce Cytotoxicity to Raji cells in the Presence of Activated T-cells

[0226] The ability of CD20 x CD3 bispecific antibodies to redirect T-cell mediated killing to CD20-expressing Raji cells was tested in an *in vitro* cytotoxicity assay. In addition, the ability of both bispecific and parental anti-CD3 antibodies to kill U937 cells via Fc/FcR interactions was also studied.

[0227] Calcein killing assays were carried out using the following protocol: Human and cynomolgus PBMC were isolated over ficoll-Plaque or via Lympholyte Mammal cell separation media, respectively. The isolated PBMCs were activated over a course of several days with media containing recombinant human IL-2 (30U/ml) and T-cell activation beads (anti-CD3/CD28 for human PBMC, anti-CD2/CD3/CD28 for cynomolgus PBMC).

[0228] Target cells (Raji for CD20 mediated killing and U937 for FcR mediated killing) were labeled with calcein, and incubated with activated T-cells at a 10:1 effector: target ratio using 3-fold serial dilutions of antibodies over a course of 3 hours at 37°C. Following incubation, the plates were centrifuged and supernatants were transferred to a translucent black clear bottom plate for fluorescence analysis. EC_{50}s defined as the molar concentration of bispecific antibody that induces 50% cytotoxicity was determined using Prism. Values were calculated using a 4-parameter non-linear regression analysis. Results are summarized in Table 27.

Table 27. EC_{50} values for CD20 x CD3-Induced Cytotoxicity to Raji and U937 cells

Antibody	Raji Cytotoxicity Human T-cells [M]	U937 Cytotoxicity Human T-cells [M]	Raji Cytotoxicity Monkey T-cells [M]
Control I (anti-CD3)	NA	3.04E-12	NA
BS3/20-001	5.63E-11*	8.86E-11*	1.27E-12*
BS3/20-002	7.71E-11*	8.24E-10	NT
BS3/20-003	7.38E-11*	8.10E-11*	4.36E-14
BS3/20-004	1.29E-11*	6.07E-11	NT
BS3/20-005	1.95E-11	1.48E-10	NT

(*) Data are median values of 3 or more independent assays. Data without a (*) are representative/average values of 1 or 2 independent assays. NA = No Activity; NT = Not Tested.

[0229] As shown in Table 27, bispecific CD20 x CD3 antibodies containing human-specific or human/cynomolgus cross reactive anti-CD3 arms were able to specifically redirect cytotoxicity to Raji cells in the presence of human activated T cells. In the presence of cynomolgus activated T cells, Raji were killed when they were incubated with BS3/20-001 or BS3/20-003, bispecific antibodies that have anti-CD3 arms that activate monkey T-cells. All bispecific antibodies as well as Control I, an anti-CD3 mAb, showed activity in the U937 Fc/FcR dependent killing assay. This activity could be blocked by the addition of blocking non-specific human IgG to the reaction (Data not shown).

Example 14. CD3 x CD20 Bispecific Antibodies Can Deplete CD19+ B-cells in Mice Reconstituted with Human Immune Cells

[0230] To determine the *in vivo* potency of CD3xCD20 bispecific antibody administration, changes in CD19+ B-cell and CD2+ T-cell levels were examined via FACS after administration of 10 µg or 0.1 µg of anti-CD3xCD20 bispecific antibody into mice, which were reconstituted with human immune cells.

[0231] Briefly, newborn BALB/$Rag2^{null}/\gamma_c^{null}$ mice were irradiated with 2 x 150 Rads and reconstituted with $4x10^5$ human $CD34^+$ hematopoietic progenitor cells via intrahepatic injection. After 12 weeks, the composition of reconstituted human immune system in peripheral blood was determined by flow cytometry. Typically by three months post reconstitution, between 10%-60% percent of peripheral white blood cells are human CD45+ of which 40%-70% are B cells, 15%-40% are T-cells and the remaining are small populations of natural killer and dendritic cells.

[0232] Five months post-reconstitution, mice were injected intraperitoneally with 10 µg or 0.1 µg of anti-CD3xCD20 bispecific antibody BS3/20-007, 10 µg of a monovalent 1-arm CD3 antibody (BS3/20-009, see Table 1) or 10 µg of an irrelevant hIgG isotype control. One, eight, and twenty-five days post injection, mice were bled retro-orbitally and immune cell populations in the peripheral blood were determined by flow cytometry (FACS).

[0233] For FACS analysis, 100 µl of blood was incubated with 1.5 ml RBC lysis buffer in Eppendorf tubes for three minutes. Cells were centrifuged for five minutes at 0.4xg, washed 2x with FACS wash (PBS+3%FBS), and blocked for 10 minutes at room temperature with mouse Fc blocking reagent. Cells were then incubated for 30 minutes at 4°C with directly conjugated antibodies to CD2, CD3, CD19, CD4, CD8, hCD45, hHLA-DR, and mCD45. After staining, cells were washed two times before FACS acquisition by a FACSCanto cytometer and analysis with FlowJo software. Results are shown in Table 28.

Table 28: Percentage of circulating CD45, CD19 and CD2 positive cells in mice reconstituted with human immune cells

		Isotype Ctrl (10 µg)		**BS3/20-007 (10 µg)**		**BS3/20-007 (0.1 µg)**			**BS3/20-009 [one-arm CD3] (10 µg)**	
Mouse ID		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
	Day									
%huCD45+	Pre	13.7	14.8	16.1	30.9	37.2	22.5	25.5	26.6	33.3
	1d	7.7	10.8	0.01	0.13	1.7	1.2	0.8	2.7	8.9
	8d	14.1	12.7	0.12	0.16	3.3	7.7	3.9	3.2	4.5
	25d	13.0	7.3	0.15	0.12	9.0	1.2	1.0	2.8	5.1
%CD19+ (of huCD45+)	1d	58.7	66.8	0.00	7.69	20.2	7.0	5.2	75.3	87.1
	8d	66.2	56.2	0.00	0.00	21.3	0.4	0.0	70.4	76.6
	25d	37.3	62.8	9.7	2.6	58.3	0.7	0.6	38.9	51.3
%CD2+ (of huCD45+)	1d	58.7	66.8	0.00	7.69	20.2	7.0	5.2	75.3	87.1
	8d	66.2	56.2	0.00	0.00	21.3	0.4	0.0	70.4	76.6
	25d	37.3	62.8	9.7	2.6	58.3	0.7	0.6	38.9	51.3

[0234] As shown in Table 28, a single 10 µg dose of anti-CD3xCD20 bispecific antibody BS3/20-007 resulted in a disappearance of circulating hCD45+ cells in 2 of 2 treated mice which did not recover over the length of the experiment. A single 0.1 µg dose of BS3/20-007 reduced circulating hCD45+ cells, including CD19+ B-cells and CD2+ T-cells 24 hours post injection in 2 of 3 treated mice. Once depleted, the percentage of hCD45+ cells did not recover significantly in the responding mice treated with 0.1 µg BS3/20-007. However, what cells remained in these mice were predominantly hCD2+ T-cells, and CD19+ B cells were not present in the responding mice even at 25 days post treatment. A single 10 µg dose of a monovalent 1-arm CD3 antibody

(BS3/20-009) also resulted in a persistent but modest reduction in CD45+ cells, notably CD2+ T-cells, in 2 of 2 treated mice. A single 10 µg dose of an irrelevant hIgG1 control had no significant effect on the percentage of circulating hCD45+, hCD19+, or hCD2+ cells.

Example 15. Treatment with CD20 x CD3 Bispecific Antibody Decreases Raji Tumor Volume in NOD/SCID Mice

[0235] To assess the efficacy of selected anti-CD3xCD20 bispecific antibodies in reducing Raji tumor growth, NOD/SCID mice (Taconic) were implanted subcutaneously with a mixture of 2×10^6 Raji tumor cells and 8×10^6 human PBMC. Mice were treated three times per week, starting on the day of tumor implantation, with either human Fc (hFc) or CD3xCD20 bispecific antibody (BS3/20-007) at a dose of 1 µg per mouse (N=20 mice per treatment group). Reagents were delivered by intraperitoneal (i.p.) injection. Tumor size was measured three times per week using calipers, and tumor volume calculated as Volume = (length x width^2)/2. Results are shown in Figure 1.

[0236] In a second experiment, NOD/SCID mice were implanted subcutaneously with a mixture of 2×10^6 Raji tumor cells and 4×10^6 human PBMC. Treatment with CD3xCD20 bispecific antibody (BS3/20-007) or control reagent (hFc) began 7 days post tumor implantation to allow tumors to become palpable. Mice were treated two times per week at a dose of 1 µg per mouse (N=6 mice per treatment group). Reagents were injected subcutaneously, away from the site of tumor implantation. Tumor size was measured two times per week using calipers, and tumor volume calculated as Volume = (length x width^2)/2. Results are shown in Figure 2.

[0237] This Example demonstrates that treatment with CD3xCD20 bispecific antibody BS3/20-007 was effective in inhibiting tumor growth both at the time of tumor implantation and once tumors were established. Tumor volume in mice was decreased 25 days post implantation in both studies, relative to control.

Example 16. CD20 x CD3 Bispecific Antibodies Deplete B-cell Populations in Cynomolgus Monkeys and Have a Pharmacokinetic Profile Typical of Monoclonal Antibodies

[0238] A pilot non-GLP toxicology and pharmacology study was performed in cynomolgus monkeys (*Macaca fascicularis*) to determine the ability of the CD3xCD20 bispecific antibodies to deplete B-cell populations in these animals. Male animals were organized into three cohorts. Cohort 1 received bispecific antibody BS3/20-001 and included three different dosing groups (0.01, 0.10 and 1.00 mg/kg) with 3-4 animals per dosing group. Cohort 2 was a two-animal cohort that received a low dose of anti-CD20 control antibody (Control V; 0.01 mg/kg). Cohort 3 was a four-animal cohort that received a high dose of anti-CD20 control antibody (Control III; 1.0 mg/kg). Blood was drawn at day -7 and immediately prior to dosing in order to establish baseline levels for B and T cells in these animals. Doses of drug at 0.01, 0.10, or 1.00 mg/kg were administered by i.v. infusion and blood was drawn at 5 minutes, 5 hours, and 1, 4, 7, and

14 days post dosing. Following day 14 post-dose, blood was drawn every two weeks until the conclusion of the study. Blood samples were analyzed by FACS for B and T cell markers and the absolute number of these cell types was determined. Serum samples were also analyzed for cytokine levels (IFNγ, IL-2, IL-6 and TNFα) using standard analytic methods. Results are shown in Figure 3 (B-cells), Figure 4 (T-cells), and Figures 5A-5D (cytokines).

[0239] As shown in this Example, administration of the CD3xCD20 bispecific antibody resulted in depletion of circulating B-cells to baseline levels by the first time point measured (day 1). This depletion was not seen in the control animal cohort. B-cell depletion in the bispecific cohort was maintained until two weeks after dosing and in the 0.01 and 0.10 mg/kg dose cohorts was followed by a gradual recovery of B-cell levels until the experiment was concluded at around 11 weeks post dosing. In the 1.0 mg/kg cohort, however, no recovery of B-cell levels was seen for the duration of the experiment (11 weeks). T-cell levels were also monitored in this experiment. A transient loss of circulating T-cells was observed at day 1 post-dose in the bispecific cohorts. T-cell levels returned to baseline levels in these cohorts by the day 4 time-point and maintained at those baseline levels until the end of the experiment. In addition, serum cytokine levels for BS3/20-001 at 5 hours exhibited a dose- and time-dependent response that is consistent with T-cell activation (see Figures 5A-5D).

[0240] Gene expression levels in the peripheral blood were also analyzed during this experiment. Blood samples were obtained from animals at two pre-dose time points (Day 7 pre-dose and immediately pre-dose) and at 5, 24, 72, 96, and 168 hours post-dosing. RNA was isolated from these samples and analyzed by microarray. When compared to pre-dose levels and gene expression levels from the control group, a notable decrease in the gene expression of B-cell markers in animals treated with the bispecific antibody was observed; this effect was similar to the effect observed in samples obtained from animals treated with 1.0 mg/kg Control III (anti-CD20 antibody corresponding to Rituximab). The observed change in B-cell marker expression corresponds to the loss of B-cells detected in the blood of treated animals. The expression of T-cell marker genes in samples from animals treated with the CD3xCD20 bispecific antibody showed an initial decrease followed by a return to normal levels by the 24 hour time point. In addition, genes associated with an inflammatory response showed an initial upregulation in animals in the bispecific cohort but returned to normal or below normal levels after 24 hours. Finally, examination of the raw intensity of the CD20 gene expression signal suggests that a greater depletion of B-cells arises from treatment of animals with the CD3xCD20 bispecific antibody than with the control anti-CD20 antibodies. (*See* Figure 6 and Table 29).

Table 29. CD20 Gene Expression Levels at Day 7

Antibody	Dose mg/kg	CD20 Expression (Raw Intensity)
Control V (anti-CD20)	0.01	26485.44
	0.01	24335.17
Control III (anti-CD20)	1.0	1813.46
	1.0	47.09
	1.0	98.88
	1.0	70.52
BS3/20-001	0.01	24.93
	0.01	226.45
	0.01	4.78
	0.01	8.12
	0.1	8.26
	0.1	5.62
	0.1	4.82
	0.1	23.61
	1.0	9.38
	1.0	9.19
	1.0	8.22

[0241] As shown in Table 29, at seven days post-dosing the raw intensity of CD20 signal remained at background levels in all but one of the CD3xCD20 animals while 3 of 4 animals treated with 1 mg/kg of Control III showed either marginal or detectable CD20 signal levels.

[0242] In the same experiment the pharmacokinetic profile of the bispecific antibody (Figure 7) was evaluated by obtaining blood samples at pre-dose and at 0.083, 5, 24, 48, 72, 168, 336, 504 and 840 hours. The resultant serum samples were analyzed by a direct enzyme linked immunosorbent assay (ELISA) to determine the concentration of total bispecific antibody. Serum total bispecific (BS3/20-001) concentration data were analyzed by non-compartmental analysis (Phoenix WinNonLin) to determine pharmacokinetic parameters Results are shown in Table 30 (AUC = area under the curve vs. time; C_{max} = maximum concentration of compound observed in matrix of interest).

Table 30: Pharmacokinetic Parameters of BS3/20-001 in Cynomolgus Monkey

Parameter	Units	0.01 mg/kg		0.10 mg/kg		1.0 mg/kg	
		Mean	SD	Mean	SD	Mean	SD
C_{max}	μg/mL	0.261	0.0413	2.32	0.274	33.4	4.20
C_{max}/Dose	kg*μg/mL/mg	26.1	4.13	23.2	2.74	33.4	4.20
t_{max}	hr	0.083	0.00	0.083	0.00	0.083	0.00
AUC_{all}	μg*hr/mL	4.42	2.37	289	87.2	4940	1080
AUC_{all}/Dose	hr*kg*μg/mL/mg	442	237	2890	872	4940	1080

[0243] Following a single intravenous dose of 0.01, 0.10 or 1.0 mg/kg of BS3/20-001 in cynomolgus monkeys, mean peak concentrations (C_{max}) of 0.261, 2.32 and 33.4 μg/mL, respectively, were observed at the first sampling time point (0.083 hr). Mean AUC_{all} values of 4.42, 289 and 4940 μg*hr/mL were observed at doses of 0.01, 0.1 and 1.0 mg/kg. Dose-normalized AUC values (AUC_{all}/Dose) of 442, 2890 and 4940 μg*hr/mL per mg/kg indicate that plasma exposure (AUC_{all}) increases with increasing dose in a non-linear fashion. Greater than proportional increase in plasma drug exposure was observed with increased antibody dose, suggesting that BS3/20-001 may be undergoing some target-mediated clearance. The overall pharmacokinetic profile of BS3/20-001 is typical of monoclonal antibodies dosed in cynomolgus monkey.

[0244] The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and the accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

What is claimed is:

1. An isolated human antibody or antigen-binding fragment thereof that binds human CD3 with a binding dissociation equilibrium constant (K_D) of less than 2 nM as measured in a surface plasmon resonance assay at 25ºC in an antigen-capture format, wherein the antibody or antigen-binding fragment comprises six complementarity determining regions (CDRs) within a heavy chain variable region (HCVR)/light chain variable region (LCVR) amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346, 354/362, 386/394, 402/410, 418/426, 434/442, 466/474, 482/490, 514/522, 594/602, 610/618, 626/634, 722/730, 770/778, 786/794, 802/810, 850/858, 882/890, 898/906, 930/938, 946/954, 1042/1234, 1050/1234, 1066/1234, 1074/1234, 1098/1234, 1106/1234, 1114/1234, 1122/1234, 1138/1234, 1146/1234, 1162/1234, and 1178/1234, and

wherein the CDRs are identified by the Kabat definition, the Chothia definition or the AbM definition.

2. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment thereof binds human CD3 with a K_D of less than 500 pM as measured in a surface plasmon resonance assay at 25ºC in an antigen-capture format, wherein the antibody or antigen-binding fragment comprises the CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 18/26, 34/42, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 210/218, 242/250, 258/266, 274/282, 290/298, 306/314, 338/346, 354/362, 402/410, 418/426, 434/442, 482/490, 514/522, 722/730, 770/778, 786/794, 850/858, 882/890, 898/906, 930/938, 946/954, 1042/1234, 1050/1234, 1066/1234, 1074/1234, and 1098/1234.

3. The isolated antibody or antigen-binding fragment of claim 2, wherein the antibody or antigen-binding fragment thereof binds human CD3 with a K_D of less than 100 pM as measured in a surface plasmon resonance assay at 25ºC in an antigen-capture format, wherein the antibody or antigen-binding fragment comprises the CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 98/106, 114/122, 338/346, 354/362, 418/426, 482/490, 514/522, and 770/778.

4. The isolated antibody or antigen-binding fragment of claim 1 that binds human CD3 with a dissociative half-life ($t½$) of greater than 10 minutes as measured in a surface plasmon resonance assay at 25ºC in an antigen-capture format, wherein the

antibody or antigen-binding fragment comprises the CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346, 354/362, 386/394, 402/410, 418/426, 434/442, 466/474, 482/490, 514/522, 594/602, 610/618, 626/634, 722/730, 770/778, 786/794, 802/810, 850/858, 882/890, 898/906, 930/938, 946/954, 1042/1234, 1050/1234, 1066/1234, 1074/1234, 1098/1234, 1106/1234, 1114/1234, 1122/1234, 1138/1234, 1146/1234, 1162/1234, and 1178/1234.

5. The isolated antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment thereof binds human CD3 with a t½ of greater than 100 minutes as measured in a surface plasmon resonance assay at 25ºC in an antigen-capture format, wherein the antibody or antigen-binding fragment comprises the CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 50/58, 82/90, 98/106, 114/122, 130/138, 338/346, 354/362, 466/474, 482/490, 514/522, 610/618, 770/778, 1042/1234, 1050/1234, 1066/1234, and 1098/1234.

6. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment comprises HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3, respectively, selected from the group consisting of SEQ ID NOs: 4-6-8-12-14-16, 20-22-24-28-30-32, 36-38-40-44-46-48, 52-54-56-60-62-64, 68-70-72-76-78-80, 84-86-88-92-94-96, 100-102-104-108-110-112, 116-118-120-124-126-128, 132-134-136-140-142-144, 148-150-152-156-158-160, 164-166-168-172-174-176, 180-182-184-188-190-192, 196-198-200-204-206-208, 212-214-216-220-222-224, 244-246-248-252-254-256, 260-262-264-268-270-272, 276-278-280-284-286-288, 292-294-296-300-302-304, 308-310-312-316-318-320, 324-326-328-332-334-336, 340-342-344-348-350-352, 356-358-360-364-366-368, 388-390-392-396-398-400, 404-406-408-412-414-416, 420-422-424-428-430-432, 436-438-440-444-446-448, 468-470-472-476-478-480, 484-486-488-492-494-496, 516-518-520-524-526-528, 596-598-600-604-606-608, 612-614-616-620-622-624, 628-630-632-636-638-640, 724-726-728-732-734-736, 772-774-776-780-782-784, 788-790-792-796-798-800, 804-806-808-812-814-816, 852-854-856-860-862-864, 884-886-888-892-894-896, 900-902-904-908-910-912, 932-934-936-940-942-944, 948-950-952-956-958-960, 1044-1046-1048-1236-1248-1240, 1052-1054-1056-1236-1248-1240, 1068-1070-1072-1236-1248-1240, 1076-1078-1080-1236-1248-1240, 1100-1102-1104-1236-1248-1240, 1108-1110-1112-1236-1248-1240, 1116-1118-1120-1236-1248-1240, 1124-1126-1128-1236-1248-1240, 1140-1142-1144-1236-1248-1240, 1148-

1150-1152-1236-1248-1240, 1164-1166-1168-1236-1248-1240, and 1180-1182-1184-1236-1248-1240.

7. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment comprises a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346, 354/362, 386/394, 402/410, 418/426, 434/442, 466/474, 482/490, 514/522, 594/602, 610/618, 626/634, 722/730, 770/778, 786/794, 802/810, 850/858, 882/890, 898/906, 930/938, 946/954, 1042/1234, 1050/1234, 1066/1234, 1074/1234, 1098/1234, 1106/1234, 1114/1234, 1122/1234, 1138/1234, 1146/1234, 1162/1234, and 1178/1234.

8. The isolated antibody or antigen-binding fragment of claim 6, wherein the antibody or antigen-binding fragment comprises a HCVR/LCVR amino acid sequence pair selected from the group consisting of: SEQ ID NOs: 2/10; 114/122; 162/170; and 178/186.

9. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment induces human T-cell proliferation and monkey T-cell proliferation *in vitro*, and wherein the antibody or antigen-binding fragment comprises the heavy and light chain CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 114/122, 722/730, 770/778, 786/794, 802/810, 1042/1234, 1050/1234, 1066/1234, 1074/1234, 1098/1234, 1106/1234, 1114/1234, 1122/1234, 1138/1234, 1146/1234, 1162/1234, and 1178/1234.

10. The isolated antibody or antigen-binding fragment of claim 9, wherein the antibody or antigen-binding fragment comprises HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3, respectively, selected from the group consisting of SEQ ID NOs: 4-6-8-12-14-16, 116-118-120-124-126-128, 724-726-728-732-734-736, 772-774-776-780-782-784, 788-790-792-796-798-800, 804-806-808-812-814-816, 1044-1046-1048-1236-1248-1240, 1052-1054-1056-1236-1248-1240, 1068-1070-1072-1236-1248-1240, 1076-1078-1080-1236-1248-1240, 1100-1102-1104-1236-1248-1240, 1108-1110-1112-1236-1248-1240, 1116-1118-1120-1236-1248-1240, 1124-1126-1128-1236-1248-1240, 1140-1142-1144-1236-1248-1240, 1148-1150-1152-1236-1248-1240, 1164-1166-1168-1236-1248-1240, and 1180-1182-1184-1236-1248-1240.

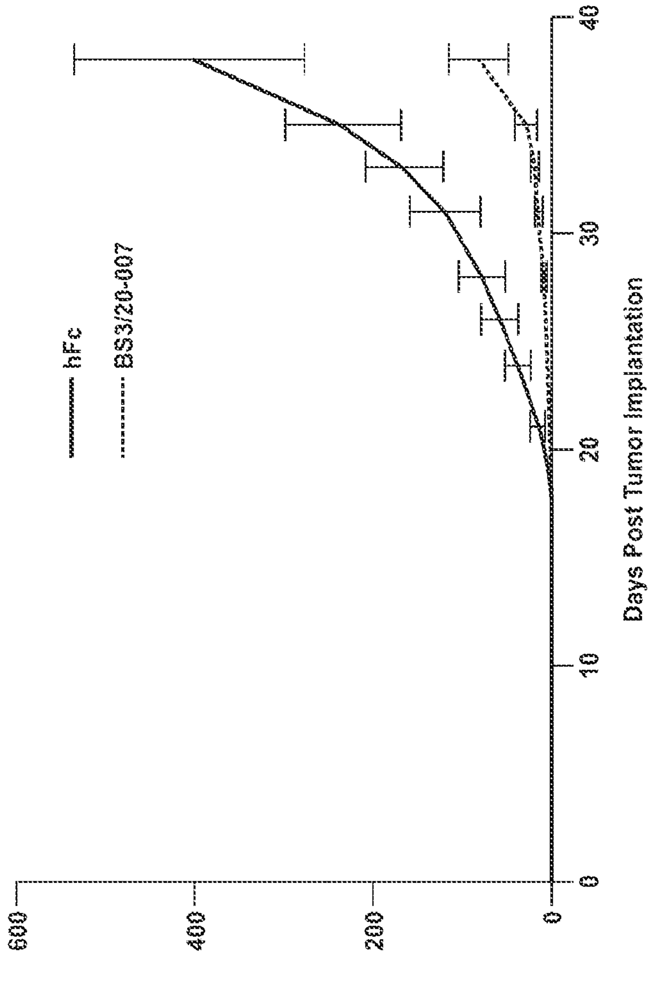
11. The isolated antibody or antigen-binding fragment of claim 9, wherein the antibody or antigen-binding fragment comprises a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 2/10, 114/122, 722/730, 770/778, 786/794, 802/810, 1042/1234, 1050/1234, 1066/1234, 1074/1234, 1098/1234, 1106/1234, 1114/1234, 1122/1234, 1138/1234, 1146/1234, 1162/1234, and 1178/1234.

12. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any one of claims 1 to 11, and a pharmaceutically acceptable carrier or diluent.

REGENERON PHARMACEUTICALS, INC.

