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(54) **Title:** TETRAVALENT FZD AND WNT CO-RECEPTOR BINDING ANTIBODY MOLECULES AND USES THEREOF

(57) **Abstract:** Described herein are tetravalent binding antibody molecules comprising a FZD receptor binding domain and an LRP5/6 co-receptor binding domain on opposite termini of an Fc domain that activate a Wnt beta-catenin signaling pathway and methods for their use.

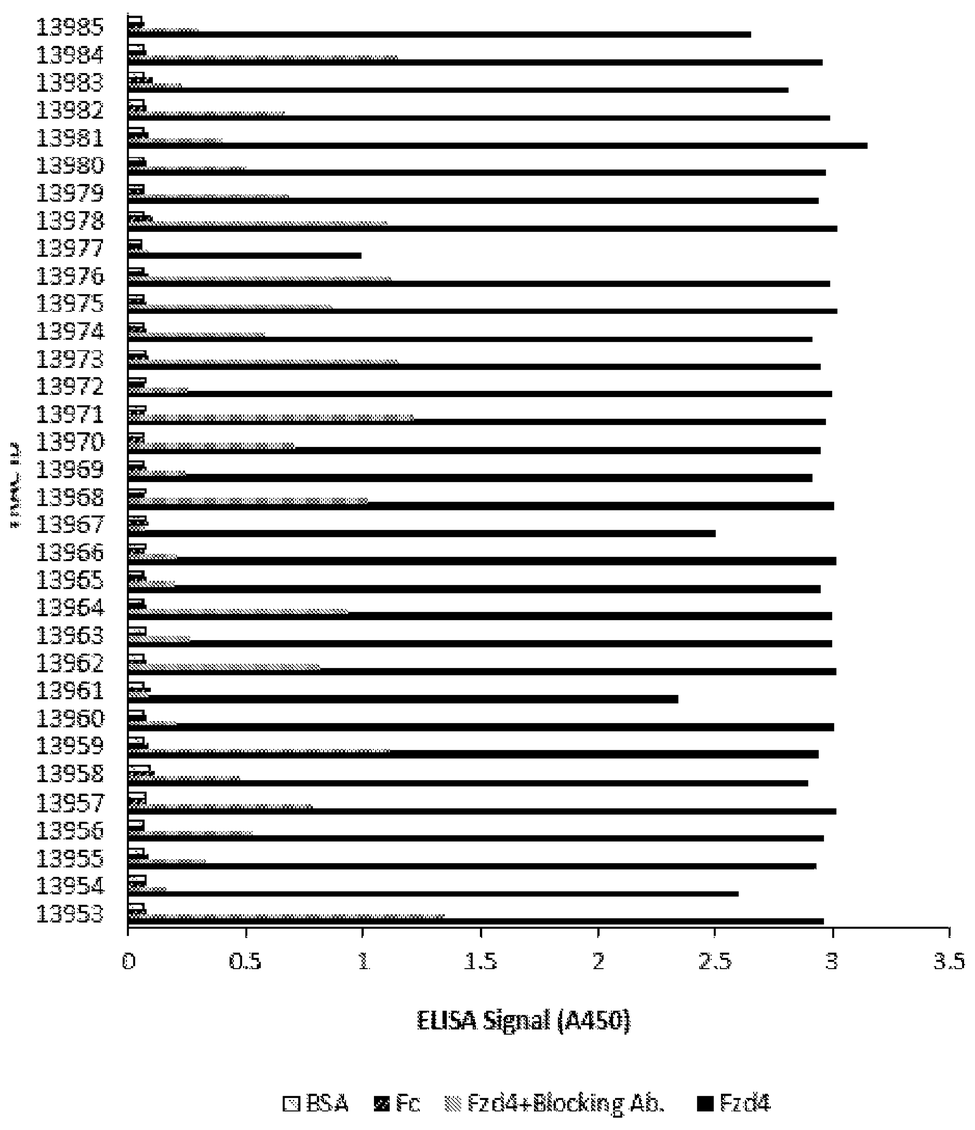

FIG 1A

[Continued on next page]

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TETRAVALENT FZD AND WNT CO-RECEPTOR BINDING ANTIBODY MOLECULES AND USES THEREOF

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on December 16, 2021, is named 117946_PD606WO_FINAL.txt and is 989,432 bytes in size.