WATERMARK INTELLECTUAL PROPERTY PTY LTD

P40122AU00


hFc
BS3/20-007
Tumor Volume (mm3)
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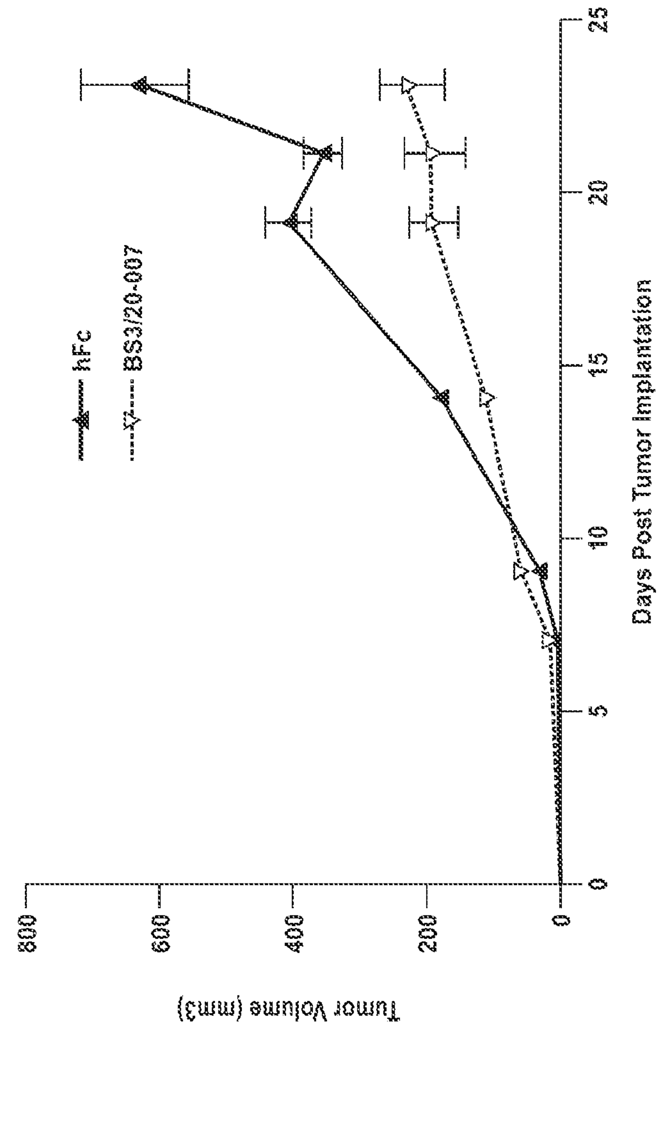
400
200
0
0
10
20
30
40
Days Post Tumor Implantation

FIG. 1


Tumor Volume (mm3)
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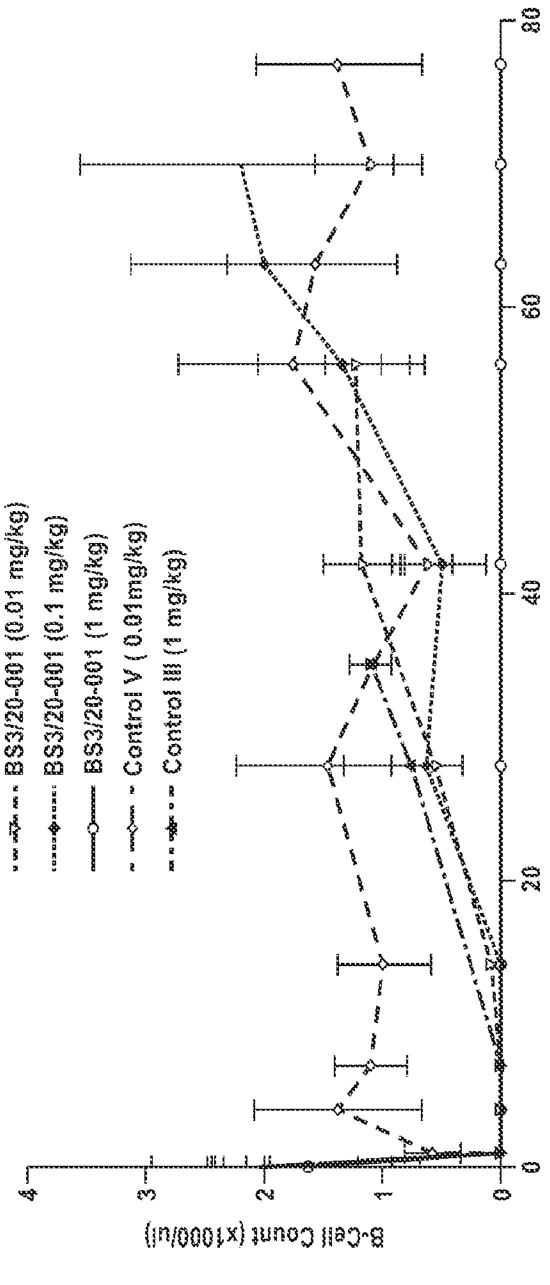
0
5
10
15
20
25
Days Post Tumor Implantation
hFc
BS3/20-007

FIG. 2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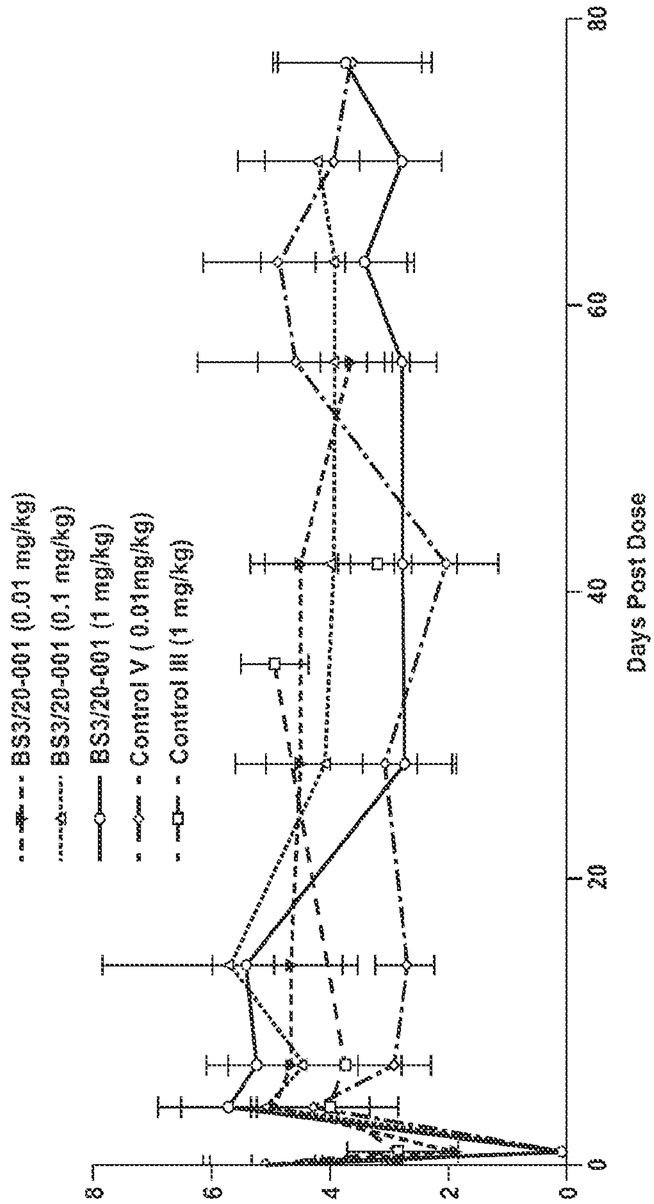
BS3/20-001 (0.1 mg/kg)
BS3/20-001 (1 mg/kg)
Control V (0.01mg/kg)
Control III (1 mg/kg)
B-Cell Count (x1000/ul)
4
3
2
1
0
0
20
40
60
80
Days Post Dose

FIG. 3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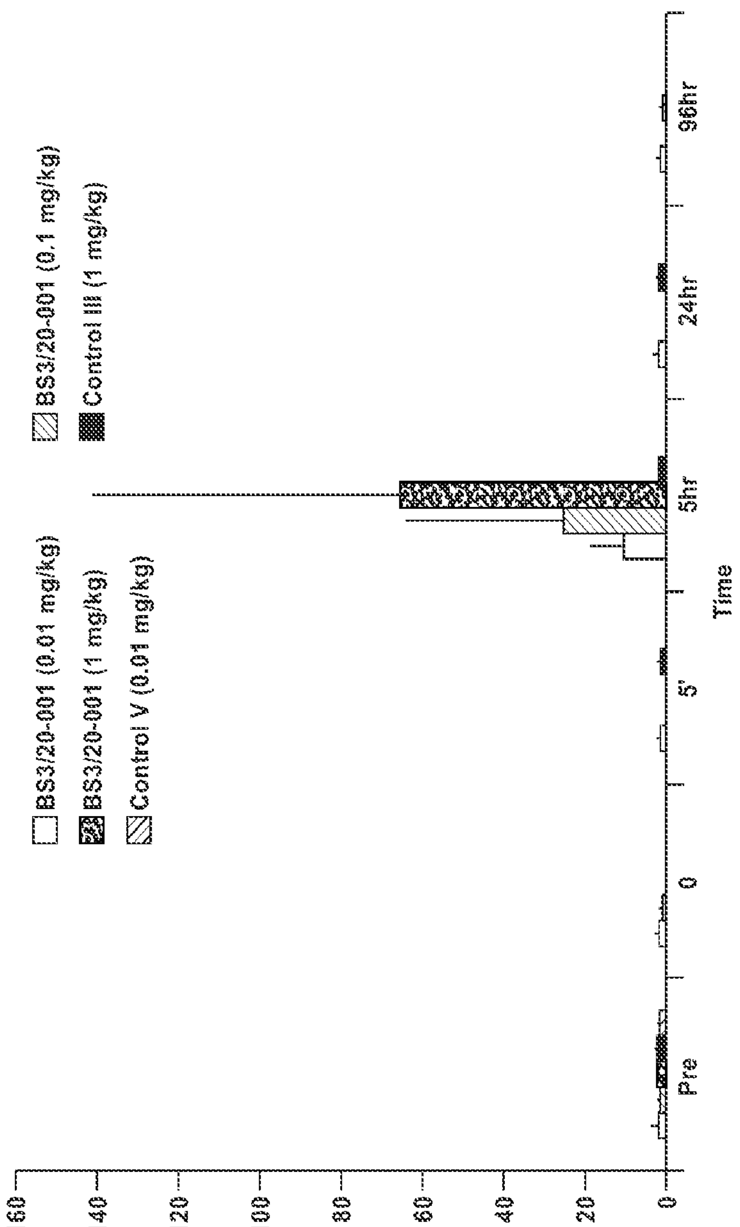
BS3/20-001 (0.1 mg/kg)
BS3/20-001 (1 mg/kg)
Control V (0.01mg/kg)
Control III (1 mg/kg)
T-Cell Count (x1000/ul)
0
2
4
6
8
0
20
40
60
80
Days Post Dose

FIG. 4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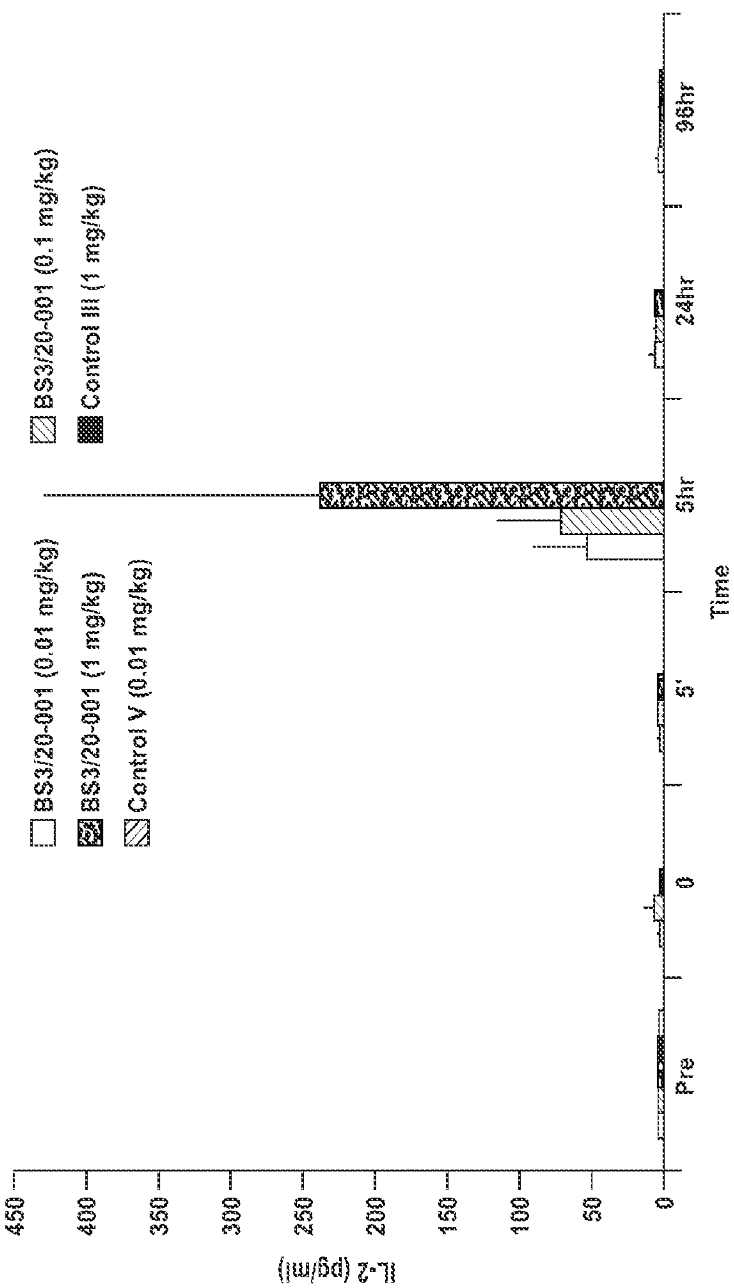
BS3/20-001 (1 mg/kg)
Control V (0.01 mg/kg)
BS3/20-001 (0.1 mg/kg)
Control III (1 mg/kg)
IFN-gamma (pg/ml)
0
20
40
60
80
100
120
140
160
Pre
0
5'
5hr
24hr
96hr
Time

FIG. 5A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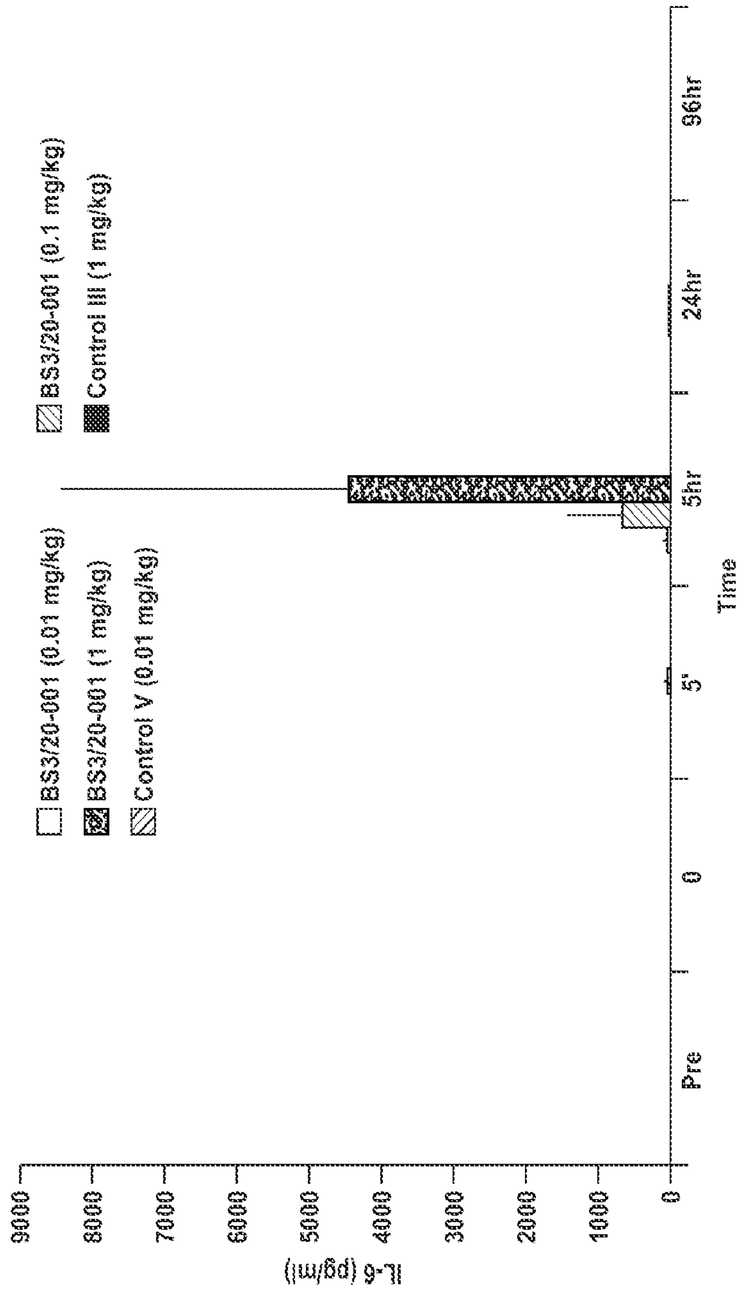
BS3/20-001 (1 mg/kg)
Control V (0.01 mg/kg)
BS3/20-001 (0.1 mg/kg)
Control III (1 mg/kg)
IL-2 (pg/ml)
450
400
350
300
250
200
150
100
50
0
Pre
0
5'
5hr
24hr
96hr
Time

FIG. 5B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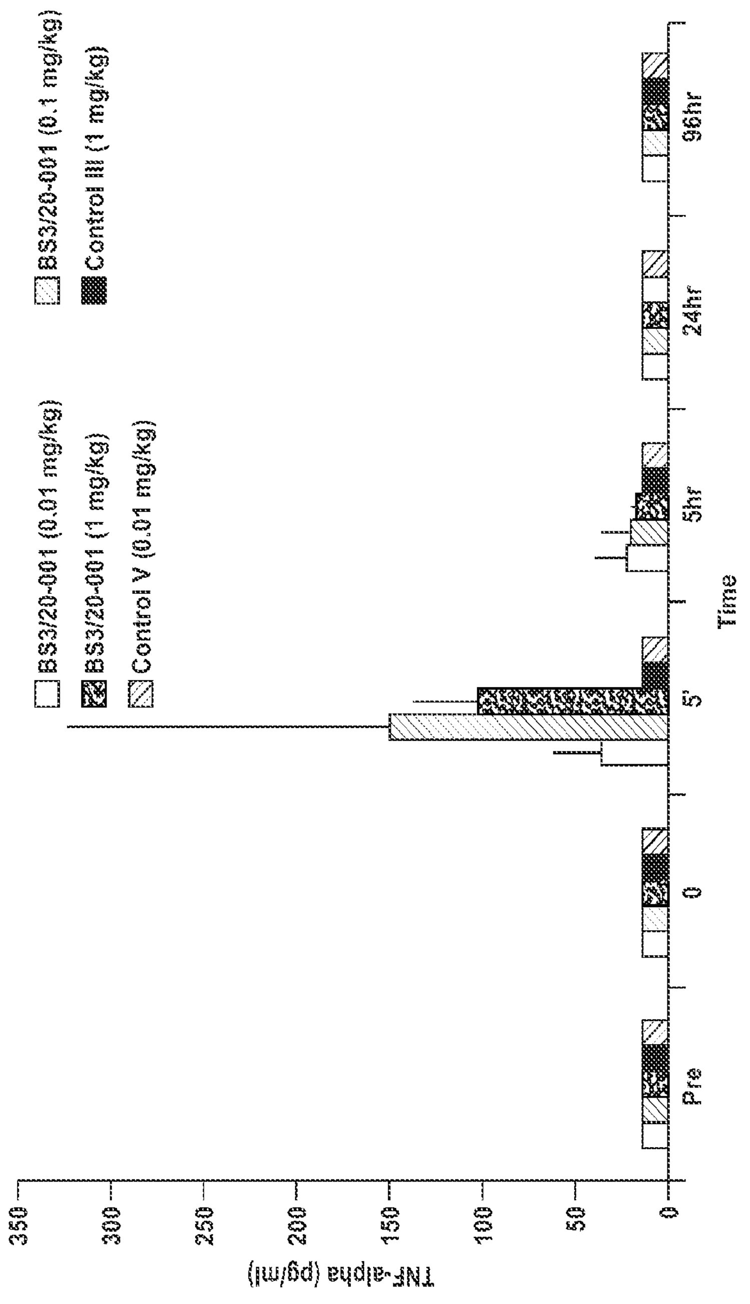
BS3/20-001 (1 mg/kg)
Control V (0.01 mg/kg)
BS3/20-001 (0.1 mg/kg)
Control III (1 mg/kg)
IL-6 (pg/ml)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Pre
0
5'
5hr
24hr
96hr
Time

FIG. 5C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BS3/20-001 (1 mg/kg)
Control V (0.01 mg/kg)
BS3/20-001 (0.1 mg/kg)
Control III (1 mg/kg)
TNF-alpha (pg/ml)
350
300
250
200
150
100
50
0
Pre
0
5'
5hr
24hr
96hr
Time

FIG. 5D

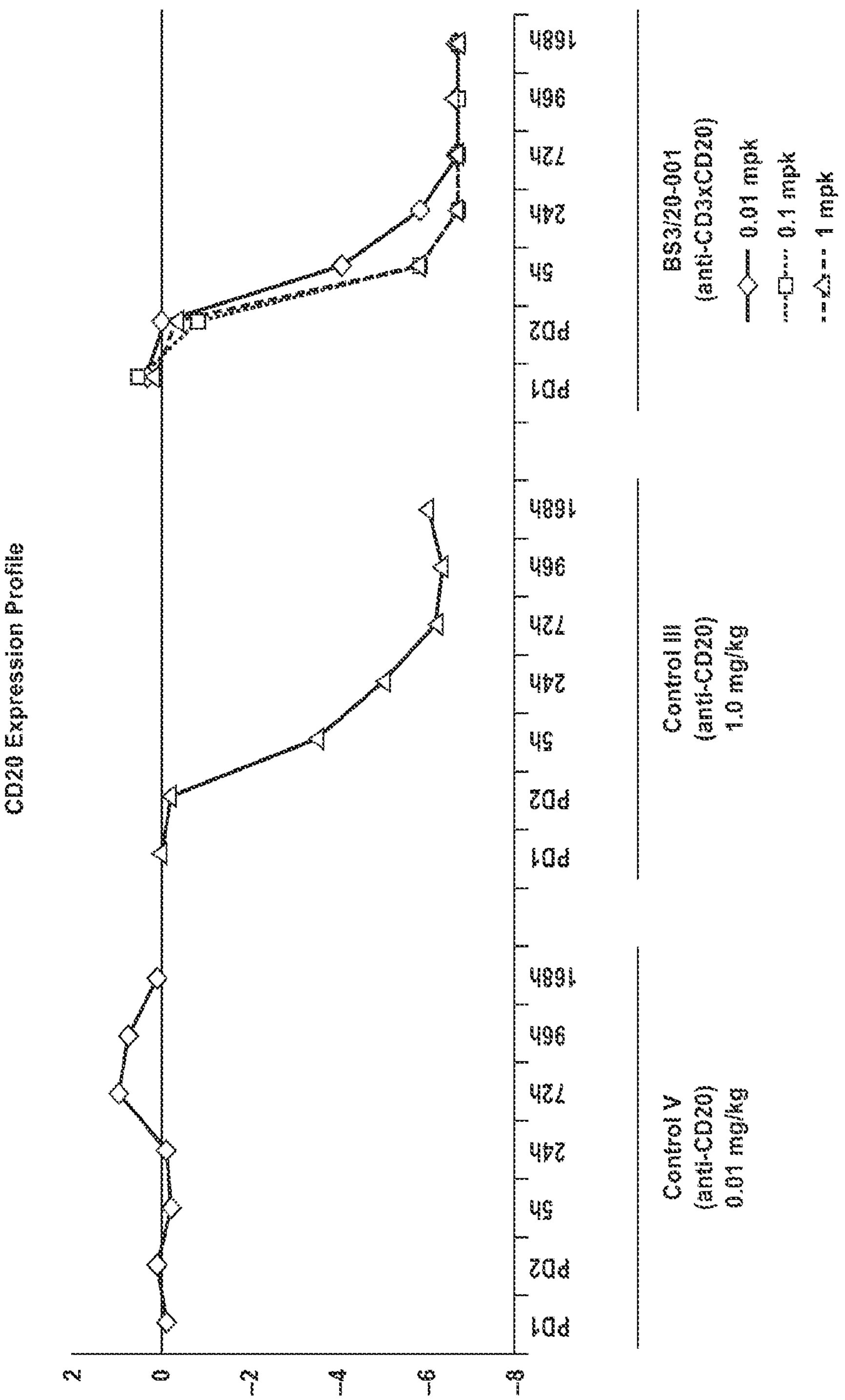
CD20 Expression Profile
Log2 Fold Change
2
0
-2
-4
-6
-8
PD1
PD2
5h
24h
72h
96h
168h
Control V
(anti-CD20)
0.01 mg/kg
Control III
(anti-CD20)
1.0 mg/kg
BS3/20-001
(anti-CD3xCD20)
0.01 mpk
0.1 mpk
1 mpk

FIG. 6

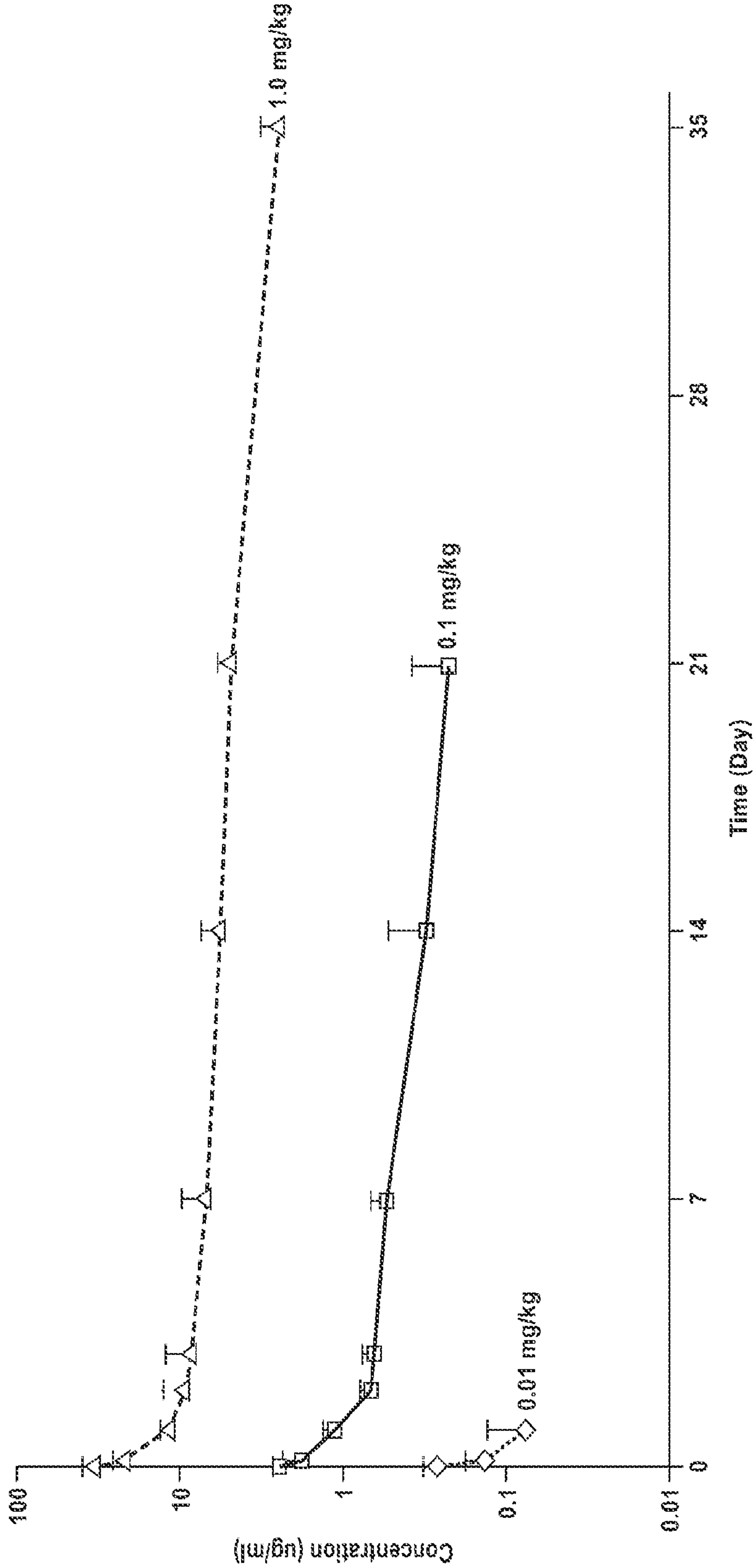
Concentration (ug/ml)
100
10
1
0.1
0.01
0
7
14
21
28
35
Time (Day)
1.0 mg/kg
0.1 mg/kg
0.01 mg/kg

FIG. 7

9250A-WO SEQUENCE LISTING

<110> REGENERON PHARMACEUTICALS, INC.

<120> Anti-CD3 Antibodies, Bispecific Antigen-Binding Molecules That Bind CD3 and CD20, and Uses Thereof

<130> 9250A-WO

<140> To be assigned
<141> Filed herewith

<150> 61/704,029
<151> 2012-09-21

<150> 61/753,461
<151> 2013-01-17

<150> 61/763,110
<151> 2013-02-11

<150> 61/827,098
<151> 2013-05-24

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<220>
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ccagggaagg gcctggagtg ggtctcaggt atcagttgga atagtggtag cataggctat 180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt actactgtgc aaaagataat 300
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gtctcctca 369

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<213> Artificial Sequence

<220>
<223> Synthetic

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

            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

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<210> 4
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<220>
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1   5

<210> 5
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<400> 5
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<210> 6
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<220>
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<400> 6
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1   5

<210> 7
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 7
gcaaaagata atagtggcta cggctattat tactacggta tggacgtc   48

<210> 8
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 8
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Gly Met Asp Val
 1   5   10   15

<210> 9
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 9
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca cagtgttagc aggaactcag cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240
gaagattttg caatttatta ctgtcagcag tataataatt ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 10
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 10
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser His Ser Val Ser Arg Asn
            20   25   30
Ser Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 11
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 11
cacagtgtta gcaggaac 18

<210> 12
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 12
His Ser Val Ser Arg Asn
1 5

<210> 13
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 13
ggtgcatcc 9

<210> 14
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 14
Gly Ala Ser
1

<210> 15
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 15
cagcagtata ataattggcc tctcact 27

<210> 16
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 16
Gln Gln Tyr Asn Asn Trp Pro Leu Thr
1 5

<210> 17
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 17
gaagtgcaac tggtggaatc gggggaggc ttggtacagc ctggcgggtc cctgagactc 60
tcctgtgcag cctctggatt ctcctttgat gattatacca tgcactgggt ccggcaacct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag cataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctggggac acggccttgt actactgtgc aaaagataat 300

agtggctacg gctattacta ctactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 18
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 18
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Asp Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 19
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 19
ggattctcct ttgatgatta tacc 24

<210> 20
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 20
Gly Phe Ser Phe Asp Asp Tyr Thr
1 5

<210> 21
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 21
attagttgga atagtggtag cata 24

<210> 22
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 22
Ile Ser Trp Asn Ser Gly Ser Ile
 1   5

<210> 23
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 23
gcaaaagata atagtggcta cggctattac tactactacg gtatggacgt c   51

<210> 24
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 24
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Tyr Gly Met Asp
 1   5   10   15
Val

<210> 25
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 25
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct 120
ggccaggctc ccagactcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tattataact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a   321

<210> 26
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 26
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly

```
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65                  70                  75                  80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Asn Trp Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 27
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 27
cagagtgtta gcagcaac                                                    18

<210> 28
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 28
Gln Ser Val Ser Ser Asn
 1               5


<210> 29
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 29
ggtgcatcc                                                              9

<210> 30
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 30
Gly Ala Ser
 1


<210> 31
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 31
cagcagtatt ataactggcc tctcact                                          27
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<210> 32
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 32
Gln Gln Tyr Tyr Asn Trp Pro Leu Thr
 1   5

<210> 33
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 33
gaagtacagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgtag cctctggatt cccctttgct gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag caaaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag aactgaggac acggccttct attactgtgc aaaagatatg 300
agtggctacg cccactactt ctactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 34
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 34
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Pro Phe Ala Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Phe Tyr Tyr Cys
                85   90   95
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Phe Tyr Tyr Gly Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 35
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 35
ggattcccct ttgctgatta tacc 24

<210> 36
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 36
Gly Phe Pro Phe Ala Asp Tyr Thr
 1   5

<210> 37
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 37
attagttgga atagtggtag caaa   24

<210> 38
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 38
Ile Ser Trp Asn Ser Gly Ser Lys
 1   5

<210> 39
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 39
gcaaaagata tgagtggcta cgcccactac ttctactacg gtatggacgt c   51

<210> 40
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 40
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Phe Tyr Tyr Gly Met Asp
 1   5   10   15
Val

<210> 41
<211> 324
<212> DNA
<213> Artificial Sequence

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<220>
<223> Synthetic

<400> 41
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc ggccaagtca gagcattagc agctatttaa attggtttca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta cccctccgat caccttcggc 300
caagggacac gactggagat taaa                                        324

<210> 42
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 42
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Pro Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30
Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
                85                  90                  95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105


<210> 43
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 43
cagagcatta gcagctat                                               18

<210> 44
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 44
Gln Ser Ile Ser Ser Tyr
1               5


<210> 45
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic
```

<400> 45
gctgcatcc 9

<210> 46
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 46
Ala Ala Ser
1

<210> 47
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 47
caacagagtt acagtacccc tccgatcacc 30

<210> 48
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 48
Gln Gln Ser Tyr Ser Thr Pro Pro Ile Thr
1 5 10

<210> 49
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 49
gaagtacaac tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctaagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagtt 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggcag cttggcctac 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ttccctgtat 240
ctgcaaatga acagtcttca ccctgaggac acggccctct attactgtgt aaaagatggt 300
agtggctacg gccactactc ctactacggt ttggacgtct ggggccaggg gaccacggtc 360
accgtctcct ca 372

<210> 50
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 50
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Val Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Leu Ala Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu His Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Val Lys Asp Gly Ser Gly Tyr Gly His Tyr Ser Tyr Tyr Gly Leu Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 51
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 51
ggattcacct ttgatgatta tacc                                          24

<210> 52
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 52
Gly Phe Thr Phe Asp Asp Tyr Thr
 1               5


<210> 53
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 53
attagttgga atagtggcag cttg                                          24

<210> 54
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 54
Ile Ser Trp Asn Ser Gly Ser Leu
 1               5


<210> 55
<211> 51
<212> DNA
<213> Artificial Sequence
```

<220>
<223> Synthetic

<400> 55
gtaaaagatg gtagtggcta cggccactac tcctactacg gtttggacgt c 51

<210> 56
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 56
```
Val Lys Asp Gly Ser Gly Tyr Gly His Tyr Ser Tyr Tyr Gly Leu Asp
 1               5                  10                  15
Val
```

<210> 57
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 57
```
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gttcaccttg gacgttcggc 300
caagggacca aggtggaaat caaa                                        324
```

<210> 58
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 58
```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 59
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 59
cagagtgtta gcagcagcta c 21

<210> 60
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 60
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 61
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 61
ggtgcatcc 9

<210> 62
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 62
Gly Ala Ser
1

<210> 63
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 63
cagcagtatg gtagttcacc ttggacg 27

<210> 64
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 64
Gln Gln Tyr Gly Ser Ser Pro Trp Thr
1 5

<210> 65

<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 65
gaagtacagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgtag cctctggatt cccctttgct gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag cataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag aactgaggac acggccttgt attactgtgc aaaagatatg 300
agtggctacg cccactactt ctactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 66
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 66
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Pro Phe Ala Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Phe Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 67
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 67
ggattcccct ttgctgatta tacc 24

<210> 68
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 68
Gly Phe Pro Phe Ala Asp Tyr Thr
1 5

<210> 69

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 69
attagttgga atagtggtag cata 24

<210> 70
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 70
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 71
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 71
gcaaaagata tgagtggcta cgcccactac ttctactacg gtatggacgt c 51

<210> 72
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 72
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Phe Tyr Tyr Gly Met Asp
1 5 10 15
Val

<210> 73
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 73
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctttgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta cccctccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 74
<211> 108
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 74
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Phe Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
                85                  90                  95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105
```

<210> 75
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 75
cagagcatta gcagctat 18

<210> 76
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 76
```
Gln Ser Ile Ser Ser Tyr
 1               5
```

<210> 77
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 77
gctgcatcc 9

<210> 78
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 78
```
Ala Ala Ser
 1
```

```
<210> 79
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 79
caacagagtt acagtacccc tccgatcacc                                      30

<210> 80
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 80
Gln Gln Ser Tyr Ser Thr Pro Pro Ile Thr
 1               5                   10


<210> 81
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 81
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgaaactc 60
tcctgtacag cctctggatt cacctttgct gattatacca tgcactgggt ccgacaaggt 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag taaaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag aactgaggac acggccttgt attactgtgc aaaagatatg 300
agtggctacg cccactacta ctactacgct ttggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca                                                         372

<210> 82
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 82
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Lys Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ala Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Tyr Tyr Tyr Ala Leu Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 83
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 83
ggattcacct ttgctgatta tacc 24

<210> 84
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 84
Gly Phe Thr Phe Ala Asp Tyr Thr
1 5

<210> 85
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 85
attagttgga atagtggtag taaa 24

<210> 86
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 86
Ile Ser Trp Asn Ser Gly Ser Lys
1 5

<210> 87
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 87
gcaaaagata tgagtggcta cgcccactac tactactacg ctttggacgt c 51

<210> 88
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 88
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Tyr Tyr Tyr Ala Leu Asp
1   5   10   15
Val

<210> 89
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 89
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagc aactatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta accccccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 90
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 90
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Asn Tyr
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Asn Pro Pro
                85   90   95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100   105

<210> 91
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 91
cagagcatta gcaactat 18

<210> 92
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 92
Gln Ser Ile Ser Asn Tyr
 1   5

<210> 93
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 93
gctgcatcc 9

<210> 94
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 94
Ala Ala Ser
 1

<210> 95
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 95
caacagagtt acagtaaccc cccgatcacc 30

<210> 96
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 96
Gln Gln Ser Tyr Ser Asn Pro Pro Ile Thr
 1   5   10

<210> 97
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 97
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt agaaaaggca tgcactgggt ccgccaggct 120
ccagtcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgac agctgaggac acggctgtgt attactgtgc gaaagaaggg 300
gggcatgact atggtggtac ctttgactac tggggccagg gaaccctggt caccgtctcc 360

tca 363

<210> 98
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 98
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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Lys
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Val Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Thr Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Lys Glu Gly Gly His Asp Tyr Gly Gly Thr Phe Asp Tyr Trp Gly
            100                 105                 110
Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 99
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 99
ggattcacct tcagtagaaa aggc 24

<210> 100
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 100
```
Gly Phe Thr Phe Ser Arg Lys Gly
 1               5
```

<210> 101
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 101
atatcatatg atggaagtaa taaa 24

<210> 102
<211> 8
<212> PRT
<213> Artificial Sequence

```
<220>
<223> Synthetic

<400> 102
Ile Ser Tyr Asp Gly Ser Asn Lys
 1               5


<210> 103
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 103
gcgaaagaag gggggcatga ctatggtggt acctttgact ac                    42

<210> 104
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 104
Ala Lys Glu Gly Gly His Asp Tyr Gly Gly Thr Phe Asp Tyr
 1               5                   10


<210> 105
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 105
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc aggcgagtca ggacattaac aactatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagttcct gatctacgat gcatccaatt tggaaacagg ggtcccatca 180
aggttcagtg gaagtggatc tgggacagat tttactttca ccatcagcag cctgcagcct 240
gaagatattg caacatatta ctgtcaacag tatgatgatc tcccattcac tttcggccct 300
gggaccaaag tggatatcaa a                                           321

<210> 106
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 106
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Asn Asn Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile
        35                  40                  45
Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
```

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asp Leu Pro Phe
85 90 95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 107
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 107
caggacatta acaactat 18

<210> 108
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 108
Gln Asp Ile Asn Asn Tyr
1 5

<210> 109
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 109
gatgcatcc 9

<210> 110
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 110
Asp Ala Ser
1

<210> 111
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 111
caacagtatg atgatctccc attcact 27

<210> 112
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 112
```
Gln Gln Tyr Asp Asp Leu Pro Phe Thr
 1               5
```

<210> 113
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 113
```
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa gtccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataat 300
agtggctacg gtcactacta ctacggaatg gacgtctggg gccaagggac cacggtcacc 360
gtcgcctca                                                         369
```

<210> 114
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 114
```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
        115                 120
```

<210> 115
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 115
```
ggattcacct ttgatgatta tacc                                        24
```

<210> 116
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 116
Gly Phe Thr Phe Asp Asp Tyr Thr
1   5

<210> 117
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 117
attagttgga atagtggtag tata   24

<210> 118
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 118
Ile Ser Trp Asn Ser Gly Ser Ile
1   5

<210> 119
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 119
gcaaaagata atagtggcta cggtcactac tactacggaa tggacgtc   48

<210> 120
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 120
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 121
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 121
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcac tatattaact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 122
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 122
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Ile Asn Trp Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 123
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 123
cagagtgtta gcagcaac 18

<210> 124
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 124
Gln Ser Val Ser Ser Asn
1 5

<210> 125
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 125
ggtgcatcc 9

<210> 126
<211> 3

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 126
Gly Ala Ser
 1

<210> 127
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 127
cagcactata ttaactggcc tctcact 27

<210> 128
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 128
Gln His Tyr Ile Asn Trp Pro Leu Thr
 1 5

<210> 129
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 129
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa gtccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataat 300
agtggctacg gtcactacta ctacggaatg gacgtctggg gccaagggac cacggtcacc 360
gtcgcctca 369

<210> 130
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 130
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
 20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val

```
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
        115                 120


<210> 131
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 131
ggattcacct ttgatgatta tacc                                          24

<210> 132
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 132
Gly Phe Thr Phe Asp Asp Tyr Thr
1               5


<210> 133
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 133
attagttgga atagtggtag tata                                          24

<210> 134
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 134
Ile Ser Trp Asn Ser Gly Ser Ile
1               5


<210> 135
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 135
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gcaaaagata atagtggcta cggtcactac tactacggaa tggacgtc 48

<210> 136
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 136
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 137
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 137
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcac tatattaact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 138
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 138
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Ile Asn Trp Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 139
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 139
cagagtgtta gcagcaac 18

<210> 140

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 140
Gln Ser Val Ser Ser Asn
1   5

<210> 141
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 141
ggtgcatcc   9

<210> 142
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 142
Gly Ala Ser
1

<210> 143
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 143
cagcactata ttaactggcc tctcact   27

<210> 144
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 144
Gln His Tyr Ile Asn Trp Pro Leu Thr
1   5

<210> 145
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 145
caggtgcagt tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtggtg cgtctggatt caccttcaga agttatggca tgcactgggt ccgccagact 120
ccaggcaggg ggctggagtg ggtggcaatg atatattatg atggaaataa taaatactat 180
gcagactccg tgaggggccg attcaccgtt tccagagaca attccaagaa caccctgtat 240
ctgcaaatga gcagcctgag agccgaggac acggctctat atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 146
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 146
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Gly Ala Ser Gly Phe Thr Phe Arg Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Thr Pro Gly Arg Gly Leu Glu Trp Val
35 40 45
Ala Met Ile Tyr Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Arg Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Phe Cys
85 90 95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
115

<210> 147
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 147
ggattcacct tcagaagtta tggc 24

<210> 148
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 148
Gly Phe Thr Phe Arg Ser Tyr Gly
1 5

<210> 149
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 149

atatattatg atggaaataa taaa 24

<210> 150
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 150
Ile Tyr Tyr Asp Gly Asn Asn Lys
1 5

<210> 151
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 151
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 152
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 152
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1 5 10

<210> 153
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 153
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtattagc aggaacttgg cctggtacca gcaraaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataacc ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a 321

<210> 154
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<220>
<221> VARIANT
<222> 38
<223> Xaa = any amino acid

<220>
<221> VARIANT
<222> 38
<223> Xaa = Any Amino Acid

<400> 154
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Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1               5                   10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Arg Asn
            20                  25                  30
Leu Ala Trp Tyr Gln Xaa Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65                  70                  75                  80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
            100                 105
```

<210> 155
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 155
cagagtatta gcaggaac 18

<210> 156
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 156
```
Gln Ser Ile Ser Arg Asn
 1               5
```

<210> 157
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 157
ggtgcatcc 9

<210> 158
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 158
```
Gly Ala Ser
 1
```

```
<210> 159
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 159
cagcagtata ataaccggcc tctcact                                          27

<210> 160
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 160
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1               5


<210> 161
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 161
caggtgcagt tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
gcctgtgttg cgtctggatt caccttcaga agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg gactgcagtg ggtggcaatg atttactatg atggtaagaa taaatattat 180
gcagactccg tgaggggccg attcaccatc tccagagaca attccaagaa cacactgtat 240
ctgcaaatga acaatctgag agtcgaggac acggctatgt atttctgtgc gcgagggcct 300
gggtacaatt ggctcgaccc ctggggccag ggaaccctgg tcactgtttc ctca       354

<210> 162
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 162
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ala Cys Val Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gln Trp Val
        35                  40                  45
Ala Met Ile Tyr Tyr Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Asn Leu Arg Val Glu Asp Thr Ala Met Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115
```

<210> 163
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 163
ggattcacct tcagaagtta tggc 24

<210> 164
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 164
Gly Phe Thr Phe Arg Ser Tyr Gly
1 5

<210> 165
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 165
atttactatg atggtaagaa taaa 24

<210> 166
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 166
Ile Tyr Tyr Asp Gly Lys Asn Lys
1 5

<210> 167
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 167
gcgcgagggc ctgggtacaa ttggctcgac ccc 33

<210> 168
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 168
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 169
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 169
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagaattagc agcaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tagcccagcc 180
aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctgcagtct 240
gaggatgttg cagtttatta ctgtcagcaa catcataact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a   321

<210> 170
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 170
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Ile Ser Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ser Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His His Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 171
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 171
cagagaatta gcagcaac   18

<210> 172
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 172
Gln Arg Ile Ser Ser Asn
 1   5

<210> 173
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 173
ggtgcatcc 9

<210> 174
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 174
Gly Ala Ser
1

<210> 175
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 175
cagcaacatc ataactggcc tctcact 27

<210> 176
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 176
Gln Gln His His Asn Trp Pro Leu Thr
1 5

<210> 177
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 177
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttatgcca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcaatg gtatactatg atggaaataa tcaatactat 180
gcagactccg tgaggggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgatgac acggctgtgt atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 178
<211> 118

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 178
```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Val Tyr Tyr Asp Gly Asn Asn Gln Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115
```

<210> 179
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 179
ggatttacct tcagaagtta tgcc 24

<210> 180
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 180
```
Gly Phe Thr Phe Arg Ser Tyr Ala
1               5
```

<210> 181
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 181
gtatactatg atggaaataa tcaa 24

<210> 182
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 182
Val Tyr Tyr Asp Gly Asn Asn Gln
 1   5

<210> 183
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 183
gcgcgagggc ctgggtacaa ctggctcgac ccc   33

<210> 184
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 184
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 185
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 185
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc aggaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccggcc 180
aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataact ggcctctcac tttcggcgga 300
gggaccaagg tggtgatcaa a   321

<210> 186
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 186
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala 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 Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Val Ile Lys
            100   105

<210> 187
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 187
cagagtgtta gcaggaac   18

<210> 188
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 188
Gln Ser Val Ser Arg Asn
1   5

<210> 189
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 189
ggtgcatcc   9

<210> 190
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 190
Gly Ala Ser
1

<210> 191
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 191
cagcagtata ataactggcc tctcact   27

<210> 192
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

```
<400> 192
Gln Gln Tyr Asn Asn Trp Pro Leu Thr
 1               5


<210> 193
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 193
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtattg cgtctggatt taccttcaga agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcaatg atatattatg atggaaacaa taaatactat 180
gcagactccg tgaggggccg attcaccatc tccagagaca actccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgatgac acggctgtgt atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca       354

<210> 194
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 194
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ile Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115


<210> 195
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 195
ggatttacct tcagaagtta tggc                                        24

<210> 196
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic
```

<400> 196
Gly Phe Thr Phe Arg Ser Tyr Gly
 1   5

<210> 197
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 197
atatattatg atggaaacaa taaa 24

<210> 198
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 198
Ile Tyr Tyr Asp Gly Asn Asn Lys
 1   5

<210> 199
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 199
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 200
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 200
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 201
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 201
gaaatagtga tgacgcagtc tccagccaca ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataaca ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 202
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 202
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 203
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 203
cagagtgtta gcagcaac   18

<210> 204
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 204
Gln Ser Val Ser Ser Asn
 1   5

<210> 205
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 205
ggtgcatcc   9

<210> 206
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 206
Gly Ala Ser
 1

<210> 207
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 207
cagcagtata ataacaggcc tctcact 27

<210> 208
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 208
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1   5

<210> 209
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 209
caggtgcagc tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatatttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gtagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 210
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 210
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35   40   45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
                85   90   95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr

100 105 110
Leu Val Thr Val Ser Ser
115

<210> 211
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 211
ggattcacct tcagaagttt tggc 24

<210> 212
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 212
Gly Phe Thr Phe Arg Ser Phe Gly
1 5

<210> 213
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 213
atatattttg atggaaaaaa taaa 24

<210> 214
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 214
Ile Tyr Phe Asp Gly Lys Asn Lys
1 5

<210> 215
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 215
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 216
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 216
```
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1               5                   10
```

<210> 217
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 217
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gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagtcacc 60
ctctcctgta gggccagtca gagtattagc aggaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttca ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a                                           321
```

<210> 218
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 218
```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1               5                   10                  15
Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Arg Asn
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65                  70                  75                  80
Glu Asp Phe Ala Val Phe His Cys Gln Gln Tyr Asn Asn Arg Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
            100                 105
```

<210> 219
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 219
```
cagagtatta gcaggaac                                               18
```

<210> 220
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 220
Gln Ser Ile Ser Arg Asn
 1   5

<210> 221
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 221
ggtgcatcc 9

<210> 222
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 222
Gly Ala Ser
 1

<210> 223
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 223
cagcagtata ataataggcc tctcact 27

<210> 224
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 224
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1   5

<210> 225
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 225
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gtagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300

```
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca       354
```

<210> 226
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 226
```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115
```

<210> 227
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 227
```
ggattcacct tcagaagttt tggc                                        24
```

<210> 228
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 228
```
Gly Phe Thr Phe Arg Ser Phe Gly
1               5
```

<210> 229
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 229
```
atatattttg atggaaaaaa taaa                                        24
```

<210> 230
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 230
Ile Tyr Phe Asp Gly Lys Asn Lys
 1   5

<210> 231
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 231
gcgcgagggc ctgggtacaa ctggctcgac ccc   33

<210> 232
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 232
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 233
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 233
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagtcacc 60
ctctcctgta gggccagtca gagtattagc aggaacttgg cctggtacca gcaraaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttca ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a   321

<210> 234
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<220>
<221> VARIANT
<222> 38
<223> Xaa = Any amino acid

<220>
<221> VARIANT
<222> 38
<223> Xaa = Any Amino Acid

<400> 234

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

<210> 235
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 235
cagagtatta gcaggaac 18

<210> 236
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 236
Gln Ser Ile Ser Arg Asn
1   5

<210> 237
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 237
ggtgcatcc 9

<210> 238
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 238
Gly Ala Ser
1

<210> 239
<211> 27
<212> DNA
<213> Artificial Sequence

```
<220>
<223> Synthetic

<400> 239
cagcagtata ataataggcc tctcact                                      27

<210> 240
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 240
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1               5


<210> 241
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 241
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gcagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaatt ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca       354

<210> 242
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 242
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115


<210> 243
<211> 24
<212> DNA
<213> Artificial Sequence
```

<220>
<223> Synthetic

<400> 243
ggattcacct tcagaagttt tggc 24

<210> 244
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 244
Gly Phe Thr Phe Arg Ser Phe Gly
1 5

<210> 245
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 245
atatattttg atggaaaaaa taaa 24

<210> 246
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 246
Ile Tyr Phe Asp Gly Lys Asn Lys
1 5

<210> 247
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 247
gcgcgagggc ctgggtacaa ttggctcgac ccc 33

<210> 248
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 248
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1 5 10

<210> 249

<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 249
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgta gggccagtca gagtgttagc aggaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttca ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a 321

<210> 250
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 250
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Phe His Cys Gln Gln Tyr Asn Asn Arg Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
100 105

<210> 251
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 251
cagagtgtta gcaggaac 18

<210> 252
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 252
Gln Ser Val Ser Arg Asn
1 5

<210> 253
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 253
ggtgcatcc 9

<210> 254
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 254
Gly Ala Ser
1

<210> 255
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 255
cagcagtata ataataggcc tctcact 27

<210> 256
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 256
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
1 5

<210> 257
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 257
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gcagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaatt ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 258
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 258
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
35 40 45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
115

<210> 259
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 259
ggattcacct tcagaagttt tggc 24

<210> 260
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 260
Gly Phe Thr Phe Arg Ser Phe Gly
1 5

<210> 261
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 261
atatattttg atggaaaaaa taaa 24

<210> 262
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 262
Ile Tyr Phe Asp Gly Lys Asn Lys
1 5

<210> 263

<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 263
gcgcgagggc ctgggtacaa ttggctcgac ccc 33

<210> 264
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 264
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1 5 10

<210> 265
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 265
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgta gggccagtca gagtgttagc aggaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttca ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a 321

<210> 266
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 266
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Phe His Cys Gln Gln Tyr Asn Asn Arg Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
100 105

<210> 267
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 267
cagagtgtta gcaggaac 18

<210> 268
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 268
Gln Ser Val Ser Arg Asn
1 5

<210> 269
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 269
ggtgcatcc 9

<210> 270
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 270
Gly Ala Ser
1

<210> 271
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 271
cagcagtata ataataggcc tctcact 27

<210> 272
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 272
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
1 5

<210> 273
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 273
caggtgcagt tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgttg cgtctggatt caccttcaga agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg gactgcagtg ggtggcaatg atttactatg atggtaagaa taaatattat 180
gcagactccg tgaggggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagtctgag agccgaagac acggctatgt atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcactgtctc ctca 354

<210> 274
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 274
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Arg Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gln Trp Val
35 40 45
Ala Met Ile Tyr Tyr Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Phe Cys
85 90 95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
115

<210> 275
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 275
ggattcacct tcagaagtta tggc 24

<210> 276
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 276
Gly Phe Thr Phe Arg Ser Tyr Gly
1 5

<210> 277

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 277
atttactatg atggtaagaa taaa 24

<210> 278
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 278
Ile Tyr Tyr Asp Gly Lys Asn Lys
1 5

<210> 279
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 279
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 280
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 280
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1 5 10

<210> 281
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 281
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagaattagc agcaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tagcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagatgttg cagtttatta ctgtcagcaa cataataact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 282
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 282
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Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1               5                   10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Ile Ser Ser Asn
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ser Pro Ala Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65                  70                  75                  80
Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Asn Trp Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 283
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 283
cagagaatta gcagcaac 18

<210> 284
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 284
```
Gln Arg Ile Ser Ser Asn
1               5
```

<210> 285
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 285
ggtgcatcc 9

<210> 286
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 286
```
Gly Ala Ser
1
```

```
<210> 287
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 287
cagcaacata ataactggcc tctcact                                         27

<210> 288
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 288
Gln Gln His Asn Asn Trp Pro Leu Thr
1               5


<210> 289
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 289
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggttt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgagggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gtagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca       354

<210> 290
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 290
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115


<210> 291
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<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 291
ggtttcacct tcagaagttt tggc 24

<210> 292
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 292
Gly Phe Thr Phe Arg Ser Phe Gly
1 5

<210> 293
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 293
atatattttg atggaaaaaa taaa 24

<210> 294
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 294
Ile Tyr Phe Asp Gly Lys Asn Lys
1 5

<210> 295
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 295
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 296
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 296
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro

1   5   10

<210> 297
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 297
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagtcatc 60
ctctcctgta gggccagtca gagtattagc aggaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcaaccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttta ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a 321

<210> 298
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 298
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Val Ile Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Arg Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Thr Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Phe Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
            100   105

<210> 299
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 299
cagagtatta gcaggaac 18

<210> 300
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 300
Gln Ser Ile Ser Arg Asn
1   5

<210> 301
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 301
ggtgcaacc 9

<210> 302
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 302
Gly Ala Thr
1

<210> 303
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 303
cagcagtata ataataggcc tctcact 27

<210> 304
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 304
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
1 5

<210> 305
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 305
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggttt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gtagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 306
<211> 118
<212> PRT
<213> Artificial Sequence

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<220>
<223> Synthetic

<400> 306
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115


<210> 307
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 307
ggtttcacct tcagaagttt tggc                                              24

<210> 308
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 308
Gly Phe Thr Phe Arg Ser Phe Gly
 1               5


<210> 309
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 309
atatattttg atggaaaaaa taaa                                              24