BACKGROUND

Wnt signaling pathways are critical for embryonic development and tissue homeostasis in adults. Wnt signaling is initiated when a Frizzled (FZD) receptor on the cell surface membrane binds with a Wnt ligand. Wnt ligands are secreted growth factors that regulate various cellular processes such as proliferation, differentiation, survival and migration.

Nineteen Wnt ligands exist in humans that interact with a network of ten Frizzled cell surface receptors (FZD) and one of several co-receptors that guide the selective engagement of different intracellular signaling branches (Wodarz, A. and Nusse, R. Annu. Rev. Cell Dev. Biol. 14, 59–88 (1998); Angers, S and Moon, R.T., transduction. Nat. Rev. Mol. Cell Biol. 10, 468–477 (2009)). FZDs have conserved structural features including seven hydrophobic transmembrane domains and a cysteine-rich ligand-binding domain. FZDs are known to function in three distinct signaling pathways, known as the Wnt planar cell polarity (PCP) pathway, the canonical Wnt/β-catenin pathway, and the Wnt/calcium pathway. The presence of Wnt co-receptors is also required to direct the differential engagement of the intracellular signaling cascades listed above. For example, Wnt ligands bind to a Frizzled receptor and a member of the low-density lipoprotein receptor-related proteins 5 and 6 (LRP5/6) co-receptor family to activate the Wnt/ β-catenin pathway, or with a receptor tyrosine kinase-like orphan receptors 1 and 2 (ROR1/2), related to receptor tyrosine kinase (RYK) or protein tyrosine kinase 7 (PTK7) co-receptor to activate alternate β- catenin-independent signaling pathways.

Wnt ligands are universally important for the control of tissue stem cells self-renewal and regulation of many progenitor cell populations, but the hydrophobicity and sensitive tertiary structure of Wnt proteins makes their biochemical purification challenging and their use *in*

vitro and *in vivo* inefficient. Described herein are tetravalent binding antibody molecules that activate a Wnt signaling pathway and methods for their use.

SUMMARY OF THE INVENTION

Described herein are tetravalent binding antibody molecules that activate a Wnt signaling pathway and methods for their use. The tetravalent binding antibody molecules bind to both an FZD receptor, e.g., Frizzled Class Receptor 1 (FZD1), Frizzled Class Receptor 2(FZD2), Frizzled Class Receptor 3 (FZD3), Frizzled Class Receptor 4 (FZD4), Frizzled Class Receptor 5 (FZD5), Frizzled Class Receptor 6 (FZD6), Frizzled Class Receptor 7 (FZD7), Frizzled Class Receptor 8 (FZD8), Frizzled Class Receptor 9 (FZD9), or Frizzled Class Receptor 10 (FZD10) and a Wnt co-receptor, e.g., LRP5 or LRP6 (LRP5/6), thereby activating a Wnt signaling pathway. In an embodiment, the tetravalent binding antibody molecules bind to both a FZD4 receptor and LRP5 and/or LRP6 and activate the Wnt/β-catenin signaling pathway. The tetravalent binding antibody molecules of this invention are also referred herein as "FZD Agonists", Frizzled and LRP5/6 Agonist (FLAg), and in some embodiments as "ANTs".

The tetravalent binding antibody molecules include an Fc domain comprised of CH2 and CH3 domains or fragment thereof comprising the CH3 domain, and a first bivalent binding domain that interacts with one or more FZD receptor, e.g., one or more of FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, and FZD10, and a second bivalent binding domain that binds a WNT co-receptor, e.g., LRP5 or LRP6, wherein the FZD binding domain is linked to one terminus of the Fc domain and the co-receptor binding domain is linked to the other terminus of the Fc domain. Thus, the binding domain for the FZD receptor and the binding domain for the WNT co-receptor are not directly linked rather they are separated by the Fc domain, or fragment thereof comprising the CH3 domain.

The Fc domain of the FZD Agonists may be an Fc domain of an immunoglobulin with or without effector function. The immunoglobulin may be an IgG, e.g., an IgG_1. In an embodiment of this invention the tetravalent binding antibody molecule comprises two polypeptides containing an Fc region that dimerize via the intrinsic ability of the Fc region in each polypeptide to dimerize or via a knob-in-holes configuration within the Fc. Thus, the Fc dimer may be a heterodimer or a homodimer. Methods for dimerizing peptides via a knob-in-hole configuration are described in WO2018/026942, inventors Van Dyk et al., Carter P.

(2001) J. Immunol. Methods 248, 7–15; Ridgway et al. (1996) Protein Eng. 9, 617–621; Merchant, et al. (1998) Nat. Biotechnol. 16, 677–681, and; Atwell et al., (1997) J. Mol. Biol. 270, 26–35, all incorporated herein by reference.

In an embodiment, each of the binding domains of the FZD Agonists described herein are bivalent and each may be monospecific, having two binding sites for the same epitope of an FZD receptor, e.g., FZD4, or Wnt co-receptor, e.g. LRP5/6, or bispecific having two binding sites with each site binding a different epitope on an FZD or Wnt co-receptor, e.g., a Wnt1 binding (domain E1-E2 within the extracellular domain of LRP5/6) site and a Wnt3 binding site (domain E3-E4 within the extracellular domain of LRP5/6) within the LRP5/6 co-receptor. In an embodiment, the LRP5/6 binding domain binds to a Wnt3A site (domain E3-E4) on LRP5 and binds to a Wnt3A site (domain E3-E4) on LRP6.

In embodiments of this invention the FZD binding domain linked to the Fc domain of the FZD Agonist comprises one or more immunoglobulin heavy-chain variable domain (VH) fragments and/or one or more immunoglobulin light-chain variable domain (VL) fragments that bind the FZD, e.g., FZD4. In an embodiment of this invention the FZD binding domain may comprise Fabs, a diabody or single chain variable fragments (scFv) single-domain antibody fragments, e.g., V_HH, or combinations thereof that bind to the same or different epitopes on the FZD.

In an embodiment of this invention the VHs and/or VLs of the FZD binding domain binds FZD4 or FZD5 and comprise the light chain CDRs and the heavy chain CDRs of a FZD4 or FZD5 binding antibody of Table 1, Table 2, or Table 6, and/or comprise light chain CDRs and heavy chain CDRs that are 50%, 55%, 60%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to the CDRs of an FZD4 antibody of Table 1, Table 2 or Table 6, and still retain binding to the FZD4 or FZD5 receptor. For example, in an embodiment of the invention, the FZD binding domain may comprise a first heavy chain (CDR-H1), a second heavy chain (CDR-H2), and/or a third heavy chain (CDR-H3), wherein the VH that binds FZD may comprise CDR-H1 of SEQ ID NO: 24, SEQ ID NO: 365, or SEQ ID NO: 893, a CDR-H2 of SEQ ID NO: 51, SEQ ID NO: 61, SEQ ID NO: 462, or SEQ ID NO: 894 and/or CDR-H3 of SEQ ID NO: 79, SEQ ID NO: 90, SEQ ID NO: 484, or SEQ ID NO: 895 and a first light chain (CDR-L1), a second light chain (CDR-L2), and/or a third light chain (CDR-L3), wherein the VL that binds FZD may comprise CDR-L1 of SEQ ID NO: 1, SEQ ID NO:

3 or SEQ ID NO: 12, a CDR-L2 of SEQ ID NO: 2, SEQ ID NO: 3 or SEQ ID NO: 12 and/or a CDR-L3 of SEQ ID NO: 3, SEQ ID NO: 12, SEQ ID NO: 285, or SEQ ID NO: 896.