<210> 310
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 310
Ile Tyr Phe Asp Gly Lys Asn Lys
```

1   5

<210> 311
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 311
gcgcgagggc ctgggtacaa ctggctcgac ccc   33

<210> 312
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 312
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1   5   10

<210> 313
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 313
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagtcatc 60
ctctcctgta gggccagtca gagtattagc aggaacttgg cctggtacca gcaraaacct 120
ggccaggctc ccaggctcct catctatggt gcaaccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttta ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a   321

<210> 314
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<220>
<221> VARIANT
<222> 38
<223> Xaa = Any amino acid

<220>
<221> VARIANT
<222> 38
<223> Xaa = Any Amino Acid

<400> 314
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Val Ile Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Arg Asn
            20   25   30
Leu Ala Trp Tyr Gln Xaa Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Gly Ala Thr Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Phe Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
            100   105

<210> 315
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 315
cagagtatta gcaggaac 18

<210> 316
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 316
Gln Ser Ile Ser Arg Asn
1   5

<210> 317
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 317
ggtgcaacc 9

<210> 318
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 318
Gly Ala Thr
1

<210> 319
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 319
cagcagtata ataataggcc tctcact 27

<210> 320
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 320
```
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1               5
```

<210> 321
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 321
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caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtattg cgtctggatt taccttcaga agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcaatg atatattatg atggaaacaa taaatactat 180
gcagactccg tgaggggccg attcaccatc tccagagaca actccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgatgac acggctgtgt atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca       354
```

<210> 322
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 322
```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ile Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115
```

<210> 323
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 323
```
ggatttacct tcagaagtta tggc                                        24
```

<210> 324
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 324
Gly Phe Thr Phe Arg Ser Tyr Gly
 1   5

<210> 325
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 325
atatattatg atggaaacaa taaa   24

<210> 326
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 326
Ile Tyr Tyr Asp Gly Asn Asn Lys
 1   5

<210> 327
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 327
gcgcgagggc ctgggtacaa ctggctcgac ccc   33

<210> 328
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 328
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 329
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 329
gaaatagtga tgacgcagtc tccagccaca ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataaca ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 330
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 330
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 331
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 331
cagagtgtta gcagcaac 18

<210> 332
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 332
Gln Ser Val Ser Ser Asn
1 5

<210> 333
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 333
ggtgcatcc 9

<210> 334
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 334
Gly Ala Ser
 1

<210> 335
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 335
cagcagtata ataacaggcc tctcact 27

<210> 336
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 336
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1   5

<210> 337
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 337
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattattcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtcgtag catagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgt aaaagataat 300
agtggctatg gccgctatta ctactacggg atggacgtct ggggccaagg gaccacggtc 360
tccgtctcct ca 372

<210> 338
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 338
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30

Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Arg Ser Ile Asp Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Val Lys Asp Asn Ser Gly Tyr Gly Arg Tyr Tyr Tyr Tyr Gly Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Ser Val Ser Ser
        115   120

<210> 339
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 339
ggattcacct ttgatgatta ttcc   24

<210> 340
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 340
Gly Phe Thr Phe Asp Asp Tyr Ser
1   5

<210> 341
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 341
attagttgga atagtcgtag cata   24

<210> 342
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 342
Ile Ser Trp Asn Ser Arg Ser Ile
1   5

<210> 343
<211> 51
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 343
gtaaaagata atagtggcta tggccgctat tactactacg ggatggacgt c 51

<210> 344
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 344
Val Lys Asp Asn Ser Gly Tyr Gly Arg Tyr Tyr Tyr Tyr Gly Met Asp
1 5 10 15
Val

<210> 345
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 345
aaaatagtga tgacgcagtc tcccgccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc ggcaacttag cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactag tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttattt ctgtcagcac tattataact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcag a 321

<210> 346
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 346
Lys Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Gly Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Ser Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Phe Cys Gln His Tyr Tyr Asn Trp Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Arg
100 105

<210> 347
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 347
cagagtgtta gcggcaac 18

<210> 348
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 348
Gln Ser Val Ser Gly Asn
1 5

<210> 349
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 349
ggtgcatcc 9

<210> 350
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 350
Gly Ala Ser
1

<210> 351
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 351
cagcactatt ataactggcc tctcact 27

<210> 352
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 352
Gln His Tyr Tyr Asn Trp Pro Leu Thr
1 5

<210> 353
<211> 369
<212> DNA

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 353
gaagtgcaac tggtggagtc tgggggaggc ttagtacagc ctggcgggtc cctgagactc 60
tcctgtgcag ccactggatt cacctttgat gattttacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt atcagttgga atagtggtag cataggctat 180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt actactgtgc aaaagataat 300
agtggctacg gctattatta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 354
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 354
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Thr Gly Phe Thr Phe Asp Asp Phe
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Val Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Gly Met Asp Val
            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 355
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 355
ggattcacct ttgatgattt tacc 24

<210> 356
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 356
Gly Phe Thr Phe Asp Asp Phe Thr
1   5

<210> 357
<211> 24
<212> DNA

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 357
atcagttgga atagtggtag cata 24

<210> 358
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 358
Ile Ser Trp Asn Ser Gly Ser Ile
1   5

<210> 359
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 359
gcaaaagata atagtggcta cggctattat tactacggta tggacgtc 48

<210> 360
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 360
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 361
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 361
gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc 60
atcaactgca agtccagcca gagtgtttta tacagctcca acaataagaa ctacttagct 120
tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg 180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcaata ttatagtact 300
ccgtacactt ttggccaggg gaccaagctg gagatcaaa 339

<210> 362
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 362
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1   5   10   15
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
            20   25   30
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
        35   40   45
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65   70   75   80
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                85   90   95
Tyr Tyr Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
            100   105   110
Lys

<210> 363
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 363
cagagtgttt tatacagctc caacaataag aactac   36

<210> 364
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 364
Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr
1   5   10

<210> 365
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 365
tgggcatct   9

<210> 366
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 366
Trp Ala Ser
1

<210> 367
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 367
cagcaatatt atagtactcc gtacact 27

<210> 368
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 368
Gln Gln Tyr Tyr Ser Thr Pro Tyr Thr
1 5

<210> 369
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 369
caggtcacct tgaaggagtc tggtcctgcg ctggtgaaac ccacacagac cctcacactg 60
acctgcacct tctctgggtt ctcactcagc actagtggaa tgtgtgtgag ctggatccgt 120
cagcccccag ggaaggccct ggagtggctt gcacgcattg attgggatga tgataaatac 180
tacagcacat ctctgaagac caggctcacc atctccaagg acacctccaa aaaccaggtg 240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca cgtattactg tgcacggatg 300
gatatagtgg gagctagagg ggggtggttc gacccctggg gccagggaac cctggtcacc 360
gtctcctca 369

<210> 370
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 370
Gln Val Thr Leu Lys Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30
Gly Met Cys Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45
Trp Leu Ala Arg Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser
50 55 60
Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95
Cys Ala Arg Met Asp Ile Val Gly Ala Arg Gly Gly Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 371
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 371
gggttctcac tcagcactag tggaatgtgt   30

<210> 372
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 372
Gly Phe Ser Leu Ser Thr Ser Gly Met Cys
1   5   10

<210> 373
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 373
attgattggg atgatgataa a   21

<210> 374
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 374
Ile Asp Trp Asp Asp Asp Lys
1   5

<210> 375
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 375
gcacggatgg atatagtggg agctagaggg gggtggttcg acccc   45

<210> 376
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 376

Ala Arg Met Asp Ile Val Gly Ala Arg Gly Gly Trp Phe Asp Pro
1   5   10   15

<210> 377
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 377
gacatccaga tgacccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcgagtca gggcattagc aattatttag cctggtttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aagttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgccaacag tataatagtt acccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 378
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 378
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
            20   25   30
Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
        35   40   45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 379
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 379
cagggcatta gcaattat 18

<210> 380
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 380
Gln Gly Ile Ser Asn Tyr
1   5

<210> 381
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 381
gctgcatcc 9

<210> 382
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 382
Ala Ala Ser
1

<210> 383
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 383
caacagtata atagttaccc gctcact 27

<210> 384
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 384
Gln Gln Tyr Asn Ser Tyr Pro Leu Thr
1 5

<210> 385
<211> 404
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 385
caggtgcagt tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcaatg atatattatg atggaaataa taaaaagtat 180
gcagactccg tgagggggccg attcaccatt tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agtcgaggac acggctgtgt atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctcagccaaa 360
acaacagccc cacccgttta tccactggcc cctggaagct tggg 404

<210> 386
<211> 134

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 386
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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Met Ile Tyr Tyr Asp Gly Asn Asn Lys Lys Tyr Ala Asp Ser Val
    50                  55                  60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser Ala Lys Thr Thr Ala Pro Pro Val Tyr Pro
        115                 120                 125
Leu Ala Pro Gly Ser Leu
    130
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<210> 387
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 387
ggattcacct tcagaagtta tggc 24

<210> 388
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 388
```
Gly Phe Thr Phe Arg Ser Tyr Gly
 1               5
```

<210> 389
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 389
atatattatg atggaaataa taaa 24

<210> 390
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 390
Ile Tyr Tyr Asp Gly Asn Asn Lys
 1   5

<210> 391
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 391
gcgcgagggc ctgggtacaa ctggctcgac ccc   33

<210> 392
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 392
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 393
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 393
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc aggaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactga tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcattctca acatcagcag cctgcagtct 240
gaagattttg cactttatta ctgtcaacaa tatagtaact ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a   321

<210> 394
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 394
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Asp Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Ile Leu Asn Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Leu Tyr Tyr Cys Gln Gln Tyr Ser Asn Trp Pro Leu
                85   90   95

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

<210> 395
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 395
cagagtgtta gcaggaac   18

<210> 396
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 396
Gln Ser Val Ser Arg Asn
1   5

<210> 397
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 397
ggtgcatcc   9

<210> 398
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 398
Gly Ala Ser
1

<210> 399
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 399
caacaatata gtaactggcc tctcact   27

<210> 400
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 400
Gln Gln Tyr Ser Asn Trp Pro Leu Thr
 1   5

<210> 401
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 401
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggttt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gtagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca   354

<210> 402
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 402
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35   40   45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
                85   90   95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100   105   110
Leu Val Thr Val Ser Ser
        115

<210> 403
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 403
ggtttcacct tcagaagttt tggc   24

<210> 404
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 404
Gly Phe Thr Phe Arg Ser Phe Gly
 1   5

<210> 405
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 405
atatattttg atggaaaaaa taaa 24

<210> 406
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 406
Ile Tyr Phe Asp Gly Lys Asn Lys
 1   5

<210> 407
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 407
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 408
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 408
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 409
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 409
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagtcatc 60
ctctcctgta gggccagtca gagtattagc aggaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcaaccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240

gaagattttg cagtttttta ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a 321

<210> 410
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 410
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Val Ile Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Arg Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Thr Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Phe Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
100 105

<210> 411
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 411
cagagtatta gcaggaac 18

<210> 412
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 412
Gln Ser Ile Ser Arg Asn
1 5

<210> 413
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 413
ggtgcaacc 9

<210> 414
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 414
Gly Ala Thr
 1

<210> 415
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 415
cagcagtata ataataggcc tctcact   27

<210> 416
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 416
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
 1   5

<210> 417
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 417
caggtgcaat tggtggagtc tgggggaggc gtggtccagc cggggaggtc cctgagactc 60
tcctgtgctg cgtctggttt caccttcaga agttttggca tgcactgggt ccgccaggct 120
ccaggcaggg gactggagtg ggtggcaatg atatattttg atggaaaaaa taaatactat 180
gcagactccg tgaggggccg attcaccatt tccagagaca attccaagaa caccctgtat 240
ctggaaatga gtagcctgag agccgaggac acggctgtat atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca   354

<210> 418
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 418
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
        35   40   45
Ala Met Ile Tyr Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Glu Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys

```
                85                  90                  95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115


<210> 419
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 419
ggtttcacct tcagaagttt tggc                                            24

<210> 420
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 420
Gly Phe Thr Phe Arg Ser Phe Gly
1               5


<210> 421
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 421
atatattttg atggaaaaaa taaa                                            24

<210> 422
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 422
Ile Tyr Phe Asp Gly Lys Asn Lys
1               5


<210> 423
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 423
gcgcgagggc ctgggtacaa ctggctcgac ccc                                  33

<210> 424
<211> 11
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<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 424
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
 1   5   10

<210> 425
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 425
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagtcatc 60
ctctcctgta gggccagtca gagtattagc aggaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcaaccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctacagtct 240
gaagattttg cagtttttta ctgtcagcag tataataata ggcctctcac tttcggcgga 300
gggaccgagg tggagatcaa a   321

<210> 426
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 426
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Val Ile Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Arg Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Thr Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Phe Tyr Cys Gln Gln Tyr Asn Asn Arg Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Glu Val Glu Ile Lys
            100   105

<210> 427
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 427
cagagtatta gcaggaac   18

<210> 428
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 428
Gln Ser Ile Ser Arg Asn
1   5

<210> 429
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 429
ggtgcaacc   9

<210> 430
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 430
Gly Ala Thr
1

<210> 431
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 431
cagcagtata ataataggcc tctcact   27

<210> 432
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 432
Gln Gln Tyr Asn Asn Arg Pro Leu Thr
1   5

<210> 433
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 433
caggtgcacc tggaagagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgttcag cgtctggttt caccttcagt agttatgcca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atatggtatg atggaactaa taaatattat 180

ttagattccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgttt 240
ctgcaaatga acagcctgag agccgaagac acggctgtgt attactgtgc gagagatcgg 300
ggaagtataa taacccactg gggccaggga accctggtca ccgtctcctc a 351

<210> 434
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 434
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Gln Val His Leu Glu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ser Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Tyr Asp Gly Thr Asn Lys Tyr Tyr Leu Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Arg Gly Ser Ile Ile Thr His Trp Gly Gln Gly Thr Leu
            100                 105                 110
Val Thr Val Ser Ser
        115
```

<210> 435
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 435
ggtttcacct tcagtagtta tgcc 24

<210> 436
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 436
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Gly Phe Thr Phe Ser Ser Tyr Ala
 1               5
```

<210> 437
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 437
atatggtatg atggaactaa taaa 24

<210> 438
<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 438
Ile Trp Tyr Asp Gly Thr Asn Lys
 1   5

<210> 439
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 439
gcgagagatc ggggaagtat aataacccac   30

<210> 440
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 440
Ala Arg Asp Arg Gly Ser Ile Ile Thr His
 1   5   10

<210> 441
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 441
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctataggaga cagagtcacc 60
atcacttgcc gggcaagtca gaacattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag acttacagta cccctccgat caccttcggc 300
caagggacac gactggagat taaa   324

<210> 442
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 442
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Ile Gly
 1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Ser Ser Tyr
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Tyr Ser Thr Pro Pro
                85   90   95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100   105

<210> 443
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 443
cagaacatta gcagctat   18

<210> 444
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 444
Gln Asn Ile Ser Ser Tyr
1   5

<210> 445
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 445
gctgcatcc   9

<210> 446
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 446
Ala Ala Ser
1

<210> 447
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 447
caacagactt acagtacccc tccgatcacc   30

<210> 448

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

<220>
<223> Synthetic

<400> 448
Gln Gln Thr Tyr Ser Thr Pro Pro Ile Thr
 1   5   10

<210> 449
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 449
gaagtacagc tggtggagtc tgggggaggc ttggtacggc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccgccaagct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtgggac cataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgc aaaagatatg 300
agtggctacg cccactacta ctactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca   372

<210> 450
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 450
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Arg Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Ser Trp Asn Ser Gly Thr Ile Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Tyr Tyr Tyr Gly Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 451
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 451
ggattcacct ttgatgatta tacc   24

<210> 452

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 452
Gly Phe Thr Phe Asp Asp Tyr Thr
 1   5

<210> 453
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 453
attagttgga atagtgggac cata   24

<210> 454
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 454
Ile Ser Trp Asn Ser Gly Thr Ile
 1   5

<210> 455
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 455
gcaaaagata tgagtggcta cgcccactac tactactacg gtatggacgt c   51

<210> 456
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 456
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Tyr Tyr Tyr Gly Met Asp
 1   5   10   15
Val

<210> 457
<211> 324
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 457
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta cccctccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 458
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 458
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 459
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 459
cagagcatta gcagctat 18

<210> 460
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 460
Gln Ser Ile Ser Ser Tyr
1 5

<210> 461
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 461

gctgcatcc 9

<210> 462
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 462
Ala Ala Ser
1

<210> 463
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 463
caacagagtt acagtacccc tccgatcacc 30

<210> 464
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 464
Gln Gln Ser Tyr Ser Thr Pro Pro Ile Thr
1 5 10

<210> 465
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 465
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctccgat attagttgga atagtggtag cataggctat 180
gcggactctg tgaagggccg attcaccgtc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag aggtgaggac acggccctgt attactgtgc aaaagatatg 300
agtggctacg cccactacgg ctactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 466
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 466
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr

```
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Gly Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Gly Tyr Tyr Gly Met Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 467
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 467
ggattcacct ttgatgatta tacc                                            24

<210> 468
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 468
Gly Phe Thr Phe Asp Asp Tyr Thr
1               5


<210> 469
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 469
attagttgga atagtggtag cata                                            24

<210> 470
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 470
Ile Ser Trp Asn Ser Gly Ser Ile
1               5


<210> 471
<211> 51
<212> DNA
<213> Artificial Sequence
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<220>
<223> Synthetic

<400> 471
gcaaaagata tgagtggcta cgcccactac ggctactacg gtatggacgt c 51

<210> 472
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 472
Ala Lys Asp Met Ser Gly Tyr Ala His Tyr Gly Tyr Tyr Gly Met Asp
1 5 10 15
Val

<210> 473
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 473
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagg aactatttaa attggtatca gcagaaacca 120
gggaaagtcc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta accctccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 474
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 474
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Asn Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Asn Pro Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 475
<211> 18
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 475
cagagcatta ggaactat 18

<210> 476
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 476
Gln Ser Ile Arg Asn Tyr
1 5

<210> 477
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 477
gctgcatcc 9

<210> 478
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 478
Ala Ala Ser
1

<210> 479
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 479
caacagagtt acagtaaccc tccgatcacc 30

<210> 480
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 480
Gln Gln Ser Tyr Ser Asn Pro Pro Ile Thr
1 5 10

<210> 481
<211> 369

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 481
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gaagcgcagc tggtggaatc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtacaa cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg gatctctgat attagttgga atggtggaac caaaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaaaaa ctccctgtat 240
ctgcaaatgg acagtctgag aggtgaggac acggccttat attactgtgt aaaagataaa 300
agtggctacg ggcacttcta cttcggtttg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca                                                         369
```

<210> 482
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 482
```
Glu Ala Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Thr Thr Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45
Ser Asp Ile Ser Trp Asn Gly Gly Thr Lys Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asp Ser Leu Arg Gly Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Val Lys Asp Lys Ser Gly Tyr Gly His Phe Tyr Phe Gly Leu Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 483
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 483
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ggattcacct ttgatgatta tacc                                        24
```

<210> 484
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 484
```
Gly Phe Thr Phe Asp Asp Tyr Thr
 1               5
```

<210> 485
<211> 24

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 485
attagttgga atggtggaac caaa 24

<210> 486
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 486
Ile Ser Trp Asn Gly Gly Thr Lys
1 5

<210> 487
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 487
gtaaaagata aaagtggcta cgggcacttc tacttcggtt tggacgtc 48

<210> 488
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 488
Val Lys Asp Lys Ser Gly Tyr Gly His Phe Tyr Phe Gly Leu Asp Val
1 5 10 15

<210> 489
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 489
gacatccaga tgacccagtc tccatcctcc ctgactgcgt ctgtaggaga cagagtcacc 60
ttcacttgcc gggcaagtca gagcattagc aggcatttaa gttggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tggaaagtgg ggtcccttca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaccct 240
gaagattttg caacttacta ctgtcaacag agctacagta accctccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 490
<211> 108
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 490
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Thr Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Phe Thr Cys Arg Ala Ser Gln Ser Ile Ser Arg His
            20                  25                  30
Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu His Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Asn Pro Pro
                85                  90                  95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105
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<210> 491
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 491
cagagcatta gcaggcat 18

<210> 492
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 492
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Gln Ser Ile Ser Arg His
1               5
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<210> 493
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 493
gctgcatcc 9

<210> 494
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 494
```
Ala Ala Ser
1
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<210> 495

<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 495
caacagagct acagtaaccc tccgatcacc 30

<210> 496
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 496
Gln Gln Ser Tyr Ser Asn Pro Pro Ile Thr
1 5 10

<210> 497
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 497
gaagtgcagt tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt caagtttgct gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcagag attagttgga atagtggtag cataggttat 180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgt aaaagataaa 300
agtggctacg ggcactacta tatcggtatg gacgtctggg gccaagggac cacggtcatc 360
gtctcctcc 369

<210> 498
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 498
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Lys Phe Ala Asp Tyr
20 25 30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Glu Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Val Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Asp Lys Ser Gly Tyr Gly His Tyr Tyr Ile Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Ile Val Ser Ser
115 120

<210> 499

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 499
ggattcaagt ttgctgatta tgcc 24

<210> 500
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 500
Gly Phe Lys Phe Ala Asp Tyr Ala
1 5

<210> 501
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 501
attagttgga atagtggtag cata 24

<210> 502
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 502
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 503
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 503
gtaaaagata aaagtggcta cgggcactac tatatcggta tggacgtc 48

<210> 504
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 504
Val Lys Asp Lys Ser Gly Tyr Gly His Tyr Tyr Ile Gly Met Asp Val

1 5 10 15

<210> 505
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 505
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagtattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta cccctccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 506
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 506
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 507
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 507
cagagtatta gcagctat 18

<210> 508
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 508
Gln Ser Ile Ser Ser Tyr
1 5

<210> 509
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 509
gctgcatcc 9

<210> 510
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 510
Ala Ala Ser
1

<210> 511
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 511
caacagagtt acagtacccc tccgatcacc 30

<210> 512
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 512
Gln Gln Ser Tyr Ser Thr Pro Pro Ile Thr
1 5 10

<210> 513
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 513
gaagtgcacc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctccgat attagttgga atagtggtag cataggctat 180
gcggactctg tgaagggccg attcaccgtc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag aggtgaggac acggccttgt attactgtgc aaaagatatg 300
agtggctacg gccactacgg caagtacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 514
<211> 124
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 514
Glu Val His Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Gly Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Met Ser Gly Tyr Gly His Tyr Gly Lys Tyr Gly Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 515
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 515
ggattcacct ttgatgatta tacc   24

<210> 516
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 516
Gly Phe Thr Phe Asp Asp Tyr Thr
 1   5

<210> 517
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 517
attagttgga atagtggtag cata   24

<210> 518
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 518

Ile Ser Trp Asn Ser Gly Ser Ile
 1   5

<210> 519
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 519
gcaaaagata tgagtggcta cggccactac ggcaagtacg gtatggacgt c   51

<210> 520
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 520
Ala Lys Asp Met Ser Gly Tyr Gly His Tyr Gly Lys Tyr Gly Met Asp
 1   5   10   15
Val

<210> 521
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 521
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagg agctatttaa attggtatca gcagaaacca 120
gggaaagtcc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcaacag tctgcaacct 240
gacgattttg caacttacta ctgtcaacag acttacagta accctccgat caccttcggc 300
caagggacac gactggagat taaa   324

<210> 522
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 522
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser Tyr
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35   40   45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
65   70   75   80
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Tyr Ser Asn Pro Pro
                85   90   95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys

100 105

<210> 523
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 523
cagagcatta ggagctat 18

<210> 524
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 524
Gln Ser Ile Arg Ser Tyr
1 5

<210> 525
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 525
gctgcatcc 9

<210> 526
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 526
Ala Ala Ser
1

<210> 527
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 527
caacagactt acagtaaccc tccgatcacc 30

<210> 528
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 528
Gln Gln Thr Tyr Ser Asn Pro Pro Ile Thr
1 5 10

<210> 529
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 529
gaggtgcagc tggtggagtc tgggggagac ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaatt attagttgga atggtaatac cattgactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
cttcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataag 300
agtggctacg gacacttcta ctattacgtt ttggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 530
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 530
Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ile Ile Ser Trp Asn Gly Asn Thr Ile Asp Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Lys Ser Gly Tyr Gly His Phe Tyr Tyr Tyr Val Leu Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 531
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 531
ggattcacct ttgatgatta tacc 24

<210> 532
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 532
Gly Phe Thr Phe Asp Asp Tyr Thr
 1   5

<210> 533
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 533
attagttgga atggtaatac catt   24

<210> 534
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 534
Ile Ser Trp Asn Gly Asn Thr Ile
 1   5

<210> 535
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 535
gcaaaagata agagtggcta cggacacttc tactattacg ttttggacgt c   51

<210> 536
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 536
Ala Lys Asp Lys Ser Gly Tyr Gly His Phe Tyr Tyr Tyr Val Leu Asp
 1   5   10   15
Val

<210> 537
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 537
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattaac aactatttaa attggtatca gcagaaacca 120

gggaaagccc ctaaactcct gatctatgct gcttccagtt tgcaaagtgg ggtcccgtca 180
aggttcagtg gcagtggttc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctctcaacag agttacagtt tcccgtggac gttcggccaa 300
gggaccaagg tggaaatcaa a 321

<210> 538
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 538
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Asn Asn Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Ser Gln Gln Ser Tyr Ser Phe Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 539
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 539
cagagcatta acaactat 18

<210> 540
<211> 6
<212> PRT
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<220>
<223> Synthetic

<400> 540
Gln Ser Ile Asn Asn Tyr
1 5

<210> 541
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 541
gctgcttcc 9

<210> 542
<211> 3
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 542
Ala Ala Ser
 1

<210> 543
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 543
caacagagtt acagtttccc gtggacg 27

<210> 544
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 544
Gln Gln Ser Tyr Ser Phe Pro Trp Thr
 1   5

<210> 545
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 545
caggtgcagc tggtggagtc gggggaggc gtggtccagc ctgggaggtc cctgagaccc 60
tcctgtgcag cgtctggatt tagtttcagg gactatggca tgcactgggt ccgccaggct 120
ccaggtaagg gactagagtg gatggcacac atatggtata atggaaagaa taaatattat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctatat 240
ctgcaaatga acagcctgag acccgaggac acggctgtat attattgtgc gagagatggt 300
gtatcagcac gtggtactcc atttgactac tggggccagg gaaccctggt caccgtctcc 360
tca 363

<210> 546
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 546
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Pro Ser Cys Ala Ala Ser Gly Phe Ser Phe Arg Asp Tyr
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45
Ala His Ile Trp Tyr Asn Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Asp Gly Val Ser Ala Arg Gly Thr Pro Phe Asp Tyr Trp Gly
            100   105   110
Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 547
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 547
ggatttagtt tcagggacta tggc   24

<210> 548
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 548
Gly Phe Ser Phe Arg Asp Tyr Gly
1   5

<210> 549
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 549
atatggtata atggaaagaa taaa   24

<210> 550
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 550
Ile Trp Tyr Asn Gly Lys Asn Lys
1   5

<210> 551
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 551
gcgagagatg gtgtatcagc acgtggtact ccatttgact ac   42

<210> 552
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 552
Ala Arg Asp Gly Val Ser Ala Arg Gly Thr Pro Phe Asp Tyr
1 5 10

<210> 553
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 553
gaaacgacac tcacgcagtc tccagcattc atgtcagcgg ctccaggaga caaagtcagc 60
atctcctgca ttgccagcca gtacattgat gatgatgtga actggtacca acagaaacca 120
ggagaaactg ctattttcat tattcaagaa gcttctactc tcgttcctgg aatctcacct 180
cgattcagtg gcagcgggta tggaacacat tttaccctca caattaataa catagattct 240
gaggatgctg cattttactt ctgtctccaa catgataatt tcccgtacac ttttggccag 300
gggaccaagc tggagatcaa a 321

<210> 554
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 554
Glu Thr Thr Leu Thr Gln Ser Pro Ala Phe Met Ser Ala Ala Pro Gly
1 5 10 15
Asp Lys Val Ser Ile Ser Cys Ile Ala Ser Gln Tyr Ile Asp Asp Asp
20 25 30
Val Asn Trp Tyr Gln Gln Lys Pro Gly Glu Thr Ala Ile Phe Ile Ile
35 40 45
Gln Glu Ala Ser Thr Leu Val Pro Gly Ile Ser Pro Arg Phe Ser Gly
50 55 60
Ser Gly Tyr Gly Thr His Phe Thr Leu Thr Ile Asn Asn Ile Asp Ser
65 70 75 80
Glu Asp Ala Ala Phe Tyr Phe Cys Leu Gln His Asp Asn Phe Pro Tyr
85 90 95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 555
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 555
cagtacattg atgatgat 18