In an embodiment of this invention the co-receptor (LRP5/6) binding domain linked to the Fc domain of the FZD Agonist comprises one or more immunoglobulin heavy-chain variable domain (VH) fragments and/or one or more immunoglobulin light-chain variable domain (VL) fragments that bind to the Wnt co-receptor, e.g., LRP5 and/or LRP6. For example, in an embodiment of the invention, the LRP binding domain may comprise a first heavy chain (CDR-H1), a second heavy chain (CDR-H2), and/or a third heavy chain (CDR-H3), wherein the VH that binds LRP may comprise a CDR-H1 of SEQ ID NO: 527, SEQ ID NO: 528, SEQ ID NO: 536, SEQ ID NO: 716, or SEQ ID NO: 720, a CDR-H2 of SEQ ID NO: 552, SEQ ID NO: 553, or SEQ ID NO: 566, SEQ ID NO: 785, or SEQ ID NO: 791 and/or a CDR-H3 of SEQ ID NO: 584, SEQ ID NO: 585, SEQ ID NO: 586 or SEQ ID NO: 603, SEQ ID NO: 856 or SEQ ID NO: 862 CDR-H3 and and a first light chain (CDR-L1), a second light chain (CDR-L2), and/or a third light chain (CDR-L3), wherein the VL that binds LRP may comprise CDR-L1 of SEQ ID NO: 1, a CDR-L2 of SEQ ID NO: 2, or SEQ ID NO: 491 and/or a CDR-L3 of SEQ ID NO: 130, SEQ ID NO: 492, SEQ ID NO: 493, SEQ ID NO: 510, SEQ ID NO: 623 or SEQ ID NO: 665.

In an embodiment of this invention, the Wnt co-receptor binding domain is bivalent and may comprise a diabody, or may comprise a Fab, a single chain variable fragment (scFv) or a single domain antibody fragments (V_HH) or combinations thereof for binding to the same or different epitopes on the co-receptor. In embodiments of this invention the VHs and VLs of the Wnt coreceptor binding domain comprise the light chain CDRs and/or the heavy chain CDRs of a LRP5 and/or LRP6 binding antibody of Table 3, Table 4 or Table 6, or comprise light chain CDRs and/or heavy chain CDRs that are 50%, 55%, 60%, 75%. 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to the CDRs of an LRP5 and/or LRP6 antibody of Table 3, Table 4 or Table 6, and still retain binding to the LRP5 and/or LRP6 co-receptor.

In an embodiment of this invention the Wnt co-receptor binding domain linked to the Fc domain of the FZD Agonists described herein comprises a diabody, formed by two peptides each peptide comprising a heavy-chain variable domain (VH or VH domain) linked to a light-chain variable domain (VL or VL domain) wherein the VH and the VL from one peptide pair with the VL and VH of the other peptide forming the diabody. In this configuration, the binding domain has two binding sites that bind to the Wnt co-receptor, e.g., LRP5 or LRP6.

The diabody may be monospecific binding the same site on the co-receptor or may be bispecific (bs) binding two different sites on the co-receptor. By using a knobs-in-holes Fc configuration, the peptides comprising the VH and VL linked to Fc regions, can be non-identical but will still pair to form a bispecific binding domain capable of binding to two different sites on the Wnt co-receptor (e.g. LRP5 or LRP6).

The peptides forming the diabodies, the V_HH, the scFv, and the Fabs that form the binding domains may be derived from an antibody selected for its binding to a desired target, a "source antibody". For the FZD binding domain, the "FZD source antibody" may be an antibody that binds to one or more of the FZD receptor(s), e.g., one or more of FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, and FZD10, and antagonizes Wnt signaling or inhibits Wnt binding to the given FZD receptor(s). Alternatively, the FZD source antibody may be an antibody that binds to the FZD receptor(s) without antagonizing Wnt signaling or without inhibiting Wnt binding to the FZD receptor. Likewise, for the co-receptor binding domain, the "co-receptor source antibody" may be an antibody that binds to the Wnt co-receptor, e.g., LRP5/6, and antagonizes Wnt signaling or inhibits Wnt binding to the Wnt co-receptor. Alternatively, the co-receptor source antibody may be an antibody that binds to a co-receptor, e.g., LRP5/6, without antagonizing Wnt signaling or without inhibiting Wnt binding to the co-receptor.