<210> 556
<211> 6

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 556
Gln Tyr Ile Asp Asp Asp
 1   5

<210> 557
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 557
gaagcttct   9

<210> 558
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 558
Glu Ala Ser
 1

<210> 559
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 559
ctccaacatg ataatttccc gtacact   27

<210> 560
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 560
Leu Gln His Asp Asn Phe Pro Tyr Thr
 1   5

<210> 561
<211> 384
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 561

caggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc 60
tcctgtgcag cctcttattt cacctttagc agttttgcca tgaactgggt ccgccaggct 120
ccagggcagg gcctggagtg ggtctcagct attagtggta gggtctcagc tattagtggt 180
agtggtggta tcacatacta cgcagactcc gtgaagggcc ggttcatcat ctccagagac 240
aattccaaga acacgctgta tctgcaaatg agcggcctga gagccgagga cacggccgta 300
tattactgtg cgaaaggccc ctatttgact acagtcaccc cctttgacta ctggggccag 360
ggaaccctgg tcaccgtctc ctca 384

<210> 562
<211> 128
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 562
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Tyr Phe Thr Phe Ser Ser Phe
20 25 30
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Val
35 40 45
Ser Ala Ile Ser Gly Arg Val Ser Ala Ile Ser Gly Ser Gly Gly Ile
50 55 60
Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Ile Ile Ser Arg Asp
65 70 75 80
Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Ser Gly Leu Arg Ala Glu
85 90 95
Asp Thr Ala Val Tyr Tyr Cys Ala Lys Gly Pro Tyr Leu Thr Thr Val
100 105 110
Thr Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 563
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 563
tatttcacct ttagcagttt tgcc 24

<210> 564
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 564
Tyr Phe Thr Phe Ser Ser Phe Ala
1 5

<210> 565
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 565

attagtggta gtggtggtat caca 24

<210> 566
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 566
Ile Ser Gly Ser Gly Gly Ile Thr
1 5

<210> 567
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 567
gcgaaaggcc cctatttgac tacagtcacc ccctttgact ac 42

<210> 568
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 568
Ala Lys Gly Pro Tyr Leu Thr Thr Val Thr Pro Phe Asp Tyr
1 5 10

<210> 569
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 569
gacatccagt tgacccagtc tccatcttcc gtgtctgcat ctgtcggaga cagagtcacc 60
atcacttgtc gggcgagtca ggggattagc agctggttag cctggtatca gcagaaacca 120
gggaaagccc ctaaactcct gatctatgct gtatccagtt tgcaaaatgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagat ttcaccctca ccatcagcag cctgcagcct 240
gaagactttg caacttacta ttgtcaacag gctaacagtt tcccattcac tttcggccct 300
gggaccaagc tggagatcaa acga 324

<210> 570
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 570
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20 25 30

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


&lt;210&gt; 571
&lt;211&gt; 18
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 571
caggggatta gcagctgg                                                  18

&lt;210&gt; 572
&lt;211&gt; 6
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 572
Gln Gly Ile Ser Ser Trp
 1               5


&lt;210&gt; 573
&lt;211&gt; 9
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 573
gctgtatcc                                                            9

&lt;210&gt; 574
&lt;211&gt; 3
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 574
Ala Val Ser
 1


&lt;210&gt; 575
&lt;211&gt; 27
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic
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<400> 575
caacaggcta acagtttccc attcact 27

<210> 576
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 576
Gln Gln Ala Asn Ser Phe Pro Phe Thr
1   5

<210> 577
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 577
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgct gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag tataggttat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttat attactgtgt aaaagataat 300
agtggctacg catcctacta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 578
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 578
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
            20   25   30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Val Lys Asp Asn Ser Gly Tyr Ala Ser Tyr Tyr Tyr Gly Met Asp Val
            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 579
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 579
ggattcacct ttgctgatta tgcc 24

<210> 580
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 580
Gly Phe Thr Phe Ala Asp Tyr Ala
1 5

<210> 581
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 581
attagttgga atagtggtag tata 24

<210> 582
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 582
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 583
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 583
gtaaaagata atagtggcta cgcatcctac tactacggta tggacgtc 48

<210> 584
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 584
Val Lys Asp Asn Ser Gly Tyr Ala Ser Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 585
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 585
gacatccagt tgacccagtc cccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctacgat gcatccaatt tggaaacagg ggtcccatca 180
aggttcagtg gaagtggatc tgggacagat tttactttca ccatcagcag cctgcagcct 240
gaagatattg caacatatta ctgtcaacag tatgataatc tcccattcac tttcggccct 300
gggaccaaag tggatatcaa acga 324

<210> 586
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 586
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Phe
85 90 95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg
100 105

<210> 587
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 587
cagagcatta gcagctat 18

<210> 588
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 588
Gln Ser Ile Ser Ser Tyr
1 5

<210> 589
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 589
gatgcatcc 9

<210> 590
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 590
Asp Ala Ser
1

<210> 591
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 591
caacagtatg ataatctccc attcact 27

<210> 592
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 592
Gln Gln Tyr Asp Asn Leu Pro Phe Thr
1 5

<210> 593
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 593
gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt aactatggca tgcactgggt ccgccaggct 120
ccaggcaaag ggctggagtg ggtgacagtt atattacatg atggaagtta taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctacat 240
ctgcaaatga acagcctgag aactgaggac acggctgtat attactgtgc gaaagggcct 300
atgtttcggg gagtccctta caaccactac tatggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

<210> 594
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 594
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg

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


<210> 595
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 595
ggattcacct tcagtaacta tggc                                              24

<210> 596
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 596
Gly Phe Thr Phe Ser Asn Tyr Gly
 1               5


<210> 597
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 597
atattacatg atggaagtta taaa                                              24

<210> 598
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 598
Ile Leu His Asp Gly Ser Tyr Lys
 1               5


<210> 599
<211> 57
<212> DNA
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<213> Artificial Sequence

<220>
<223> Synthetic

<400> 599
gcgaaagggc ctatgtttcg gggagtccct tacaaccact actatggtat ggacgtc 57

<210> 600
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 600
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Ala Lys Gly Pro Met Phe Arg Gly Val Pro Tyr Asn His Tyr Tyr Gly
 1               5                  10                  15
Met Asp Val
```

<210> 601
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 601
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gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcatcaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtctcatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300
gggaccaagg tggaaatcaa acga                                        324
```

<210> 602
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 602
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Ser Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Tyr
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 603
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 603
cagggcatca gaaatgat 18

<210> 604
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 604
Gln Gly Ile Arg Asn Asp
1 5

<210> 605
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 605
gctgcatcc 9

<210> 606
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 606
Ala Ala Ser
1

<210> 607
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 607
ctacagcata atagttaccc gtacact 27

<210> 608
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 608
Leu Gln His Asn Ser Tyr Pro Tyr Thr
1 5

<210> 609
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 609
gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtacag cgtcaggttt ccccttcagt cgctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggaatg ggtgacattt atatggtatg atggaagtaa taaatactat 180
gcagactccg cgaagggccg attcaccatc accagagaca attccaagaa cacggtgtat 240
ctgcaaatgg acagcctgag agccgatgac acggctgttt attattgtgt gagagatcag 300
gcagctctct actattttga ctcttggggc cagggaaccc tggtcaccgt ctcctca 357

<210> 610
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 610
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Pro Phe Ser Arg Tyr
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Thr Phe Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Ala
    50   55   60
Lys Gly Arg Phe Thr Ile Thr Arg Asp Asn Ser Lys Asn Thr Val Tyr
65   70   75   80
Leu Gln Met Asp Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Val Arg Asp Gln Ala Ala Leu Tyr Tyr Phe Asp Ser Trp Gly Gln Gly
            100   105   110
Thr Leu Val Thr Val Ser Ser
        115

<210> 611
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 611
ggtttcccct tcagtcgcta tggc 24

<210> 612
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 612
Gly Phe Pro Phe Ser Arg Tyr Gly
1   5

<210> 613

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 613
atatggtatg atggaagtaa taaa 24

<210> 614
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 614
Ile Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> 615
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 615
gtgagagatc aggcagctct ctactatttt gactct 36

<210> 616
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 616
Val Arg Asp Gln Ala Ala Leu Tyr Tyr Phe Asp Ser
1 5 10

<210> 617
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 617
gacatccaga tgacccagtc tccatcttcc gtgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcgagtca gggtattagc aggtggttag cctggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctctgct gcatccagtt tgcaaagtgg agtcccatca 180
aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcgg cctgcagcct 240
gaagattttg caacttacta ttgtcaaaag gctaacagtt tccctttcac tttcggccct 300
gggaccaagc tggagatcaa acga 324

<210> 618
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 618
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Arg Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Ser Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Lys Ala Asn Ser Phe Pro Phe
                85                  90                  95
Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105
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<210> 619
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 619
cagggtatta gcaggtgg 18

<210> 620
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 620
```
Gln Gly Ile Ser Arg Trp
 1               5
```

<210> 621
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 621
gctgcatcc 9

<210> 622
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 622
```
Ala Ala Ser
 1
```

```
<210> 623
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 623
caaaaggcta acagtttccc tttcact                                          27

<210> 624
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 624
Gln Lys Ala Asn Ser Phe Pro Phe Thr
 1               5


<210> 625
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 625
gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtgacagtt atattacatg atggaagtaa tagatactct 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctttat 240
ctgcaaatga acatcctgag agttgaggac acggctgtgt attactgtac gaaaggggct 300
atggttcggg gagtccctta caatcactac tacggcatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca                                                378

<210> 626
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 626
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Thr Val Ile Leu His Asp Gly Ser Asn Arg Tyr Ser Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ile Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Thr Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn His Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 627
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 627
ggattcacct tcagtagtta tggc 24

<210> 628
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 628
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 629
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 629
atattacatg atggaagtaa taga 24

<210> 630
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 630
Ile Leu His Asp Gly Ser Asn Arg
1 5

<210> 631
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 631
acgaaagggg ctatggttcg gggagtccct tacaatcact actacggcat ggacgtc 57

<210> 632
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 632

Thr Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn His Tyr Tyr Gly
 1   5   10   15
Met Asp Val

<210> 633
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 633
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct aatctatgct gcatccattt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300
gggaccaagc tggagatcaa acga   324

<210> 634
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 634
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20   25   30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35   40   45
Tyr Ala Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Tyr
                85   90   95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
            100   105

<210> 635
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 635
cagggcatta gaaatgat   18

<210> 636
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 636
Gln Gly Ile Arg Asn Asp

1   5

<210> 637
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 637
gctgcatcc 9

<210> 638
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 638
Ala Ala Ser
1

<210> 639
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 639
ctacagcata atagttaccc gtacact 27

<210> 640
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 640
Leu Gln His Asn Ser Tyr Pro Tyr Thr
1   5

<210> 641
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 641
gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtgacagtt atattacatg atggaagtaa tagatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctttat 240
ctgcaaatga acatcctgag agctgaggac acggctgtgt attactgtac gaaaggggct 300
atggttcggg gagtccctta caatcactac tacggcatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

<210> 642
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 642
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Thr Val Ile Leu His Asp Gly Ser Asn Arg Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ile Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Thr Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn His Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 643
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 643
ggattcacct tcagtagcta tggc 24

<210> 644
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 644
```
Gly Phe Thr Phe Ser Ser Tyr Gly
 1               5
```

<210> 645
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 645
atattacatg atggaagtaa taga 24

<210> 646
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 646
Ile Leu His Asp Gly Ser Asn Arg
1   5

<210> 647
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 647
acgaaagggg ctatggttcg gggagtccct tacaatcact actacggcat ggacgtc 57

<210> 648
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 648
Thr Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn His Tyr Tyr Gly
1   5   10   15
Met Asp Val

<210> 649
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 649
gacatcgtga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccaatt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300
gggaccaagc tggagatcaa acga 324

<210> 650
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 650
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20   25   30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35   40   45
Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Tyr
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105


<210> 651
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 651
cagggcatta gaaatgat                                                    18

<210> 652
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 652
Gln Gly Ile Arg Asn Asp
 1               5


<210> 653
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 653
gctgcatcc                                                              9

<210> 654
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 654
Ala Ala Ser
 1


<210> 655
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 655
ctacagcata atagttaccc gtacact                                          27

<210> 656
<211> 9
<212> PRT
```

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 656
Leu Gln His Asn Ser Tyr Pro Tyr Thr
1   5

<210> 657
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 657
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagact attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt tttactgtgc gaaaggggct 300
atggttcggg gagtccctta caactactac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

<210> 658
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 658
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Tyr Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Phe Tyr Cys
                85   90   95
Ala Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn Tyr Tyr Tyr Gly
            100   105   110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120   125

<210> 659
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 659
ggattcacct tcagtagcta tggc 24

<210> 660
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 660
Gly Phe Thr Phe Ser Ser Tyr Gly
 1   5

<210> 661
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 661
atatcatatg atggaagtaa taaa   24

<210> 662
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 662
Ile Ser Tyr Asp Gly Ser Asn Lys
 1   5

<210> 663
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 663
gcgaaagggg ctatggttcg gggagtccct tacaactact actacggtat ggacgtc   57

<210> 664
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 664
Ala Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn Tyr Tyr Tyr Gly
 1   5   10   15
Met Asp Val

<210> 665
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 665
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtttca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300
gggaccaagc tggagatcaa a 321

<210> 666
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 666
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Tyr
85 90 95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 667
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 667
cagggcatta gaaatgat 18

<210> 668
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 668
Gln Gly Ile Arg Asn Asp
1 5

<210> 669
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 669
gctgcatcc 9

<210> 670
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 670
Ala Ala Ser
 1

<210> 671
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 671
ctacagcata atagttaccc gtacact 27

<210> 672
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 672
Leu Gln His Asn Ser Tyr Pro Tyr Thr
 1   5

<210> 673
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 673
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggact caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180
acagactccg tgaagggccg attcaccatc tccagagaca attctaagaa cacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggcc 300
atggttcggg gagtccctta caactactac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

<210> 674
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 674
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Thr Phe Ser Ser Tyr
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

```
        35                  40                  45
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Thr Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn Tyr Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
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<210> 675
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 675
ggactcacct tcagtagcta tggc 24

<210> 676
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 676
```
Gly Leu Thr Phe Ser Ser Tyr Gly
 1               5
```

<210> 677
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 677
atatcatatg atggaagtaa taaa 24

<210> 678
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 678
```
Ile Ser Tyr Asp Gly Ser Asn Lys
 1               5
```

<210> 679
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 679
gcgaaagggg ccatggttcg gggagtccct tacaactact actacggtat ggacgtc   57

<210> 680
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 680
Ala Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn Tyr Tyr Tyr Gly
1   5   10   15
Met Asp Val

<210> 681
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 681
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcgtccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300
gggaccaagc tggagatcaa a   321

<210> 682
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 682
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20   25   30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35   40   45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Tyr
                85   90   95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 683
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 683
cagggcatta gaaatgat 18

<210> 684
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 684
Gln Gly Ile Arg Asn Asp
1 5

<210> 685
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 685
gctgcgtcc 9

<210> 686
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 686
Ala Ala Ser
1

<210> 687
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 687
ctacagcata atagttaccc gtacact 27

<210> 688
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 688
Leu Gln His Asn Ser Tyr Pro Tyr Thr
1 5

<210> 689
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 689
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagg agctttggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atttcatatg atggaaatta taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtac attactgtgc gaaaggggct 300
atggttcggg gagtccctta caacttctac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

<210> 690
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 690
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Phe
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ala Val Ile Ser Tyr Asp Gly Asn Tyr Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val His Tyr Cys
                85   90   95
Ala Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn Phe Tyr Tyr Gly
            100   105   110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120   125

<210> 691
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 691
ggattcacct tcaggagctt tggc 24

<210> 692
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 692
Gly Phe Thr Phe Arg Ser Phe Gly
1   5

<210> 693
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 693
atttcatatg atggaaatta taaa 24

<210> 694
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 694
Ile Ser Tyr Asp Gly Asn Tyr Lys
1 5

<210> 695
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 695
gcgaaagggg ctatggttcg gggagtccct tacaacttct actacggtat ggacgtc 57

<210> 696
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 696
Ala Lys Gly Ala Met Val Arg Gly Val Pro Tyr Asn Phe Tyr Tyr Gly
1 5 10 15
Met Asp Val

<210> 697
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 697
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca ggtcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg gatcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300
gggaccaagc tggagatcaa a 321

<210> 698
<211> 107
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 698
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Val Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Tyr
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 699
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 699
caggtcatta gaaatgat 18

<210> 700
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 700
```
Gln Val Ile Arg Asn Asp
 1               5
```

<210> 701
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 701
gctgcatcc 9

<210> 702
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 702
```
Ala Ala Ser
 1
```

<210> 703

<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 703
ctacagcata atagttaccc gtacact 27

<210> 704
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 704
Leu Gln His Asn Ser Tyr Pro Tyr Thr
1 5

<210> 705
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 705
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagtt 120
ccaggaaagg gcctggagtg gatctcaggt attagttgga atagtggtag catggactat 180
gcggactctg tgaagggccg attcaccatc tctagagaca acgccaggaa ctccctgttt 240
ctgcaaatga acagtgtgag aactgaggac acggccttgt attactgtgc aaaagataag 300
agtggctacg gctccttcta ctacggtatg gacgtctggg gccaggggac cacggtcacc 360
gtctcctca 369

<210> 706
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 706
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Val Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Met Asp Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Val Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Phe Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 707

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 707
ggattcacct ttgatgatta tacc 24

<210> 708
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 708
Gly Phe Thr Phe Asp Asp Tyr Thr
1 5

<210> 709
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 709
attagttgga atagtggtag catg 24

<210> 710
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 710
Ile Ser Trp Asn Ser Gly Ser Met
1 5

<210> 711
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 711
gcaaaagata agagtggcta cggctccttc tactacggta tggacgtc 48

<210> 712
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 712
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Phe Tyr Tyr Gly Met Asp Val

1 5 10 15

<210> 713
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 713
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga cagagccacc 60
ctctcctgca gggccagtca gagtgtcagc agcatctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatccat ggtgcgtcca ccagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcagggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagttta ttactgtcag cagcgtgctc actcaccgta cacttttggc 300
caggggacca agctggagat caaa 324

<210> 714
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 714
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ile
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile His Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ala His Ser Pro
85 90 95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 715
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 715
cagagtgtca gcagcatcta c 21

<210> 716
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 716
Gln Ser Val Ser Ser Ile Tyr
1 5

<210> 717
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 717
ggtgcgtcc 9

<210> 718
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 718
Gly Ala Ser
1

<210> 719
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 719
cagcagcgtg ctcactcacc gtacact 27

<210> 720
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 720
Gln Gln Arg Ala His Ser Pro Tyr Thr
1 5

<210> 721
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 721
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggctt cagctttgat aattatgcca tgcactgggt ccggcaagct 120
ccaggacagg gcctggagtg ggtctcaggt attagttgga atagtggtag cagagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca atgccaggaa ctccctgttt 240
ctgcaaatga acagtctgag taatgaggac acggccatgt attactgcgc aaaagataag 300
agtggctacg gctcctactt ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 722
<211> 123
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 722
```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Asp Asn Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Arg Asp Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ser Leu Phe
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Ser Asn Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Phe Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 723
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 723
ggcttcagct ttgataatta tgcc   24

<210> 724
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 724
```
Gly Phe Ser Phe Asp Asn Tyr Ala
 1               5
```

<210> 725
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 725
attagttgga atagtggtag caga   24

<210> 726
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 726

Ile Ser Trp Asn Ser Gly Ser Arg
 1   5

<210> 727
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 727
gcaaaagata agagtggcta cggctcctac ttctacggta tggacgtc   48

<210> 728
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 728
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Phe Tyr Gly Met Asp Val
 1   5   10   15

<210> 729
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 729
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga cagagccacc 60
ctctcctgca gggccagtca gagtattaga aacatctatt tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatccat ggtgcgtcca ccagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcagggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagttta ttactgtcag cagcgtgtta gtttaccgta cacttttggc 300
caggggacca agctggagat caaa   324

<210> 730
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 730
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1   5   10   15
Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Arg Asn Ile
            20   25   30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35   40   45
Ile His Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50   55   60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Val Ser Leu Pro
                85   90   95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 731
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 731
cagagtatta gaaacatcta t 21

<210> 732
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 732
Gln Ser Ile Arg Asn Ile Tyr
1 5

<210> 733
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 733
ggtgcgtcc 9

<210> 734
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 734
Gly Ala Ser
1

<210> 735
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 735
cagcagcgtg ttagtttacc gtacact 27

<210> 736
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 736
Gln Gln Arg Val Ser Leu Pro Tyr Thr
 1   5

<210> 737
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 737
caggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggctt cagctttgat gattatgcca tgcactgggt ccggcaagct 120
ccaggacagg gcctggagtg ggtctcaggt attagttgga atggtggtag cagagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaggaa ctccctgttt 240
ctgcaaatga acagtctgtt tactgaggac acggccttgt attactgtgc aaaagataag 300
agtggctacg gctcctactt ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca   369

<210> 738
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 738
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Asp Asp Tyr
            20   25   30
Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Gly Gly Ser Arg Asp Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ser Leu Phe
65   70   75   80
Leu Gln Met Asn Ser Leu Phe Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Phe Tyr Gly Met Asp Val
            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 739
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 739
ggcttcagct ttgatgatta tgcc   24

<210> 740
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 740
Gly Phe Ser Phe Asp Asp Tyr Ala
 1   5

<210> 741
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 741
attagttgga atggtggtag caga   24

<210> 742
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 742
Ile Ser Trp Asn Gly Gly Ser Arg
 1   5

<210> 743
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 743
gcaaaagata agagtggcta cggctcctac ttctacggta tggacgtc   48

<210> 744
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 744
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Phe Tyr Gly Met Asp Val
 1   5   10   15

<210> 745
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 745
gaaattgtgt tgacgcagtc tccaggcatt ctgtctttgt ctccagggga cagagccacc 60
ctctcctgca gggccagtca gagtattaga aacatctatt tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatccat ggtgcgtcca ccagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcagggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagttta ttactgtcag cagcgtgtta gttcaccgta cacttttggc 300
caggggacca agctggagat caaa   324

<210> 746
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 746
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Glu Ile Val Leu Thr Gln Ser Pro Gly Ile Leu Ser Leu Ser Pro Gly
 1               5                   10                  15
Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Arg Asn Ile
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile His Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Val Ser Ser Pro
                85                  90                  95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
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<210> 747
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 747
cagagtatta gaaacatcta t 21

<210> 748
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 748
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Gln Ser Ile Arg Asn Ile Tyr
 1               5
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<210> 749
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 749
ggtgcgtcc 9

<210> 750
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 750
Gly Ala Ser
1

<210> 751
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 751
cagcagcgtg ttagttcacc gtacact 27

<210> 752
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 752
Gln Gln Arg Val Ser Ser Pro Tyr Thr
1 5

<210> 753
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 753
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
ccaggaaagg gcctggagtg ggtctcaggt attagttgga atagtggtag cagagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaggaa ctccctgttt 240
ctgcaaatga acagtctgag tactgaggac acggccttgt attactgtgc aaaagataag 300
agtggctacg gctcctacta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 754
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 754
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Arg Asp Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Ser Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Tyr Tyr Gly Met Asp Val
            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 755
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 755
ggattcacct ttgatgatta tgcc   24

<210> 756
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 756
Gly Phe Thr Phe Asp Asp Tyr Ala
1   5

<210> 757
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 757
attagttgga atagtggtag caga   24

<210> 758
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 758
Ile Ser Trp Asn Ser Gly Ser Arg
1   5

<210> 759
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 759
gcaaaagata agagtggcta cggctcctac tactacggta tggacgtc   48

<210> 760
<211> 16
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 760
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 761
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 761
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga cagagccacc 60
ctctcctgca gggccagtca gagtattaga agcatctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatccat ggtgcgtcca ccagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcagggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagttta ttactgtcag cagcgtgtta gctcaccgta cacttttggc 300
caggggacca agctggagat caaa 324

<210> 762
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 762
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1   5   10   15
Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Arg Ser Ile
            20   25   30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35   40   45
Ile His Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50   55   60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Val Ser Ser Pro
                85   90   95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 763
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 763
cagagtatta gaagcatcta c 21

<210> 764
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 764
Gln Ser Ile Arg Ser Ile Tyr
 1   5

<210> 765
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 765
ggtgcgtcc   9

<210> 766
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 766
Gly Ala Ser
 1

<210> 767
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 767
cagcagcgtg ttagctcacc gtacact   27

<210> 768
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 768
Gln Gln Arg Val Ser Ser Pro Tyr Thr
 1   5

<210> 769
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 769
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgtag cctctggatt cacctttgct gattttacca tgcactgggt ccggcaagcg 120
ccagggaagg gccttgagtg ggtctcaggt attagttgga atagtaatag tatagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa atccctgttt 240

ctgcaaatgt ccagtctgag agctgaggac acggccttat attactgtgt caaagacaga 300
agcggatata gcagattcta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 770
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 770
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ala Asp Phe
20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Gly Ile Ser Trp Asn Ser Asn Ser Ile Asp Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Phe
65 70 75 80
Leu Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Asp Arg Ser Gly Tyr Ser Arg Phe Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 771
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 771
ggattcacct ttgctgattt tacc 24

<210> 772
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 772
Gly Phe Thr Phe Ala Asp Phe Thr
1 5

<210> 773
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 773
attagttgga atagtaatag tata 24

<210> 774
<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 774
Ile Ser Trp Asn Ser Asn Ser Ile
 1   5

<210> 775
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 775
gtcaaagaca gaagcggata tagcagattc tactacggta tggacgtc   48

<210> 776
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 776
Val Lys Asp Arg Ser Gly Tyr Ser Arg Phe Tyr Tyr Gly Met Asp Val
 1   5   10   15

<210> 777
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 777
gaaattgtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccatc 60
ctctcctgca gggccagtca gaatattaat agcaacttgg cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tgtcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatccgcag cctgcaatct 240
gaagattttg cagtttatta ctgtcaacaa tattataatt ggccgatcac tttcggccac 300
gggacacgac tggagattaa a   321

<210> 778
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 778
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1   5   10   15
Glu Arg Ala Ile Leu Ser Cys Arg Ala Ser Gln Asn Ile Asn Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
    50   55   60

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

<210> 779
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 779
cagaatatta atagcaac   18

<210> 780
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 780
Gln Asn Ile Asn Ser Asn
 1   5

<210> 781
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 781
ggtgcatcc   9

<210> 782
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 782
Gly Ala Ser
 1

<210> 783
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 783
caacaatatt ataattggcc gatcact   27

<210> 784

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 784
Gln Gln Tyr Tyr Asn Trp Pro Ile Thr
 1   5

<210> 785
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 785
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
ccaggaaagg gcctggagtg ggtctcaggt attagttgga atggtggtag taaagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acaccaggaa ctccctgtct 240
ctgcaaatga acagtctgag aattgaagac acggccttat attactgtgc aaaagataag 300
agtggctacg gctccttcta ctacggtttg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 786
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 786
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Gly Gly Ser Lys Asp Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Thr Arg Asn Ser Leu Ser
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ile Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Phe Tyr Tyr Gly Leu Asp Val
            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 787
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 787
ggattcacct ttgatgatta tgcc 24

<210> 788

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 788
Gly Phe Thr Phe Asp Asp Tyr Ala
 1   5

<210> 789
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 789
attagttgga atggtggtag taaa 24

<210> 790
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 790
Ile Ser Trp Asn Gly Gly Ser Lys
 1   5

<210> 791
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 791
gcaaaagata agagtggcta cggctccttc tactacggtt tggacgtc 48

<210> 792
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 792
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Phe Tyr Tyr Gly Leu Asp Val
 1   5   10   15

<210> 793
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 793
gaaatagtgt tgacacagtc tccaggcacc ctgtctttgt ctccagggga cagagccacc 60
ctctcctgca gggccagtca gagtattaga agcatctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatccat ggtgcgtcca ccagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcagggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagttta ttactgtcag cagcgtgtta gctcaccgta cacttttggc 300
caggggacca agctggagat caaa 324

<210> 794
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 794
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Arg Ser Ile
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile His Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Val Ser Ser Pro
85 90 95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 795
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 795
cagagtatta gaagcatcta c 21

<210> 796
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 796
Gln Ser Ile Arg Ser Ile Tyr
1 5

<210> 797
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 797
ggtgcgtcc 9

<210> 798
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 798
Gly Ala Ser
 1

<210> 799
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 799
cagcagcgtg ttagctcacc gtacact 27

<210> 800
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 800
Gln Gln Arg Val Ser Ser Pro Tyr Thr
 1   5

<210> 801
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 801
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gatttcacca tgcactgggt ccggcaagct 120
ccaggaaagg gcctggagtg ggtctcagat attagttgga atagtggtag catagactat 180
gcggactctg tgaagggccg attcaccatt tccagagaca atgccaggaa ctccctgttt 240
ctacaaatga gcagtctgag aactgaggac acggcctcgt attactgtat aaaagataag 300
agtggctacg gctcctacaa ctacggtctg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 802
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 802
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Phe
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

```
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Ile Asp Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ser Leu Phe
65                  70                  75                  80
Leu Gln Met Ser Ser Leu Arg Thr Glu Asp Thr Ala Ser Tyr Tyr Cys
                85                  90                  95
Ile Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Asn Tyr Gly Leu Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 803
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 803
ggattcacct ttgatgattt cacc 24

<210> 804
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 804
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Gly Phe Thr Phe Asp Asp Phe Thr
 1               5
```

<210> 805
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 805
attagttgga atagtggtag cata 24

<210> 806
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 806
```
Ile Ser Trp Asn Ser Gly Ser Ile
 1               5
```

<210> 807
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

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<400> 807
ataaaagata agagtggcta cggctcctac aactacggtc tggacgtc              48

<210> 808
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 808
Ile Lys Asp Lys Ser Gly Tyr Gly Ser Tyr Asn Tyr Gly Leu Asp Val
 1               5                   10                  15


<210> 809
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 809
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga cagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcatctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatccat ggtgcgtcca ccagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcggggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcacttta ttactgtcac cagcgtgtta gttcaccgta cacttttggc 300
caggggacca agctggagat caaa                                        324

<210> 810
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 810
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                   10                  15
Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ile
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile His Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Leu Tyr Tyr Cys His Gln Arg Val Ser Ser Pro
                85                  90                  95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105


<210> 811
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 811
cagagtgtta gcagcatcta c                                           21
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<210> 812
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 812
Gln Ser Val Ser Ser Ile Tyr
1   5

<210> 813
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 813
ggtgcgtcc   9

<210> 814
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 814
Gly Ala Ser
1

<210> 815
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 815
caccagcgtg ttagttcacc gtacact   27

<210> 816
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 816
His Gln Arg Val Ser Ser Pro Tyr Thr
1   5

<210> 817
<211> 369
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 817
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gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
ccaggaaagg gcctggagtg ggtctcaggt attagttgga atagtggtag taaagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acaccaggaa ctccctgttt 240
ctgcaaatga acagtctgag aactgaagac acggccttat attactgtgc aaaagataag 300
agtggctacg gctccttcta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca                                                         369
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<210> 818
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 818
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Lys Asp Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Thr Arg Asn Ser Leu Phe
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Phe Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 819
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 819
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ggattcacct ttgatgatta tgcc                                        24
```

<210> 820
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 820
```
Gly Phe Thr Phe Asp Asp Tyr Ala
1               5
```

<210> 821
<211> 24
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 821
attagttgga atagtggtag taaa 24

<210> 822
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 822
Ile Ser Trp Asn Ser Gly Ser Lys
1 5

<210> 823
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 823
gcaaaagata agagtggcta cggctccttc tactacggta tggacgtc 48

<210> 824
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 824
Ala Lys Asp Lys Ser Gly Tyr Gly Ser Phe Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 825
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 825
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
gatgattttg caacttatta ctgccaacag tataatagtt attctccgtt cggccaaggg 300
accaaggtgg aaatcaaa 318

<210> 826
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 826
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly

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


<210> 827
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 827
cagagtatta gtagctgg                                                   18

<210> 828
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 828
Gln Ser Ile Ser Ser Trp
 1               5


<210> 829
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 829
aaggcgtct                                                              9

<210> 830
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 830
Lys Ala Ser
 1


<210> 831
<211> 24
<212> DNA
<213> Artificial Sequence
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<220>
<223> Synthetic

<400> 831
caacagtata atagttattc tccg 24

<210> 832
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 832
Gln Gln Tyr Asn Ser Tyr Ser Pro
1 5

<210> 833
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 833
caggtgcaac tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggact caccttcagt acctatgtca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggcgtg ggtggcagtt atagcaaatg atggaagtaa taaatattat 180
gcagactccg tgaagggccg attcaccatc tccagagaca actccaagaa cacgctgtat 240
ctgcaaatga atagcctgag acctgaggac acggctgtgt atttttgtgc gaaagagggg 300
ggtaccagtg ggtcctacta ttactatgga atggacgtct ggggtcaagg gactacggtc 360
accgtctcct ca 372

<210> 834
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 834
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Thr Phe Ser Thr Tyr
20 25 30
Val Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Ala Trp Val
35 40 45
Ala Val Ile Ala Asn Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Lys Glu Gly Gly Thr Ser Gly Ser Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 835
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 835
ggactcacct tcagtaccta tgtc 24

<210> 836
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 836
Gly Leu Thr Phe Ser Thr Tyr Val
1 5

<210> 837
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 837
atagcaaatg atggaagtaa taaa 24

<210> 838
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 838
Ile Ala Asn Asp Gly Ser Asn Lys
1 5

<210> 839
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 839
gcgaaagagg ggggtaccag tgggtcctac tattactatg gaatggacgt c 51

<210> 840
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 840
Ala Lys Glu Gly Gly Thr Ser Gly Ser Tyr Tyr Tyr Tyr Gly Met Asp
1 5 10 15
Val

<210> 841
<211> 342
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 841
gacatccaga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc 60
atcaactgca agtccagcca gagtctttta ttcaactcca tcaataagaa ctacttagct 120
tggtaccagc agaaaccagg acagcctcct aagcttctcc tttactgggc atctacccgg 180
gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240
atcaccagcc tgcaggctga agatgtggca ctttattact gtcagcaata ttatagtatt 300
ccgtggacgt tcggccaagg gaccaaggtg gaaatcaaac ga 342

<210> 842
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 842
Asp Ile Gln Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Phe Asn
20 25 30
Ser Ile Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45
Pro Pro Lys Leu Leu Leu Tyr Trp Ala Ser Thr Arg Glu Ser Gly Ile
50 55 60
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80
Ile Thr Ser Leu Gln Ala Glu Asp Val Ala Leu Tyr Tyr Cys Gln Gln
85 90 95
Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110
Lys Arg

<210> 843
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 843
cagagtcttt tattcaactc catcaataag aactac 36

<210> 844
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 844
Gln Ser Leu Leu Phe Asn Ser Ile Asn Lys Asn Tyr
1 5 10

<210> 845
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 845
tgggcatct 9

<210> 846
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 846
Trp Ala Ser
1

<210> 847
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 847
cagcaatatt atagtattcc gtggacg 27

<210> 848
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 848
Gln Gln Tyr Tyr Ser Ile Pro Trp Thr
1 5

<210> 849
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 849
caggtgcagc tggtggagtc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaaga cttctggata caccttcacc ggctactata tgcactggat acgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcaacccta aaagtggtgg cacaaattat 180
gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240
atggaactga gcaggctgag atccgacgac atggccgtgt attattgtgc gagaatgggg 300
gacggtgcag tgtttgactt ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 850
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 850
Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Ile Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Lys Ser Gly Gly 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 Met Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe Trp Gly Gln Gly Thr
            100   105   110
Leu Val Thr Val Ser Ser
        115

<210> 851
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 851
ggatacacct tcaccggcta ctat   24

<210> 852
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 852
Gly Tyr Thr Phe Thr Gly Tyr Tyr
1   5

<210> 853
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 853
atcaacccta aaagtggtgg caca   24

<210> 854
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 854
Ile Asn Pro Lys Ser Gly Gly Thr

 1   5

<210> 855
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 855
gcgagaatgg gggacggtgc agtgtttgac ttc 33

<210> 856
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 856
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe
 1   5   10

<210> 857
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 857
gccatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gaggattagc agcttttttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatact gcatccaatt tacaaaatgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ctatcagcag tctgcaacct 240
gaagattttg ctacttacta ctgtcaacag agttacagga ccccgctcac tttcggcgga 300
gggaccaagg tggaaatcaa acga 324

<210> 858
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 858
Ala Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Phe
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Asn Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 859
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 859
cagaggatta gcagcttt 18

<210> 860
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 860
Gln Arg Ile Ser Ser Phe
1 5

<210> 861
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 861
actgcatcc 9

<210> 862
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 862
Thr Ala Ser
1

<210> 863
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 863
caacagagtt acaggacccc gctcact 27

<210> 864
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 864

Gln Gln Ser Tyr Arg Thr Pro Leu Thr
 1   5

<210> 865
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 865
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga acagtggtag cataggctat 180
gcggactctg tgaagggccg attcaccatt tccagagaca acgccaagaa ctccctgtat 240
ttgcaaatga acagtctgag agctgaggac acggccttgt tttactgtgc aaaagatcaa 300
agtggttacg gccactacta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca   369

<210> 866
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 866
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Phe Tyr Cys
                85   90   95
Ala Lys Asp Gln Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
            100   105   110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 867
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 867
ggattcacct ttgatgatta tacc   24

<210> 868
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 868

Gly Phe Thr Phe Asp Asp Tyr Thr
 1   5

<210> 869
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 869
attagttgga acagtggtag cata   24

<210> 870
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 870
Ile Ser Trp Asn Ser Gly Ser Ile
 1   5

<210> 871
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 871
gcaaaagatc aaagtggtta cggccactac tactacggta tggacgtc   48

<210> 872
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 872
Ala Lys Asp Gln Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
 1   5   10   15

<210> 873
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 873
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgta gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactga tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatca ctgtcagcag tataataact ggccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a   321

<210> 874
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 874
```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45
Tyr Gly Ala Ser Thr Arg Ala Thr Asp Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65                  70                  75                  80
Glu Asp Phe Ala Val Tyr His Cys Gln Gln Tyr Asn Asn Trp Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
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<210> 875
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 875
cagagtgtta gcagcaac 18

<210> 876
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 876
```
Gln Ser Val Ser Ser Asn
 1               5
```

<210> 877
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 877
ggtgcatcc 9

<210> 878
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 878
Gly Ala Ser
 1

<210> 879
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 879
cagcagtata ataactggcc gctcact 27

<210> 880
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 880
Gln Gln Tyr Asn Asn Trp Pro Leu Thr
 1   5

<210> 881
<211> 387
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 881
gaggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt tactatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atatcatttg atggaaagaa taaatattat 180
gcagactccg tgatgggccg attcaccatc tccagagaca attccaagaa tacactgtat 240
ctgcaaatga acagcctgag agctgaggac tcggctgtgt ttttctgtgc gaggtcttac 300
gacattttga ctggttatgg agccggttac agctaccact acggtatgga cgtctggggc 360
caagggacca cggtcaccgt ctcctca 387

<210> 882
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 882
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Tyr
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ala Val Ile Ser Phe Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Met Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Ser Ala Val Phe Phe Cys
                85   90   95
Ala Arg Ser Tyr Asp Ile Leu Thr Gly Tyr Gly Ala Gly Tyr Ser Tyr

```
            100                 105                 110
His Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125
Ser



<210> 883
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 883
ggattcacct tcagttacta tggc                                              24

<210> 884
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 884
Gly Phe Thr Phe Ser Tyr Tyr Gly
 1               5


<210> 885
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 885
atatcatttg atggaaagaa taaa                                              24

<210> 886
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 886
Ile Ser Phe Asp Gly Lys Asn Lys
 1               5


<210> 887
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 887
gcgaggtctt acgacatttt gactggttat ggagccggtt acagctacca ctacggtatg 60
gacgtc                                                                  66

<210> 888
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<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 888
Ala Arg Ser Tyr Asp Ile Leu Thr Gly Tyr Gly Ala Gly Tyr Ser Tyr
1   5   10   15
His Tyr Gly Met Asp Val
            20

<210> 889
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 889
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atcacttgcc gggcaagtca gaggattagc agctttttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct aatctatact gcatccaatt tacaaaatgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagga ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa acga 324

<210> 890
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 890
Ala Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Phe
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Asn Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 891
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 891
cagaggatta gcagcttt 18

<210> 892
<211> 6

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 892
Gln Arg Ile Ser Ser Phe
 1   5

<210> 893
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 893
actgcatcc   9

<210> 894
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 894
Thr Ala Ser
 1

<210> 895
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 895
caacagagtt acaggacccc gctcact   27

<210> 896
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 896
Gln Gln Ser Tyr Arg Thr Pro Leu Thr
 1   5

<210> 897
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 897

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caggtgcagc tggtggagtc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaaga cttctggata caccctctcc ggctattata tgcactggat gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg attaacccta aaagtggtgt cacaaattat 180
gcacagaagt ttcaggacag agtcgccatg accagggaca cgtccatcag cacagcctac 240
atggaactga gcaggctgag atctgacgac acggccgtgt attactgtgc gagaatgggg 300
gacggtgcag tgtttgactt ctgggcccag ggaaccctgg tcaccgtctc ctca       354

&lt;210&gt; 898
&lt;211&gt; 118
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 898
Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Thr Leu Ser Gly Tyr
            20                  25                  30
Tyr Met His Trp Met Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Lys Ser Gly Val Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Asp Arg Val Ala 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 Met Gly Asp Gly Ala Val Phe Asp Phe Trp Ala Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115


&lt;210&gt; 899
&lt;211&gt; 24
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 899
ggatacaccc tctccggcta ttat                                         24

&lt;210&gt; 900
&lt;211&gt; 8
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 900
Gly Tyr Thr Leu Ser Gly Tyr Tyr
1               5


&lt;210&gt; 901
&lt;211&gt; 24
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 901
attaacccta aaagtggtgt caca                                         24
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<210> 902
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 902
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Ile Asn Pro Lys Ser Gly Val Thr
 1               5
```

<210> 903
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 903
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gcgagaatgg gggacggtgc agtgtttgac ttc                              33
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<210> 904
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 904
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Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe
 1               5                   10
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<210> 905
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 905
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gacatccagt tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gaggattagc agctttttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct aatctatact gcatccaatt tacaaaatgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagga ccccgctcac tttcggcgga 300
gggaccaagc tggagatcaa acga                                        324
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<210> 906
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 906
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Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Phe
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
```

```
        35                  40                  45
Tyr Thr Ala Ser Asn Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105


&lt;210&gt; 907
&lt;211&gt; 18
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 907
cagaggatta gcagcttt                                                  18

&lt;210&gt; 908
&lt;211&gt; 6
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 908
Gln Arg Ile Ser Ser Phe
 1               5


&lt;210&gt; 909
&lt;211&gt; 9
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 909
actgcatcc                                                            9

&lt;210&gt; 910
&lt;211&gt; 3
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 910
Thr Ala Ser
 1


&lt;210&gt; 911
&lt;211&gt; 27
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 911
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caacagagtt acaggacccc gctcact 27

<210> 912
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 912
Gln Gln Ser Tyr Arg Thr Pro Leu Thr
1 5

<210> 913
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 913
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtgtcaact atatcatttg atggaagtaa caaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag acctgaggac acggctgtgt attactgtgc gaaagggggg 300
ggtaccagtg ggtcctactt ttactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 914
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 914
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Thr Ile Ser Phe Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Lys Gly Gly Gly Thr Ser Gly Ser Tyr Phe Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 915
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 915

ggattcacct tcagtagcta tggc 24

<210> 916
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 916
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 917
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 917
atatcatttg atggaagtaa caaa 24

<210> 918
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 918
Ile Ser Phe Asp Gly Ser Asn Lys
1 5

<210> 919
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 919
gcgaaagggg ggggtaccag tgggtcctac ttttactacg gtatggacgt c 51

<210> 920
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 920
Ala Lys Gly Gly Gly Thr Ser Gly Ser Tyr Phe Tyr Tyr Gly Met Asp
1 5 10 15
Val

<210> 921
<211> 324
<212> DNA

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<213> Artificial Sequence

<220>
<223> Synthetic

<400> 921
gccatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gaggattagc agctttttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct aatctatact gcatccaatt tacaaaatgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagga ccccgctcac tttcggcgga 300
gggaccaagc tggagatcaa acga                                        324

<210> 922
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 922
Ala Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Phe
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Asn Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105


<210> 923
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 923
cagaggatta gcagcttt                                                18

<210> 924
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 924
Gln Arg Ile Ser Ser Phe
 1               5


<210> 925
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
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<223> Synthetic

<400> 925
actgcatcc 9

<210> 926
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 926
Thr Ala Ser
1

<210> 927
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 927
caacagagtt acaggacccc gctcact 27

<210> 928
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 928
Gln Gln Ser Tyr Arg Thr Pro Leu Thr
1 5

<210> 929
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 929
caggttcagc tggtgcagtc tgggactgag gtgaagaagc ctggggcctc aatgaaggtc 60
tcctgcaagg cttctggata caccttcacc ggctactata ttcactgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtgatgt cacaaagtat 180
gcacagaagt ttcagggcag ggtcaccttg accagggaca cgtccatcag tgcagcctat 240
attgacctga gcaggctgag atctgacgac acggccattt attactgtgc gagaatgggg 300
gacggtgcag tgtttgacta ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 930
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 930
Gln Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Ala

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


&lt;210&gt; 931
&lt;211&gt; 24
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 931
ggatacacct tcaccggcta ctat                                          24

&lt;210&gt; 932
&lt;211&gt; 8
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 932
Gly Tyr Thr Phe Thr Gly Tyr Tyr
 1               5


&lt;210&gt; 933
&lt;211&gt; 24
&lt;212&gt; DNA
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 933
atcaacccta acagtgatgt caca                                          24

&lt;210&gt; 934
&lt;211&gt; 8
&lt;212&gt; PRT
&lt;213&gt; Artificial Sequence

&lt;220&gt;
&lt;223&gt; Synthetic

&lt;400&gt; 934
Ile Asn Pro Asn Ser Asp Val Thr
 1               5


&lt;210&gt; 935
&lt;211&gt; 33
&lt;212&gt; DNA
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<213> Artificial Sequence

<220>
<223> Synthetic

<400> 935
gcgagaatgg gggacggtgc agtgtttgac tac 33

<210> 936
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 936
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Ala Arg Met Gly Asp Gly Ala Val Phe Asp Tyr
 1               5                   10
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<210> 937
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 937
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gacatccagt tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca acgcattagc agctatttaa attggtatca acagaaacca 120
gggaaagccc ctaaggtgct gatctctgtt gcatccagtt tacaaagtgg ggtcccatca 180
aggttcagtg gcagtggatt tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaggattctg catcttacta ctgtcaacag agttacaata ccccgctcac tttcggcggc 300
gggaccaagc tggagatcaa acga                                         324
```

<210> 938
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 938
```
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
        35                  40                  45
Ser Val Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Phe Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Ser Ala Ser Tyr Tyr Cys Gln Gln Ser Tyr Asn Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105
```

<210> 939
<211> 18
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 939
caacgcatta gcagctat 18

<210> 940
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 940
Gln Arg Ile Ser Ser Tyr
1 5

<210> 941
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 941
gttgcatcc 9

<210> 942
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 942
Val Ala Ser
1

<210> 943
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 943
caacagagtt acaataccc gctcact 27

<210> 944
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 944
Gln Gln Ser Tyr Asn Thr Pro Leu Thr
1 5

<210> 945
<211> 354

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 945
gaggtgcagc tggtggagtc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaaga cttctggata cagtttcatt ggctattata tacactggat gcgacaggcc 120
cctggacaag ggcttgaatg gatgggatgg atcaacccta agagtggtgt cacaaattat 180
gcacagaggt ttcagggcag ggtcaccatg accagggaca cgtccatcag tactgcctac 240
atggaactga gcaggctgaa atctgacgac acggccgtgt atttctgtgc gagaatgggg 300
gacggtgcag tgtttgactt ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 946
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 946
Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Ser Phe Ile Gly Tyr
20 25 30
Tyr Ile His Trp Met Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Lys Ser Gly Val Thr Asn Tyr Ala Gln Arg 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 Lys Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
115

<210> 947
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 947
ggatacagtt tcattggcta ttat 24

<210> 948
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 948
Gly Tyr Ser Phe Ile Gly Tyr Tyr
1 5

<210> 949
<211> 24
<212> DNA

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 949
atcaacccta agagtggtgt caca 24

<210> 950
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 950
Ile Asn Pro Lys Ser Gly Val Thr
1 5

<210> 951
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 951
gcgagaatgg gggacggtgc agtgtttgac ttc 33

<210> 952
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 952
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe
1 5 10

<210> 953
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 953
gacatccagt tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gaggattagc agctttttaa attggtatca gcagaaacca 120
gggaaagtcc ctaagctcct gatctatact gcatccaatt tacaaaatgg ggtcccatca 180
aggttcagtg gcactggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagga ccccgctcac tttcggcgga 300
gggaccaaag tggatatcaa acga 324

<210> 954
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 954
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Phe
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Asn Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Thr Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Arg
            100   105

<210> 955
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 955
cagaggatta gcagcttt 18

<210> 956
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 956
Gln Arg Ile Ser Ser Phe
1   5

<210> 957
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 957
actgcatcc 9

<210> 958
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 958
Thr Ala Ser
1

<210> 959
<211> 27

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 959
caacagagtt acaggacccc gctcact 27

<210> 960
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 960
Gln Gln Ser Tyr Arg Thr Pro Leu Thr
1 5

<210> 961
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 961
gaggtgcagc tggtggagtc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaaga cttctggata caccttcacc ggctactata tgcactggat acgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcaacccta aaagtggtgg cacaaattat 180
gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240
atggaactga gcaggctgag atccgacgac atggccgtgt attattgtgc gagaatgggg 300
gacggtgcag tgtttgactt ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 962
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 962
Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Met His Trp Ile Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Lys Ser Gly Gly 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 Met Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
115

<210> 963
<211> 24
<212> DNA

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 963
ggatacacct tcaccggcta ctat 24

<210> 964
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 964
Gly Tyr Thr Phe Thr Gly Tyr Tyr
1 5

<210> 965
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 965
atcaacccta aaagtggtgg caca 24

<210> 966
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 966
Ile Asn Pro Lys Ser Gly Gly Thr
1 5

<210> 967
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 967
gcgagaatgg gggacggtgc agtgtttgac ttc 33

<210> 968
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 968
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Phe
1 5 10

<210> 969
<211> 327
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 969
gacatcgtga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta cccctccgct cactttcggc 300
ggagggacca aagtggatat caaacga 327

<210> 970
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 970
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
85 90 95
Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Arg
100 105

<210> 971
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 971
cagagcatta gcagctat 18

<210> 972
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 972
Gln Ser Ile Ser Ser Tyr
1 5

<210> 973
<211> 9

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 973
gctgcatcc 9

<210> 974
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 974
Ala Ala Ser
1

<210> 975
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 975
caacagagtt acagtacccc tccgctcact 30

<210> 976
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 976
Gln Gln Ser Tyr Ser Thr Pro Pro Leu Thr
1 5 10

<210> 977
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 977
caggttcagc tggtgcagtc tgggactgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctggata caccttcacc ggctactata tgcactgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtgatgt cacaaactat 180
gcacagaagt ttcagggcag ggtcaccttg accagggaca cgtccatcag tacagcctac 240
attgacctga gcaggctgag atctgacgac acggccattt attactgtgc gagaatgggg 300
gacggtgcag tgtttgacta ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 978
<211> 118
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 978
```
Gln Val Gln Leu Val Gln Ser Gly Thr 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 Trp Ile Asn Pro Asn Ser Asp Val Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Ile Asp Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110
Leu Val Thr Val Ser Ser
        115
```

<210> 979
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 979
ggatacacct tcaccggcta ctat 24

<210> 980
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 980
```
Gly Tyr Thr Phe Thr Gly Tyr Tyr
1               5
```

<210> 981
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 981
atcaacccta acagtgatgt caca 24

<210> 982
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 982
```
Ile Asn Pro Asn Ser Asp Val Thr
1               5
```

<210> 983
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 983
gcgagaatgg gggacggtgc agtgtttgac tac 33

<210> 984
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 984
```
Ala Arg Met Gly Asp Gly Ala Val Phe Asp Tyr
 1               5                  10
```

<210> 985
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 985
```
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gcgcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaaggtgct gatctctgtt gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccattagtag tctgcaacct 240
gaggattttg catcttacta ctgtcaacag agttacaata ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa acga                                        324
```

<210> 986
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 986
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
        35                  40                  45
Ser Val Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Tyr Asn Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 987
<211> 18

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 987
cagcgcatta gcagctat 18

<210> 988
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 988
Gln Arg Ile Ser Ser Tyr
1 5

<210> 989
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 989
gttgcatcc 9

<210> 990
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 990
Val Ala Ser
1

<210> 991
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 991
caacagagtt acaatacccc gctcact 27

<210> 992
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 992
Gln Gln Ser Tyr Asn Thr Pro Leu Thr
1 5

<210> 993
<211> 381
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 993
caggtgcagc tggtgcagtc tgggggaggc ttggtcaagc ctggggggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt agctatgaca tgagctgggt ccgccaggct 120
ccagggaagg ggctggagtg ggtttcatac attagtagta gtggtaatac catacattac 180
gcagactctg tgaagggccg attcaccatc tccagagaca attccaagaa ctcactttat 240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gaaagccggt 300
cccgctacgg tgacacggag gtactactac tactacggtt tggacgtctg gggccaaggg 360
accacggtca ccgtctcctc a 381

<210> 994
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 994
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile His Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Lys Ala Gly Pro Ala Thr Val Thr Arg Arg Tyr Tyr Tyr Tyr Tyr
100 105 110
Gly Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 995
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 995
ggattcacct tcagtagcta tgac 24

<210> 996
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 996
Gly Phe Thr Phe Ser Ser Tyr Asp
1 5

<210> 997
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 997
attagtagta gtggtaatac cata 24

<210> 998
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 998
Ile Ser Ser Ser Gly Asn Thr Ile
1 5

<210> 999
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 999
gcgaaagccg gtcccgctac ggtgacacgg aggtactact actactacgg tttggacgtc 60

<210> 1000
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1000
Ala Lys Ala Gly Pro Ala Thr Val Thr Arg Arg Tyr Tyr Tyr Tyr Tyr
1 5 10 15
Gly Leu Asp Val
20

<210> 1001
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1001
gacatcgtga tgacccagtc tccatcctcc ctgtctgcat ctgtacgaga cagagtcacc 60
atcacttgcc gggcaagtca gagaattagc agctatttaa attggtttca gcagaaacca 120
gggaaagccc ctaaggtcct gatctatact gcatccagtt tgcaaaatgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagactttg caacttacta ctgtcagcag agttacagga ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa acga 324

<210> 1002
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1002
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Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Arg
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Tyr
            20                  25                  30
Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Ser Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 1003
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1003
cagagaatta gcagctat 18

<210> 1004
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1004
```
Gln Arg Ile Ser Ser Tyr
 1               5
```

<210> 1005
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1005
actgcatcc 9

<210> 1006
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1006
Thr Ala Ser
 1

<210> 1007
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1007
cagcagagtt acaggacccc gctcact 27

<210> 1008
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1008
Gln Gln Ser Tyr Arg Thr Pro Leu Thr
 1   5

<210> 1009
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1009
caggtgcagc tggtacagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctggata cacattcatc ggctactata tgcactgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcaacccta aaagtggtgg cacaaactat 180
gcacagaagt ttcagggcag ggtcaccatg accggggaca cgtccatcag cacagcctac 240
atggagctga gcaggctgag atctgacgac acggccgtgt tttactgtgc gagaatgggg 300
gacggtgcaa tgtttgacta ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 1010
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1010
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 Ile 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 Trp Ile Asn Pro Lys Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60
Gln Gly Arg Val Thr Met Thr Gly 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 Phe Tyr Cys
                85   90   95
Ala Arg Met Gly Asp Gly Ala Met Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110
Leu Val Thr Val Ser Ser
115

<210> 1011
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1011
ggatacacat tcatcggcta ctat 24

<210> 1012
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1012
Gly Tyr Thr Phe Ile Gly Tyr Tyr
1 5

<210> 1013
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1013
atcaacccta aaagtggtgg caca 24

<210> 1014
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1014
Ile Asn Pro Lys Ser Gly Gly Thr
1 5

<210> 1015
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1015
gcgagaatgg gggacggtgc aatgtttgac tac 33

<210> 1016
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1016
```
Ala Arg Met Gly Asp Gly Ala Met Phe Asp Tyr
 1               5                  10
```

<210> 1017
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1017
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gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagaattagc agctatttaa attggtatca gcagaaagca 120
gggaaagccc ctaaggtcct gatctatact gcatccagtt tgcaaagtgg ggtcccatca 180
cgattcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a                                           321
```