In an embodiment of this invention the FZD binding domain of the FZD Agonist may bind specifically to a specific FZD, e.g., FZD4, with a higher affinity than to other FZDs, i.e., FZD1, FZD2, FZD3, FZD5, FZD6, FZD7, FZD8, FZD9, and FZD10, or may be pan-specific, binding to one or more other members of the FZD receptor family. In an embodiment the FZD binding domain binds specifically to one FZD with an affinity greater than 10-fold over the binding to any other Frizzled family member.

In an embodiment of this invention the FZD Agonist binds to FZD4, a "FZD4 Agonist". The FZD4 binding domain of the FZD4 Agonist may bind specifically to FZD4, binding with a higher affinity to FZD4 over other FZDs, or may be pan-specific, binding to FZD4 and one or more other members of the FZD receptor family, e.g., Frizzled Class Receptor 1 (FZD1), Frizzled Class Receptor 2(FZD2), Frizzled Class Receptor 3 (FZD3), Frizzled Class Receptor 5 (FZD5), Frizzled Class Receptor 6 (FZD6), Frizzled Class Receptor 7 (FZD7), Frizzled Class Receptor 8 (FZD8), Frizzled Class Receptor 9 (FZD9), or Frizzled Class Receptor 10

(FZD10). In an embodiment the FZD binding domain binds specifically to FZD4 with an affinity greater than 10-fold over any other Frizzled family member listed above.

In an embodiment of this invention the FZD Agonist binds to FZD5, a "FZD5 Agonist." The FZD5 binding domain of the FZD5 Agonist may bind specifically to FZD5, binding with a higher affinity to FZD5 over other FZDs, or may be panspecific, binding to FZD5 and one or more other members of the FZD receptor family, e.g., FZD1, FZD2, FZD3, FZD4, FZD6, FZD7, FZD8, FZD9, or FZD10. In an embodiment the FZD binding domain binds specifically to FZD5 with an affinity greater than 10-fold over any other Frizzled family member listed above.

In an embodiment of the FZD Agonists of this invention the Wnt co-receptor binding domain is a monospecific bivalent LRP5/6 co-receptor binding domain and binds to a single epitope on the LRP5 and/or LRP6 co-receptor, e.g., an epitope of the LRP5 and/or LRP6 coreceptor that binds to Wnt1(E1-E2 domain of LRP5 or LRP6) or binds Wnt3a (E3-E4 domain of LRP5 or LRP6). In an embodiment of this invention the co-receptor binding domain is a bispecific bivalent LRP5/6 binding domain that binds to two epitopes within the LRP5 and/or LRP6 co-receptor extracellular domain, e.g., the co-receptor binding domain interacts with the Wnt1 (E1-E2) and Wnt3 (E3-E4) epitopes of the LRP5 and/or LRP6 co-receptor. In an embodiment of this invention the co-receptor binding domain is a bispecific bivalent binding domain that binds to an extracellular domain of LRP5 and LPR6, e.g., the domain interacts with the Wnt1 (E1-E2) epitope of the LRP5 co-receptor and the Wnt1 (E1-E2) epitope of the LRP6 co-receptor LRP5, or the domain interacts with the Wnt3a (E3-E4) epitope of the LRP5 co-receptor and the Wnt3a (E3-E4) epitope of the LRP6 co-receptor or alternatively the domain interacts with a Wnt1 (E1-E2) epitope or LRP5 co-receptor and a Wnt3a (E3-E4) epitope of LPR6 co-receptor or vis versa.

Various formats of tetravalent binding antibody molecules described herein are depicted in Figure 6. In a particular format, Diabody-Fc-Fab, an LRP5/6 binding diabody is linked to the N-terminus of an Fc domain and two Fabs are linked to the C-terminus of the Fc domain wherein the Fab is linked to the CH3 of the Fc domain via the Fab heavy chain (VH) variable

domain. Alternatively, the Fab is linked to the CH3 of the Fc domain via the variable region (VL) of the light chain.