<210> 1018
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1018
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Tyr
            20                  25                  30
Leu Asn Trp Tyr Gln Gln Lys Ala Gly Lys Ala Pro Lys Val Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 1019
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1019
```
cagagaatta gcagctat                                               18
```

<210> 1020
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1020
Gln Arg Ile Ser Ser Tyr
1   5

<210> 1021
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1021
actgcatcc   9

<210> 1022
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1022
Thr Ala Ser
1

<210> 1023
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1023
caacagagtt acagtacccc gctcact   27

<210> 1024
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1024
Gln Gln Ser Tyr Ser Thr Pro Leu Thr
1   5

<210> 1025
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1025
caggtgcagc tggtacagtc tgggggaggc gtggtacagc ctgggggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccgtcaagct 120
ccagggaagg gtctggagtg ggtctctctt attagtgggg atggtggtag cacatactat 180
gcagactctg tgaagggccg attcaccatc tccagagaca acagcaaaaa ctccctgtat 240
ctgcaaatga acagtctgag aactgaggac accgccttgt attactgtgc aaaagatgat 300

agcagctcgt cctggtacta ctactactac ggtatggacg tctggggccg agggaccacg 360
gtcaccgtct cctca 375

<210> 1026
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1026
```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Leu Ile Ser Gly Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Asp Ser Ser Ser Ser Trp Tyr Tyr Tyr Tyr Tyr Gly Met
            100                 105                 110
Asp Val Trp Gly Arg Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 1027
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1027
ggattcacct ttgatgatta tgcc 24

<210> 1028
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1028
```
Gly Phe Thr Phe Asp Asp Tyr Ala
 1               5
```

<210> 1029
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1029
attagtgggg atggtggtag caca 24

<210> 1030
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1030
Ile Ser Gly Asp Gly Gly Ser Thr
1   5

<210> 1031
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1031
gcaaaagatg atagcagctc gtcctggtac tactactact acggtatgga cgtc   54

<210> 1032
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1032
Ala Lys Asp Asp Ser Ser Ser Ser Trp Tyr Tyr Tyr Tyr Tyr Gly Met
1   5   10   15
Asp Val

<210> 1033
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1033
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gcgcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaaggtgct gatctctgtt gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaggattttg catcttacta ctgtcaacag agttacaata ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa acga   324

<210> 1034
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1034
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Ser Ser Tyr
            20   25   30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
        35   40   45
Ser Val Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

```
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Tyr Asn Thr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 1035
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1035
cagcgcatta gcagctat                                                   18

<210> 1036
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1036
Gln Arg Ile Ser Ser Tyr
 1               5


<210> 1037
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1037
gttgcatcc                                                              9

<210> 1038
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1038
Val Ala Ser
 1


<210> 1039
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1039
caacagagtt acaatacccc gctcact                                         27
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<210> 1040
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1040
Gln Gln Ser Tyr Asn Thr Pro Leu Thr
 1   5

<210> 1041
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1041
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttggt gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctccgat attagttgga atagtggtag caaagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctctat 240
cttcaaatga acagtctgag aactgaggat acggcctttt attactgtgc aaaagatagt 300
aggggctacg gtctctacta ccacctcggt ttggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1042
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1042
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Asp Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Phe Tyr Tyr Cys
                85   90   95
Ala Lys Asp Ser Arg Gly Tyr Gly Leu Tyr Tyr His Leu Gly Leu Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1043
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1043
ggattcacct ttggtgatta tacc 24

<210> 1044
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1044
Gly Phe Thr Phe Gly Asp Tyr Thr
 1   5

<210> 1045
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1045
attagttgga atagtggtag caaa   24

<210> 1046
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1046
Ile Ser Trp Asn Ser Gly Ser Lys
 1   5

<210> 1047
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1047
gcaaaagata gtaggggcta cggtctctac taccacctcg gtttggacgt c   51

<210> 1048
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1048
Ala Lys Asp Ser Arg Gly Tyr Gly Leu Tyr Tyr His Leu Gly Leu Asp
 1   5   10   15
Val

<210> 1049
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1049
gaggtgcagc tggtggagtc tgggggaggc ttggtgcagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgct gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag tatagcctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctctat 240
cttcaaatga acagtctgag aactgaggac acggcctttt attactgtgc aaaagatagt 300
aggggctacg gtcactataa gtacctcggt ttggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1050
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1050
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Ile Ala Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Phe Tyr Tyr Cys
85 90 95
Ala Lys Asp Ser Arg Gly Tyr Gly His Tyr Lys Tyr Leu Gly Leu Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1051
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1051
ggattcacct ttgctgatta tacc 24

<210> 1052
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1052
Gly Phe Thr Phe Ala Asp Tyr Thr
1 5

<210> 1053
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1053
attagttgga atagtggtag tata 24

<210> 1054
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1054
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 1055
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1055
gcaaaagata gtaggggcta cggtcactat aagtacctcg gtttggacgt c 51

<210> 1056
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1056
Ala Lys Asp Ser Arg Gly Tyr Gly His Tyr Lys Tyr Leu Gly Leu Asp
1 5 10 15
Val

<210> 1057
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1057
gaggtgcagc tggtggagtc tgggggaggc atggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt ccccttcaat gattacacca tgcactgggt ccggcaagtc 120
ccagggaggg gcctggagtg ggtctcagat attagttgga atagcggcag taaaggctat 180
gcggactctg tgaagggtcg attcatcatc tccagagaca acgccaagaa ctccctgtac 240
ctgcaaatga acagtctgag agttgaagac acggccttgt attactgtgt aaaagatgga 300
agtggctacg ggaggttcca ttattacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1058
<211> 124
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 1058
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Met Val Gln Pro Gly Arg
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Pro Phe Asn Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Val Pro Gly Arg Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Val Lys Asp Gly Ser Gly Tyr Gly Arg Phe His Tyr Tyr Ala Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1059
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1059
ggattcccct tcaatgatta cacc   24

<210> 1060
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1060
Gly Phe Pro Phe Asn Asp Tyr Thr
1   5

<210> 1061
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1061
attagttgga atagcggcag taaa   24

<210> 1062
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1062
Ile Ser Trp Asn Ser Gly Ser Lys
1   5

<210> 1063
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1063
gtaaaagatg gaagtggcta cgggaggttc cattattacg ctatggacgt c 51

<210> 1064
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1064
Val Lys Asp Gly Ser Gly Tyr Gly Arg Phe His Tyr Tyr Ala Met Asp
1 5 10 15
Val

<210> 1065
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1065
gaggtgcagc tggtggagtc tggtggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgct gattatacca tgcactgggt ccgccaagtt 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag caaagactat 180
gcggactctg tgaagggccg cttcaccatc tccagagaca acgccaagaa tttcctgtat 240
ctgcaaatga acagtctgag agctgaagac acggccttgt attactgtgt aaaatatgga 300
agtggctacg ggaaattcta cttctacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1066
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1066
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Val Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Asp Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Phe Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Tyr Gly Ser Gly Tyr Gly Lys Phe Tyr Phe Tyr Ala Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

115 120

<210> 1067
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1067
ggattcacct ttgctgatta tacc 24

<210> 1068
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1068
Gly Phe Thr Phe Ala Asp Tyr Thr
1 5

<210> 1069
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1069
attagttgga atagtggtag caaa 24

<210> 1070
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1070
Ile Ser Trp Asn Ser Gly Ser Lys
1 5

<210> 1071
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1071
gtaaaatatg gaagtggcta cgggaaattc tacttctacg ctatggacgt c 51

<210> 1072
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 1072
Val Lys Tyr Gly Ser Gly Tyr Gly Lys Phe Tyr Phe Tyr Ala Met Asp
 1   5   10   15
Val

<210> 1073
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1073
gaggtgcagc tggtgcagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgct gattatacca tgcactgggt ccggcaaact 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag caaagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag aactgaggac acggccttgt attactgtgc aaaatatgga 300
agtggctacg ggagatattt cttctacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca   372

<210> 1074
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1074
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Thr Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Lys Asp Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Tyr Gly Ser Gly Tyr Gly Arg Tyr Phe Phe Tyr Ala Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1075
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1075
ggattcacct ttgctgatta tacc   24

<210> 1076
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1076
Gly Phe Thr Phe Ala Asp Tyr Thr
 1   5

<210> 1077
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1077
attagttgga atagtggtag caaa 24

<210> 1078
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1078
Ile Ser Trp Asn Ser Gly Ser Lys
 1   5

<210> 1079
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1079
gcaaaatatg gaagtggcta cgggagatat ttcttctacg ctatggacgt c 51

<210> 1080
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1080
Ala Lys Tyr Gly Ser Gly Tyr Gly Arg Tyr Phe Phe Tyr Ala Met Asp
 1   5   10   15
Val

<210> 1081
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1081

gaggtgcagc tggtggagtc aaggggagcc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cgcctttaat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtaatag taaagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctctat 240
ctacaaatga acagtctgag agctgaggac acggccttgt attactgtgt aaaagatgga 300
agtggctacg ggaaattttc cctctacgct ttggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1082
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1082
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Glu Val Gln Leu Val Glu Ser Arg Gly Ala Leu Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Asn Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Asn Ser Lys Asp Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Val Lys Asp Gly Ser Gly Tyr Gly Lys Phe Ser Leu Tyr Ala Leu Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 1083
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1083
ggattcgcct ttaatgatta tacc 24

<210> 1084
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1084
```
Gly Phe Ala Phe Asn Asp Tyr Thr
 1               5
```

<210> 1085
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1085

attagttgga atagtaatag taaa 24

<210> 1086
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1086
Ile Ser Trp Asn Ser Asn Ser Lys
1 5

<210> 1087
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1087
gtaaaagatg gaagtggcta cgggaaattt tccctctacg ctttggacgt c 51

<210> 1088
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1088
Val Lys Asp Gly Ser Gly Tyr Gly Lys Phe Ser Leu Tyr Ala Leu Asp
1 5 10 15
Val

<210> 1089
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1089
caggtgcagc tggtggagtc tgggggaggc ttggttcacc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt caaatttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctagagtg ggtctcagat attagttgga atagtggtag taaaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagga ttccctatat 240
ctgcagatgg acagtctgag agctgcagac acggccttct attactgtgc aaaagataaa 300
agtggctacg gccacttcta ctactacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1090
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1090
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val His Pro Gly Arg

```
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Lys Phe Asp Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asp Ser Leu Arg Ala Ala Asp Thr Ala Phe Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Lys Ser Gly Tyr Gly His Phe Tyr Tyr Tyr Ala Met Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 1091
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1091
ggattcaaat ttgatgatta tacc                                            24

<210> 1092
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1092
Gly Phe Lys Phe Asp Asp Tyr Thr
 1               5


<210> 1093
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1093
attagttgga atagtggtag taaa                                            24

<210> 1094
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1094
Ile Ser Trp Asn Ser Gly Ser Lys
 1               5


<210> 1095
<211> 51
<212> DNA
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<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1095
gcaaaagata aaagtggcta cggccacttc tactactacg ctatggacgt c 51

<210> 1096
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1096
```
Ala Lys Asp Lys Ser Gly Tyr Gly His Phe Tyr Tyr Tyr Ala Met Asp
 1               5                   10                  15
Val
```

<210> 1097
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1097
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gaggtgcagc tggtggagtc tgggggaggc ttggtacacc ctggcaggtc cctaagactc 60
tcctgtacag cctctggatt caagtttgct gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag taaaggctat 180
gcggactctg taaagggccg attcaccatc tccagagaca atgacaagaa ctccctgtat 240
ctgcaaatga acagtctgag aggtgaggac acggccttgt attactgtgc aaaagatgga 300
agtggctacg ggaggttcca cttctacgct atcgacgtct ggggccaagg gaccacggtc 360
accgtctcct ca                                                     372
```

<210> 1098
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1098
```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val His Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Lys Phe Ala Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Asp Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Gly Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Gly Ser Gly Tyr Gly Arg Phe His Phe Tyr Ala Ile Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 1099

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1099
ggattcaagt ttgctgatta tacc 24

<210> 1100
<211> 8
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<213> Artificial Sequence

<220>
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<400> 1100
Gly Phe Lys Phe Ala Asp Tyr Thr
1 5

<210> 1101
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1101
attagttgga atagtggtag taaa 24

<210> 1102
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1102
Ile Ser Trp Asn Ser Gly Ser Lys
1 5

<210> 1103
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1103
gcaaaagatg gaagtggcta cgggaggttc cacttctacg ctatcgacgt c 51

<210> 1104
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1104
Ala Lys Asp Gly Ser Gly Tyr Gly Arg Phe His Phe Tyr Ala Ile Asp

 1   5   10   15
Val

<210> 1105
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1105
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tcctgtgtag cctctggatt cacctttgat gattattcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag caaagactat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaagac acggccttgt attactgtgc aaaatatgga 300
agtggctacg ggaagttcta ccactacggt ttggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca   372

<210> 1106
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1106
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Lys Asp Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Tyr Gly Ser Gly Tyr Gly Lys Phe Tyr His Tyr Gly Leu Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1107
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1107
ggattcacct ttgatgatta ttcc   24

<210> 1108
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1108
Gly Phe Thr Phe Asp Asp Tyr Ser
 1   5

<210> 1109
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1109
attagttgga atagtggtag caaa 24

<210> 1110
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1110
Ile Ser Trp Asn Ser Gly Ser Lys
 1   5

<210> 1111
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1111
gcaaaatatg gaagtggcta cgggaagttc taccactacg gtttggacgt c 51

<210> 1112
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1112
Ala Lys Tyr Gly Ser Gly Tyr Gly Lys Phe Tyr His Tyr Gly Leu Asp
 1   5   10   15
Val

<210> 1113
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1113
caggtgcagt tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgct gattatacca tgcactgggt ccggcaggct 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag catgggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa atccctgtat 240

ctgcaaatga acagtctgag aactgaggac acggccttgt attactgtgc aaaagatgga 300
agtggctacg ggaaatactt cttctacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1114
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1114
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Met Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Gly Ser Gly Tyr Gly Lys Tyr Phe Phe Tyr Ala Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1115
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1115
ggattcacct ttgctgatta tacc 24

<210> 1116
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1116
Gly Phe Thr Phe Ala Asp Tyr Thr
1 5

<210> 1117
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 1117
attagttgga atagtggtag catg 24

<210> 1118
<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1118
Ile Ser Trp Asn Ser Gly Ser Met
 1   5

<210> 1119
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1119
gcaaaagatg gaagtggcta cgggaaatac ttcttctacg ctatggacgt c   51

<210> 1120
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1120
Ala Lys Asp Gly Ser Gly Tyr Gly Lys Tyr Phe Phe Tyr Ala Met Asp
 1   5   10   15
Val

<210> 1121
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1121
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tcctgtgcag cctctggatt caccttttct gattatacta tgcattgggt ccggcaaggt 120
ccagggaagg gcctggagtg ggtctcagat attagttgga atagtggtag taaaggctat 180
acggactctg tgaagggccg attcaccatt tccagagaca acgccaagaa gtccctgtat 240
ctacaaatga acagtctgag agctgaggac acggccttgt actactgtgt aaaagatgga 300
agtggctacg ggaaatacca cttctacgct atggacgtct ggggccaagg gaccctggtc 360
accgtctcct ca   372

<210> 1122
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1122
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val

        35   40   45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Thr Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Val Lys Asp Gly Ser Gly Tyr Gly Lys Tyr His Phe Tyr Ala Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 1123
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 1123
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<210> 1124
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1124
Gly Phe Thr Phe Ser Asp Tyr Thr
1   5

<210> 1125
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1125
attagttgga atagtggtag taaa   24

<210> 1126
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1126
Ile Ser Trp Asn Ser Gly Ser Lys
1   5

<210> 1127
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1127
gtaaaagatg gaagtggcta cgggaaatac cacttctacg ctatggacgt c 51

<210> 1128
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1128
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Val Lys Asp Gly Ser Gly Tyr Gly Lys Tyr His Phe Tyr Ala Met Asp
 1               5                   10                  15
Val
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<210> 1129
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1129
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ccagggaagg gcctggaatg ggtctcagat attagttgga atagtggtag cagaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagata atgccgagaa ctccctgtac 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataaa 300
agtggctacg gccactacta ctactacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca                                                     372
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<210> 1130
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1130
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val His Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Ser Trp Asn Ser Gly Ser Arg Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Glu Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Lys Ser Gly Tyr Gly His Tyr Tyr Tyr Tyr Ala Met Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 1131
<211> 24
<212> DNA
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<220>
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<400> 1131
ggattcacct ttgatgatta tacc 24

<210> 1132
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1132
Gly Phe Thr Phe Asp Asp Tyr Thr
1 5

<210> 1133
<211> 24
<212> DNA
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<220>
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<400> 1133
attagttgga atagtggtag caga 24

<210> 1134
<211> 8
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<400> 1134
Ile Ser Trp Asn Ser Gly Ser Arg
1 5

<210> 1135
<211> 51
<212> DNA
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<220>
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<400> 1135
gcaaaagata aaagtggcta cggccactac tactactacg ctatggacgt c 51

<210> 1136
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1136
Ala Lys Asp Lys Ser Gly Tyr Gly His Tyr Tyr Tyr Tyr Ala Met Asp
1 5 10 15
Val

<210> 1137
<211> 372
<212> DNA
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<220>
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<400> 1137
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ccagggaagg gcctggaatg ggtctcagat attagttgga atagtggcac cagaggctat 180
gcggactctg tgaggggccg attcaccatc tccagagaca acgccaagaa gtccctgtat 240
ctgcaaatga acagtctgag atctgaggac acggccttgt attactgtgt gaaagatgga 300
agtggctacg ggagatataa tttctacgct atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

<210> 1138
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1138
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Thr Phe Ala Asp Tyr
20 25 30
Thr Leu His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Ser Trp Asn Ser Gly Thr Arg Gly Tyr Ala Asp Ser Val
50 55 60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Asp Gly Ser Gly Tyr Gly Arg Tyr Asn Phe Tyr Ala Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1139
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1139
ggattcacct ttgctgatta tacc 24

<210> 1140
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1140
Gly Phe Thr Phe Ala Asp Tyr Thr
1 5

<210> 1141
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1141
attagttgga atagtggcac caga 24

<210> 1142
<211> 8
<212> PRT
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<220>
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<400> 1142
Ile Ser Trp Asn Ser Gly Thr Arg
1 5

<210> 1143
<211> 51
<212> DNA
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<400> 1143
gtgaaagatg gaagtggcta cgggagatat aatttctacg ctatggacgt c 51

<210> 1144
<211> 17
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<213> Artificial Sequence

<220>
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<400> 1144
Val Lys Asp Gly Ser Gly Tyr Gly Arg Tyr Asn Phe Tyr Ala Met Asp
1 5 10 15
Val

<210> 1145
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
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<400> 1145
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tcctgtgcag cctctggatt tacctttgct gactatacca tgcactgggt ccggcaaggt 120
ccagggaagg gcctggagtg ggtctcagat attggttgga atagtaatac tataggctat 180
gcggactctg tgaagggccg attcgccatc tccagagaca acgccaagaa ctccctgtat 240
cttcaaatga acagtctgcg acctgaggac acggccttat attactgtgt aaaggataaa 300
agtggctacg ggaaattcca atacggtttg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 1146
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1146
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Gly Trp Asn Ser Asn Thr Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Gln Tyr Gly Leu Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 1147
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
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<400> 1147
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<210> 1148
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1148
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Gly Phe Thr Phe Ala Asp Tyr Thr
 1               5
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<210> 1149
<211> 24
<212> DNA
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<220>
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<400> 1149
attggttgga atagtaatac tata 24

<210> 1150
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<212> PRT
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<400> 1150
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 1   5

<210> 1151
<211> 48
<212> DNA
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<400> 1151
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<210> 1152
<211> 16
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<220>
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<400> 1152
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 1   5   10   15

<210> 1153
<211> 369
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ccagggaagg gcctggagtg ggtctcagat attggttgga atagtaacag tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctccaaatga acagtctgag acctgaggac acggccttgt atttctgtgt aaaggataaa 300
agtggctacg ggaaattttt catcggtttg gacgtctggg gccaagggac aatggtcacc 360
gtctcttca   369

<210> 1154
<211> 123
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<220>
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<400> 1154
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Gly Trp Asn Ser Asn Ser Ile Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Phe Cys

                85   90   95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Phe Ile Gly Leu Asp Val
            100   105   110
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 1155
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 1155
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<210> 1156
<211> 8
<212> PRT
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<220>
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<400> 1156
Gly Phe Thr Phe Asp Asp Tyr Thr
1   5

<210> 1157
<211> 24
<212> DNA
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<220>
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<400> 1157
attggttgga atagtaacag tata 24

<210> 1158
<211> 8
<212> PRT
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<220>
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<400> 1158
Ile Gly Trp Asn Ser Asn Ser Ile
1   5

<210> 1159
<211> 48
<212> DNA
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<220>
<223> Synthetic

<400> 1159
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<210> 1160
<211> 16

<212> PRT
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<220>
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<400> 1160
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Phe Ile Gly Leu Asp Val
 1   5   10   15

<210> 1161
<211> 369
<212> DNA
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ccagggaagg gcctggagtg ggtctcagat attggttgga atagtaatac taaaggctat 180
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ctccaaatga acagtctgag acctgaggac acggccttgt atttctgtgt gaaggataaa 300
agtggctacg ggaaattttt catcggtttg gacgtctggg gccaagggac aatggtcacc 360
gtctcttca   369

<210> 1162
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1162
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Asp Ile Gly Trp Asn Ser Asn Thr Lys Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Phe Cys
                85   90   95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Phe Ile Gly Leu Asp Val
            100   105   110
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 1163
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 1163
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<210> 1164
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<212> PRT
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<220>
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<400> 1164
Gly Phe Thr Phe Asp Asp Tyr Thr
1   5

<210> 1165
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<400> 1165
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<210> 1166
<211> 8
<212> PRT
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<220>
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<400> 1166
Ile Gly Trp Asn Ser Asn Thr Lys
1   5

<210> 1167
<211> 48
<212> DNA
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<220>
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<400> 1167
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<210> 1168
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<220>
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<400> 1168
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Phe Ile Gly Leu Asp Val
1   5   10   15

<210> 1169
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
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<400> 1169

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ccagggacgg gcctggagtg ggtctcagat attggttgga gtggtggtag tttaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ttggaaatga acaatctgcg acctgaagac acggccttgt attattgtgt aaaggataaa 300
agtggctacg ggaaattcca gtacggtttg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 1170
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<220>
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Gly Pro Gly Thr Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Gly Trp Ser Gly Gly Ser Leu Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Glu Met Asn Asn Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Gln Tyr Gly Leu Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1171
<211> 24
<212> DNA
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<220>
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<400> 1171
ggattcacct ttgctgatta tacc 24

<210> 1172
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1172
Gly Phe Thr Phe Ala Asp Tyr Thr
1 5

<210> 1173
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 1173

attggttgga gtggtggtag ttta 24

<210> 1174
<211> 8
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<220>
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<400> 1174
Ile Gly Trp Ser Gly Gly Ser Leu
1 5

<210> 1175
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1175
gtaaaggata aaagtggcta cgggaaattc cagtacggtt tggacgtc 48

<210> 1176
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1176
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Gln Tyr Gly Leu Asp Val
1 5 10 15

<210> 1177
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
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<400> 1177
gaggtgcagc tggtggagtc tgggggaggc gtggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctgggtt taaatttgat ggttatacca tgcactgggt ccggcaaggt 120
ccagggaagg gcctggagtg ggtctcagat attggttgga atagtaacac tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctccaaatga acagtctgag accagaggac acggccttgt atttctgtgt aaaggataaa 300
agtggctacg ggaaattttt catcggtttg gacgtctggg gccaagggac aatggtcacc 360
gtctcttca 369

<210> 1178
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1178
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Lys Phe Asp Gly Tyr

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            20                  25                  30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Asp Ile Gly Trp Asn Ser Asn Thr Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Phe Cys
                85                  90                  95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Phe Ile Gly Leu Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210> 1179
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<212> DNA
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<220>
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<400> 1179
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<210> 1180
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1180
Gly Phe Lys Phe Asp Gly Tyr Thr
1               5


<210> 1181
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1181
attggttgga atagtaacac tata                                          24

<210> 1182
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1182
Ile Gly Trp Asn Ser Asn Thr Ile
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<210> 1183
<211> 48
<212> DNA
<213> Artificial Sequence
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<220>
<223> Synthetic

<400> 1183
gtaaaggata aaagtggcta cgggaaattt ttcatcggtt tggacgtc 48

<210> 1184
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1184
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Phe Ile Gly Leu Asp Val
1 5 10 15

<210> 1185
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1185
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tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaaggt 120
ccagggaagg gcctggagtg ggtctcagat attggttgga atagtaatac tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaggaa ctccctgtat 240
ctgcaaatga acagtctgcg acctgaagac acggccttat attactgtgt aaaggataaa 300
agtggctacg ggaaattcca atacggtttg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 1186
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1186
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Gly Trp Asn Ser Asn Thr Ile Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Gln Tyr Gly Leu Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1187
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1187
ggattcacct ttgatgatta tacc 24

<210> 1188
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1188
Gly Phe Thr Phe Asp Asp Tyr Thr
1 5

<210> 1189
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 1189
attggttgga atagtaatac tata 24

<210> 1190
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1190
Ile Gly Trp Asn Ser Asn Thr Ile
1 5

<210> 1191
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1191
gtaaaggata aaagtggcta cgggaaattc caatacggtt tggacgtc 48

<210> 1192
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1192
Val Lys Asp Lys Ser Gly Tyr Gly Lys Phe Gln Tyr Gly Leu Asp Val
1 5 10 15

<210> 1193

<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1193
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tcctgtgcag cctctggatt caagtttgat gattatacca tgcactgggt ccggcaaggt 120
ccagggaagg gcctggagtg ggtctcagac attagttgga gtggtggtag catagactat 180
acggactctg tgaagggccg attctccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agttgaagac acggccttgt attattgtgt aaaagataaa 300
agtggctacg ggaagtactc ttacggtttg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca 369

<210> 1194
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1194
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Lys Phe Asp Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Asp Ile Ser Trp Ser Gly Gly Ser Ile Asp Tyr Thr Asp Ser Val
50 55 60
Lys Gly Arg Phe Ser Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Val Lys Asp Lys Ser Gly Tyr Gly Lys Tyr Ser Tyr Gly Leu Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1195
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1195
ggattcaagt ttgatgatta tacc 24

<210> 1196
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1196
Gly Phe Lys Phe Asp Asp Tyr Thr
1 5

<210> 1197

<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1197
attagttgga gtggtggtag cata 24

<210> 1198
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1198
Ile Ser Trp Ser Gly Gly Ser Ile
1   5

<210> 1199
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1199
gtaaaagata aaagtggcta cgggaagtac tcttacggtt tggacgtc 48

<210> 1200
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1200
Val Lys Asp Lys Ser Gly Tyr Gly Lys Tyr Ser Tyr Gly Leu Asp Val
1   5   10   15

<210> 1201
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1201
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tcctgtgcag cctctggatt ctctttcatt aacgcctgga tgaactgggt ccgccaggct 120
ccagggaagg ggctggagtg ggttggccgt attaaaagca taagtgatgg tgggacaaca 180
gactacgctg catccgtgaa aggcagattc accatctcaa gagaagattc aaaaaatatg 240
ctgtttctgg aaatgaatag tctgaaaacc gaggacacag ccgtgtttta ctgtaccaca 300
gaggtcgcta gaactccgaa ctactggggc cggggaaccc tggtcaccgt ctcctca 357

<210> 1202
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1202
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly Phe Ser Phe Ile Asn Ala
            20                  25                  30
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Gly Arg Ile Lys Ser Ile Ser Asp Gly Gly Thr Thr Asp Tyr Ala Ala
    50                  55                  60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asp Ser Lys Asn Met
65                  70                  75                  80
Leu Phe Leu Glu Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Phe
                85                  90                  95
Tyr Cys Thr Thr Glu Val Ala Arg Thr Pro Asn Tyr Trp Gly Arg Gly
            100                 105                 110
Thr Leu Val Thr Val Ser Ser
        115
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<210> 1203
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1203
ggattctctt tcattaacgc ctgg 24

<210> 1204
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1204
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Gly Phe Ser Phe Ile Asn Ala Trp
 1               5
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<210> 1205
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1205
attaaaagca taagtgatgg tgggacaaca 30

<210> 1206
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1206
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Ile Lys Ser Ile Ser Asp Gly Gly Thr Thr
 1               5                  10
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<210> 1207
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1207
accacagagg tcgctagaac tccgaactac                                    30

<210> 1208
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1208
Thr Thr Glu Val Ala Arg Thr Pro Asn Tyr
 1               5                   10


<210> 1209
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1209
gaagtacagc ttgtagaatc cggcggagga ctggtacaac ctggaagaag tcttagactg 60
agttgcgcag ctagtgggtt tacattcgac gattacagca tgcattgggt gaggcaagct 120
cctggtaaag gattggaatg ggttagcggg atatcatgga actcaggaag caagggatac 180
gccgacagcg tgaaaggccg atttacaata tctagggaca acgcaaaaaa ctctctctac 240
cttcaaatga actctcttag ggcagaagac acagcattgt attattgcgc aaaatacggc 300
agtggttatg gcaagtttta tcattatgga ctggacgtgt ggggacaagg gacaacagtg 360
acagtgagta gc                                                     372

<210> 1210
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1210
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Lys Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Tyr Gly Ser Gly Tyr Gly Lys Phe Tyr His Tyr Gly Leu Asp
            100                 105                 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 1211
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1211
gggtttacat tcgacgatta cagc 24

<210> 1212
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1212
Gly Phe Thr Phe Asp Asp Tyr Ser
1 5

<210> 1213
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1213
atatcatgga actcaggaag caag 24

<210> 1214
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 1214
Ile Ser Trp Asn Ser Gly Ser Lys
1 5

<210> 1215
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1215
gcaaaatacg gcagtggtta tggcaagttt tatcattatg gactggacgt g 51

<210> 1216
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1216
Ala Lys Tyr Gly Ser Gly Tyr Gly Lys Phe Tyr His Tyr Gly Leu Asp
 1   5   10   15
Val

<210> 1217
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1217
gaagtacaac tggtcgaatc tggaggaggt cttgttcaac ctggtcgatc acttcgcctt 60
tcttgtgccg cttctggttt cactttcgac gattatagca tgcattgggt acgacaggct 120
cccggaaaag ggctggaatg ggtgtcagga attagttgga actcaggaag tattggatac 180
gctgattcag tcaaaggacg cttcacaatc tcaagggaca acgctaaaaa ctcactttat 240
ttgcaaatga actctctccg cgctgaagat accgctctct attattgcgc caaagatggg 300
tctggttacg gttattttta ctactatgga atggacgttt ggggccaagg aacaactgtc 360
acagtatcat cc   372

<210> 1218
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1218
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20   25   30
Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Gly Ser Gly Tyr Gly Tyr Phe Tyr Tyr Tyr Gly Met Asp
            100   105   110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1219
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1219
ggtttcactt tcgacgatta tagc   24

<210> 1220
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1220
Gly Phe Thr Phe Asp Asp Tyr Ser
 1   5

<210> 1221
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1221
attagttgga actcaggaag tatt   24

<210> 1222
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1222
Ile Ser Trp Asn Ser Gly Ser Ile
 1   5

<210> 1223
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1223
gccaaagatg ggtctggtta cggttatttt tactactatg gaatggacgt t   51

<210> 1224
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1224
Ala Lys Asp Gly Ser Gly Tyr Gly Tyr Phe Tyr Tyr Tyr Gly Met Asp
 1   5   10   15
Val

<210> 1225
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1225
gaagtgcaac tcgttgaaag cggaggagga ctggtccagc ccggcagatc tctcagattg 60

tcttgcgctg catccggatt tacatttgac gactattcaa tgcactgggt acggcaagcc 120
ccaggtaaag gactcgaatg ggtaagcggc atatcttgga actcaggcag tattggctac 180
gcagattcag taaaaggaag attcactatt tcaagggata atgctaagaa cagtctctac 240
ttgcaaatga atagcttgcg cgcagaagat acagcacttt attattgtgc aaaagatgga 300
agcggttatg ggaaatttta ttattatggt atggatgtat ggggtcaagg tacaacagtt 360
actgtgtcaa gt 372

<210> 1226
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1226
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30
Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Gly Ser Gly Tyr Gly Lys Phe Tyr Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1227
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1227
ggatttacat ttgacgacta ttca 24

<210> 1228
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1228
Gly Phe Thr Phe Asp Asp Tyr Ser
1 5

<210> 1229
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1229
atatcttgga actcaggcag tatt 24

<210> 1230
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1230
Ile Ser Trp Asn Ser Gly Ser Ile
 1   5

<210> 1231
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1231
gcaaaagatg gaagcggtta tgggaaattt tattattatg gtatggatgt a   51

<210> 1232
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1232
Ala Lys Asp Gly Ser Gly Tyr Gly Lys Phe Tyr Tyr Tyr Gly Met Asp
 1   5   10   15
Val

<210> 1233
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1233
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccgtca 180
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag agttacagta cccctccgat caccttcggc 300
caagggacac gactggagat taaa   324

<210> 1234
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1234
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr

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


<210> 1235
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1235
cagagcatta gcagctat                                                   18

<210> 1236
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1236
Gln Ser Ile Ser Ser Tyr
 1               5


<210> 1237
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1237
gctgcatcc                                                              9

<210> 1238
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1238
Ala Ala Ser
 1


<210> 1239
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic
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<400> 1239
caacagagtt acagtacccc tccgatcacc 30

<210> 1240
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1240
```
Gln Gln Ser Tyr Ser Thr Pro Pro Ile Thr
 1               5                   10
```

<210> 1241
<211> 382
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1241
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gaagtacagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgtag cctctggatt cacctttaat gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggaatg ggtctcagtt attagttgga atagtgatag cataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatgc acagtctgag agctgaggac acggccttgt attactgtgc aaaagataat 300
cactatggtt cggggagtta ttactactac caatacggta tggacgtctg ggccaaggg 360
accacggtca ccgtctcctc ag                                          382
```

<210> 1242
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1242
```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Asn Asp Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Val Ile Ser Trp Asn Ser Asp Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                      80
Leu Gln Met His Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Asn His Tyr Gly Ser Gly Ser Tyr Tyr Tyr Tyr Gln Tyr
            100                 105                 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 1243
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1243
ggattcacct ttaatgatta tgcc 24

<210> 1244
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1244
Gly Phe Thr Phe Asn Asp Tyr Ala
1 5

<210> 1245
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1245
attagttgga atagtgatag cata 24

<210> 1246
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1246
Ile Ser Trp Asn Ser Asp Ser Ile
1 5

<210> 1247
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1247
gcaaaagata atcactatgg ttcggggagt tattactact accaatacgg tatggacgtc 60

<210> 1248
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1248
Ala Lys Asp Asn His Tyr Gly Ser Gly Ser Tyr Tyr Tyr Tyr Gln Tyr
1 5 10 15
Gly Met Asp Val
20

<210> 1249
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1249
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa gtccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataat 300
agtggctacg gtcactacta ctacggaatg gacgtctggg gccaagggac cacggtcacc 360
gtcgcctca 369

<210> 1250
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1250
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
115 120

<210> 1251
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1251
ggattcacct ttgatgatta tacc 24

<210> 1252
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1252
Gly Phe Thr Phe Asp Asp Tyr Thr
1 5

<210> 1253
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1253
attagttgga atagtggtag tata 24

<210> 1254
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1254
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 1255
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1255
gcaaaagata atagtggcta cggtcactac tactacggaa tggacgtc 48

<210> 1256
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1256
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 1257
<211> 320
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1257
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcac tatattaact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa 320

<210> 1258
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1258
```
Ala Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro
 1               5                   10                  15
Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser
            20                  25                  30
Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65                  70                  75                  80
Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Ile Asn Trp Pro
                85                  90                  95
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 1259
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1259
cagagtgtta gcagcaac 18

<210> 1260
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1260
```
Gln Ser Val Ser Ser Asn
 1               5
```

<210> 1261
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1261
ggtgcatcc 9

<210> 1262
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1262
```
Gly Ala Ser
 1
```

<210> 1263
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1263
cagcactata ttaactggcc tctcact 27

<210> 1264
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1264
```
Gln His Tyr Ile Asn Trp Pro Leu Thr
 1               5
```

<210> 1265
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1265
```
gaagtgcaac tggtggagtc tgggggaggc ttagtacagc ctggcgggtc cctgagactc 60
tcctgtgcag ccactggatt cacctttgat gattttacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt atcagttgga atagtggtag cataggctat 180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt actactgtgc aaaagataat 300
agtggctacg gctattatta ctacggtatg gacgtctggg gccaagggac cacggtcacc 360
gtctcctca                                                         369
```

<210> 1266
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1266
```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Thr Gly Phe Thr Phe Asp Asp Phe
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Val Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 1267
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1267
ggattcacct ttgatgattt tacc 24

<210> 1268
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1268
Gly Phe Thr Phe Asp Asp Phe Thr
1 5

<210> 1269
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1269
atcagttgga atagtggtag cata 24

<210> 1270
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1270
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 1271
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1271
gcaaaagata atagtggcta cggctattat tactacggta tggacgtc 48

<210> 1272
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1272
Ala Lys Asp Asn Ser Gly Tyr Gly Tyr Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 1273
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1273
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca cagtgttagc aggaactcag cctggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240
gaagattttg caatttatta ctgtcagcag tataataatt ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 1274
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1274
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser His Ser Val Ser Arg Asn
            20   25   30
Ser Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 1275
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1275
cacagtgtta gcaggaac 18

<210> 1276
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1276
His Ser Val Ser Arg Asn
1   5

<210> 1277
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1277
ggtgcatcc 9

<210> 1278
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1278
Gly Ala Ser
1

<210> 1279
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1279
cagcagtata ataattggcc tctcact 27

<210> 1280
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1280
Gln Gln Tyr Asn Asn Trp Pro Leu Thr
1 5

<210> 1281
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1281
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag tataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa gtccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataat 300
agtggctacg gtcactacta ctacggaatg gacgtctggg gccaagggac cacggtcacc 360
gtcgcctca 369

<210> 1282

<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1282
```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
            100                 105                 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
        115                 120
```

<210> 1283
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1283
ggattcacct ttgatgatta tacc 24

<210> 1284
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1284
```
Gly Phe Thr Phe Asp Asp Tyr Thr
 1               5
```

<210> 1285
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1285
attagttgga atagtggtag tata 24

<210> 1286
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1286
Ile Ser Trp Asn Ser Gly Ser Ile
1   5

<210> 1287
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1287
gcaaaagata atagtggcta cggtcactac tactacggaa tggacgtc 48

<210> 1288
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1288
Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
1   5   10   15

<210> 1289
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1289
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcac tatattaact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 1290
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1290
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Ile Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

100 105

<210> 1291
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1291
cagagtgtta gcagcaac 18

<210> 1292
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1292
Gln Ser Val Ser Ser Asn
1 5

<210> 1293
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1293
ggtgcatcc 9

<210> 1294
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1294
Gly Ala Ser
1

<210> 1295
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1295
cagcactata ttaactggcc tctcact 27

<210> 1296
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 1296
Gln His Tyr Ile Asn Trp Pro Leu Thr
1   5

<210> 1297
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1297
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgctg cgtctggatt caccttcaga agttatgcca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcaatg gtatactatg atggaaataa tcaatactat 180
gcagactccg tgaggggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgatgac acggctgtgt atttctgtgc gcgagggcct 300
gggtacaact ggctcgaccc ctggggccag ggaaccctgg tcaccgtctc ctca   354

<210> 1298
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1298
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20   25   30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ala Met Val Tyr Tyr Asp Gly Asn Asn Gln Tyr Tyr Ala Asp Ser Val
    50   55   60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Phe Cys
                85   90   95
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100   105   110
Leu Val Thr Val Ser Ser
        115

<210> 1299
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1299
ggatttacct tcagaagtta tgcc   24

<210> 1300
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1300
Gly Phe Thr Phe Arg Ser Tyr Ala
1 5

<210> 1301
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1301
gtatactatg atggaaataa tcaa 24

<210> 1302
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1302
Val Tyr Tyr Asp Gly Asn Asn Gln
1 5

<210> 1303
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1303
gcgcgagggc ctgggtacaa ctggctcgac ccc 33

<210> 1304
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1304
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1 5 10

<210> 1305
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1305
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc aggaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccggcc 180
aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataact ggcctctcac tttcggcgga 300

gggaccaagg tggtgatcaa a 321

<210> 1306
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1306
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala 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 Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Val Ile Lys
100 105

<210> 1307
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1307
cagagtgtta gcaggaac 18

<210> 1308
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1308
Gln Ser Val Ser Arg Asn
1 5

<210> 1309
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1309
ggtgcatcc 9

<210> 1310
<211> 3
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 1310
Gly Ala Ser
 1

<210> 1311
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1311
cagcagtata ataactggcc tctcact   27

<210> 1312
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1312
Gln Gln Tyr Asn Asn Trp Pro Leu Thr
 1   5

<210> 1313
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1313
caggtgcagt tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
gcctgtgttg cgtctggatt caccttcaga agttatggca tgcactgggt ccgccaggct 120
ccaggcaagg gactgcagtg ggtggcaatg atttactatg atggtaagaa taaatattat 180
gcagactccg tgaggggccg attcaccatc tccagagaca attccaagaa cacactgtat 240
ctgcaaatga acaatctgag agtcgaggac acggctatgt atttctgtgc gcgagggcct 300
gggtacaatt ggctcgaccc ctggggccag ggaaccctgg tcactgtttc ctca   354

<210> 1314
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1314
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ala Cys Val Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20   25   30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gln Trp Val
        35   40   45
Ala Met Ile Tyr Tyr Asp Gly Lys Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Asn Leu Arg Val Glu Asp Thr Ala Met Tyr Phe Cys
                85   90   95

Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro Trp Gly Gln Gly Thr
            100   105   110
Leu Val Thr Val Ser Ser
        115

<210> 1315
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1315
ggattcacct tcagaagtta tggc 24

<210> 1316
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1316
Gly Phe Thr Phe Arg Ser Tyr Gly
1   5

<210> 1317
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1317
atttactatg atggtaagaa taaa 24

<210> 1318
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1318
Ile Tyr Tyr Asp Gly Lys Asn Lys
1   5

<210> 1319
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1319
gcgcgagggc ctgggtacaa ttggctcgac ccc 33

<210> 1320
<211> 11
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1320
Ala Arg Gly Pro Gly Tyr Asn Trp Leu Asp Pro
1   5   10

<210> 1321
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1321
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagaattagc agcaacttgg cctggtacca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tagcccagcc 180
aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctgcagtct 240
gaggatgttg cagtttatta ctgtcagcaa catcataact ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 1322
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1322
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Ile Ser Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ser Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His His Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 1323
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1323
cagagaatta gcagcaac 18

<210> 1324
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 1324
Gln Arg Ile Ser Ser Asn
 1   5

<210> 1325
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1325
ggtgcatcc   9

<210> 1326
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1326
Gly Ala Ser
 1

<210> 1327
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1327
cagcaacatc ataactggcc tctcact   27

<210> 1328
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1328
Gln Gln His His Asn Trp Pro Leu Thr
 1   5

<210> 1329
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1329
Asp Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

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

<210> 1330
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1330
Gly Tyr Thr Phe Thr Arg Tyr Thr
1 5

<210> 1331
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1331
Ile Asn Pro Ser Arg Gly Tyr Thr
1 5

<210> 1332
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1332
Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 1333
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1333
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 Ser Val Ser Tyr Met
20 25 30
Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60
Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Asn Ser Leu Glu Ala Glu
65   70   75   80
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 1334
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1334
Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Tyr
 1   5   10

<210> 1335
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1335
Asp Thr Ser
 1

<210> 1336
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1336
Gln Gln Trp Ser Ser Asn Pro Leu Thr
 1   5

<210> 1337
<211> 367
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1337
gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttat gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagctgga atagtgatac cataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttat attactgtac aaaagatggc 300
agctatggtc acttctactc cggtttggac gtctggggcc aagggaccac ggtcaccgtc 360
tcctcag   367

<210> 1338
<211> 122

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1338
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Asp Tyr
            20                  25                  30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Gly Ile Ser Trp Asn Ser Asp Thr Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95
Thr Lys Asp Gly Ser Tyr Gly His Phe Tyr Ser Gly Leu Asp Val Trp
            100                 105                 110
Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 1339
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1339
ggattcacct tttatgatta tgcc   24

<210> 1340
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1340
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Gly Phe Thr Phe Tyr Asp Tyr Ala
 1               5
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<210> 1341
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1341
attagctgga atagtgatac cata   24

<210> 1342
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1342
Ile Ser Trp Asn Ser Asp Thr Ile
1   5

<210> 1343
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1343
acaaaagatg gcagctatgg tcacttctac tccggtttgg acgtc 45

<210> 1344
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1344
Thr Lys Asp Gly Ser Tyr Gly His Phe Tyr Ser Gly Leu Asp Val
1   5   10   15

<210> 1345
<211> 322
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1345
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct 120
ggccaggctc ccgactcct catctatggt acatccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcaacaa tataataact ggccgctcac tttcggcgga 300
gggaccaagg tggagatcaa ac 322

<210> 1346
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1346
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Thr Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 1347
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1347
cagagtgtta gcagcaac 18

<210> 1348
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1348
Gln Ser Val Ser Ser Asn
1 5

<210> 1349
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1349
ggtacatcc 9

<210> 1350
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1350
Gly Thr Ser
1

<210> 1351
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1351
caacaatata ataactggcc gctcact 27

<210> 1352
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1352
Gln Gln Tyr Asn Asn Trp Pro Leu Thr
 1   5

<210> 1353
<211> 379
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1353
gaagagcaac tggtggagtc tgggggagac ttggtacagc ctggcaggtc cctgaggctc 60
tcctgtgcag cctctggatt cacctttcat gattacacca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggaag tctaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa gtccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttat attactgtgc aaaagatccc 300
tcttatggtt cggggtcgta tcactcctac tacggaatgg acgtctgggg ccaagggacc 360
acggtcactg tctcctcag   379

<210> 1354
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1354
Glu Glu Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Arg
 1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe His Asp Tyr
            20   25   30
Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ser Gly Ile Ser Trp Asn Ser Gly Ser Leu Gly Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85   90   95
Ala Lys Asp Pro Ser Tyr Gly Ser Gly Ser Tyr His Ser Tyr Tyr Gly
            100   105   110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120   125

<210> 1355
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1355
ggattcacct ttcatgatta cacc   24

<210> 1356
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1356
Gly Phe Thr Phe His Asp Tyr Thr
 1   5

<210> 1357
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1357
attagttgga atagtggaag tcta   24

<210> 1358
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1358
Ile Ser Trp Asn Ser Gly Ser Leu
 1   5

<210> 1359
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1359
gcaaaagatc cctcttatgg ttcggggtcg tatcactcct actacggaat ggacgtc   57

<210> 1360
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1360
Ala Lys Asp Pro Ser Tyr Gly Ser Gly Ser Tyr His Ser Tyr Tyr Gly
 1   5   10   15
Met Asp Val

<210> 1361
<211> 322
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1361
gaaattgtgt tgacacagtc tccagccacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgct gggccagtca gagtattagc aggtacttag tctggtacca acagaaatgt 120
ggccaggcac ccagactcct catctatgaa gcatctaaga gggccaccgg catcccagtc 180

aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctagagtct 240
gaagattttg cagtttatta ttgtcagcag cgtttcaatt ggcctctcac tttcggcgga 300
gggaccaagg tggagatcaa ac 322

<210> 1362
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1362
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 Trp Ala Ser Gln Ser Ile Ser Arg Tyr
20 25 30
Leu Val Trp Tyr Gln Gln Lys Cys Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Glu Ala Ser Lys Arg Ala Thr Gly Ile Pro Val Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Phe Asn Trp Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1363
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1363
cagagtatta gcaggtac 18

<210> 1364
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1364
Gln Ser Ile Ser Arg Tyr
1 5

<210> 1365
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1365
gaagcatct 9

<210> 1366
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1366
Glu Ala Ser
 1

<210> 1367
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1367
cagcagcgtt tcaattggcc tctcact 27

<210> 1368
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 1368
Gln Gln Arg Phe Asn Trp Pro Leu Thr
 1   5

<210> 1369
<211> 297
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD20

<400> 1369
Met Thr Thr Pro Arg Asn Ser Val Asn Gly Thr Phe Pro Ala Glu Pro
 1   5   10   15
Met Lys Gly Pro Ile Ala Met Gln Ser Gly Pro Lys Pro Leu Phe Arg
            20   25   30
Arg Met Ser Ser Leu Val Gly Pro Thr Gln Ser Phe Phe Met Arg Glu
        35   40   45
Ser Lys Thr Leu Gly Ala Val Gln Ile Met Asn Gly Leu Phe His Ile
    50   55   60
Ala Leu Gly Gly Leu Leu Met Ile Pro Ala Gly Ile Tyr Ala Pro Ile
65   70   75   80
Cys Val Thr Val Trp Tyr Pro Leu Trp Gly Gly Ile Met Tyr Ile Ile
                85   90   95
Ser Gly Ser Leu Leu Ala Ala Thr Glu Lys Asn Ser Arg Lys Cys Leu
            100   105   110
Val Lys Gly Lys Met Ile Met Asn Ser Leu Ser Leu Phe Ala Ala Ile
        115   120   125
Ser Gly Met Ile Leu Ser Ile Met Asp Ile Leu Asn Ile Lys Ile Ser
    130   135   140
His Phe Leu Lys Met Glu Ser Leu Asn Phe Ile Arg Ala His Thr Pro
145   150   155   160
Tyr Ile Asn Ile Tyr Asn Cys Glu Pro Ala Asn Pro Ser Glu Lys Asn
                165   170   175
Ser Pro Ser Thr Gln Tyr Cys Tyr Ser Ile Gln Ser Leu Phe Leu Gly
            180   185   190
Ile Leu Ser Val Met Leu Ile Phe Ala Phe Phe Gln Glu Leu Val Ile
        195   200   205

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Ala Gly Ile Val Glu Asn Glu Trp Lys Arg Thr Cys Ser Arg Pro Lys
    210                 215                 220
Ser Asn Ile Val Leu Leu Ser Ala Glu Glu Lys Lys Glu Gln Thr Ile
225                 230                 235                 240
Glu Ile Lys Glu Glu Val Val Gly Leu Thr Glu Thr Ser Ser Gln Pro
                245                 250                 255
Lys Asn Glu Glu Asp Ile Glu Ile Ile Pro Ile Gln Glu Glu Glu Glu
            260                 265                 270
Glu Glu Thr Glu Thr Asn Phe Pro Glu Pro Pro Gln Asp Gln Glu Ser
        275                 280                 285
Ser Pro Ile Glu Asn Asp Ser Ser Pro
    290                 295


<210> 1370
<211> 104
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD3 epsilon

<400> 1370
Asp Gly Asn Glu Glu Met Gly Gly Ile Thr Gln Thr Pro Tyr Lys Val
 1               5                  10                  15
Ser Ile Ser Gly Thr Thr Val Ile Leu Thr Cys Pro Gln Tyr Pro Gly
            20                  25                  30
Ser Glu Ile Leu Trp Gln His Asn Asp Lys Asn Ile Gly Gly Asp Glu
        35                  40                  45
Asp Asp Lys Asn Ile Gly Ser Asp Glu Asp His Leu Ser Leu Lys Glu
    50                  55                  60
Phe Ser Glu Leu Glu Gln Ser Gly Tyr Tyr Val Cys Tyr Pro Arg Gly
65                  70                  75                  80
Ser Lys Pro Glu Asp Ala Asn Phe Tyr Leu Tyr Leu Arg Ala Arg Val
                85                  90                  95
Ser Glu Asn Ser Met Glu Met Asp
            100


<210> 1371
<211> 79
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD3 delta

<400> 1371
Phe Lys Ile Pro Ile Glu Glu Leu Glu Asp Arg Val Phe Val Asn Cys
 1               5                  10                  15
Asn Thr Ser Ile Thr Trp Val Glu Gly Thr Val Gly Thr Leu Leu Ser
            20                  25                  30
Asp Ile Thr Arg Leu Asp Leu Gly Lys Arg Ile Leu Asp Pro Arg Gly
        35                  40                  45
Ile Tyr Arg Cys Asn Gly Thr Asp Ile Tyr Lys Asp Lys Glu Ser Thr
    50                  55                  60
Val Gln Val His Tyr Arg Met Ser Gln Ser Ser Val Glu Leu Asp
65                  70                  75


<210> 1372
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<223> hFc-delta-Adp
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<400> 1372
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1   5   10   15
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20   25   30
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35   40   45
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50   55   60
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65   70   75   80
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85   90   95
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100   105   110
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115   120   125
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    130   135   140
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145   150   155   160
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165   170   175
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180   185   190
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195   200   205
His Glu Ala Leu His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser
    210   215   220
Pro Gly Lys
225

<210> 1373
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<223> hFc

<400> 1373
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1   5   10   15
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20   25   30
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35   40   45
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50   55   60
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65   70   75   80
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85   90   95
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100   105   110
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115   120   125
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    130   135   140
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145   150   155   160
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165   170   175
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180   185   190
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195   200   205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210   215   220
Pro Gly Lys
225

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Ala Pro Asn Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys
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Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val
        35   40   45
Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe
    50   55   60
Val Asn Asn Val Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu
65   70   75   80
Asp Tyr Asn Ser Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His
                85   90   95
Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys
            100   105   110
Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser
        115   120   125
Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met
    130   135   140
Thr Lys Lys Gln Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro
145   150   155   160
Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn
                165   170   175
Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met
            180   185   190
Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser
        195   200   205
Tyr Ser Cys Ser Val Val His Glu Gly Leu His Asn Arg Phe Thr Thr
    210   215   220
Lys Ser Phe Ser Arg Thr Pro Gly Lys
225   230

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

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Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys
            100                 105                 110
Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser
        115                 120                 125
Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met
    130                 135                 140
Thr Lys Lys Gln Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro
145                 150                 155                 160
Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn
                165                 170                 175
Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met
            180                 185                 190
Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser
        195                 200                 205
Tyr Ser Cys Ser Val Val His Glu Gly Leu His Asn His His Thr Thr
    210                 215                 220
Lys Ser Phe Ser Arg Thr Pro Gly Lys
225                 230
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