We previously reported multivalent binding molecules comprising an Fc domain, a FZD binding domain and a Wnt co-receptor (LRP5/6) binding domain on opposite termini of the Fc domain, e.g., a molecule having a FZD4 diabody linked one terminus of an Fc domain and a LRP5/6-binding diabody linked to the other terminus of the Fc domain, see PCT/IB2019/051174 inventors Angers et al. and PCT/IB2020/055463 inventors Angers et al., both incorporated in their entirety by reference.

It has been reported that Wnt-βcatenin signaling, specifically through activation of FZD4, is important for vasculature development and for adult vasculature homeostasis. More specifically, it is critical for barrier function at the blood-retina and blood-brain barriers (BRB and BBB). Defects in FZD4 signaling can lead to endothelial cell permeability defects and genetic mutations within this pathway are known to lead to vascular defects (e.g. Norrie disease, FEVR). At the blood-retina barrier, the extracellular ligand Norrin predominantly activates a FZD4-TSPAN12-LRP5 complex to regulate endothelial cell-cell interactions, barrier functions and permeability (Wang et al. (2012) Norrin/Frizzled4 signaling in retinal vascular development and blood brain barrier plasticity. Cell. 151:1332–1344). At the blood-brain barrier the secreted Wnt7a/b growth factor chiefly activates the FZD4-GPR124-LRP6 receptor complex (Chang et al., (2017). GPR124 is essential for blood-brain barrier integrity in central nervous system disease. (Nat. Med. 23: 450–460). The FZD4 Agonists described herein, e.g., the configurations having a diabody binding domain for a LRP5/6 and an FZD4 binding domain comprised of two Fab fragments that bind FZD4, wherein the binding domains are on opposite termini of an Fc domain, produce a particularly stable and homogenous molecule with an unexpectedly high level of Wnt-βcatenin signaling pathway activation in endothelial cells that translates into increased barrier function and decreased vascular permeability (Figure 11). In essence, the FZD4 Agonists described herein function as Norrin and Wnt7a/b mimetic molecules.

This invention also includes methods for using the FZD Agonists described herein. Described herein are methods to activate a Wnt signaling pathway, e.g., the Wnt/β-catenin signaling pathway, using the tetravalent binding antibody molecules of this invention, which are contemplated to promote the proximity of FZD receptors and Wnt co-receptors, e.g., one or more of FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, and FZD10

receptors and LRP5 and/or LRP6 co-receptors, on a cell wherein binding by the FZD Agonists to both FZD receptor(s) and the LRP5 and/or LPR6 co-receptor(s) activates the Wnt signaling pathway.

Blood-retina barrier (BRB) formation and retinal angiogenesis require βcatenin signaling induced by the ligand norrin (NDP [Norrie disease protein]), the receptor FZD4, co-receptor LRP5, and the TSPAN12 (tetraspanin 12). As such, an aspect of this invention is a method for promoting and/or maintaining retinal vasculature barrier function and angiogenesis by treating eye tissue, e.g., retinal tissue, with an effective amount of a tetravalent FZD4 Agonists of this invention.

Also, an aspect of this invention is a method for promoting, restoring and/or maintaining the BRB and BBB functions by treating the BRB or BBB vasculature with an effective amount of a tetravalent FZD4 Agonist described herein. A further aspect of this invention is a method for treating a subject having a disorder or condition characterized by defective retinal or brain angiogenesis characterized by reduced endothelial cell barrier function leading to vascular leakage by administering to such subject an effective amount of a FZD4 Agonists of this invention. A further aspect of this invention is a FZD4/LRP5 tetravalent binding antibody molecule or pharmaceutical composition for use in the treatment or prevention of a disorder or condition characterized by defective retinal or brain angiogenesis and/or characterized by reduced endothelial cell barrier function and/or vascular leakage. A further aspect of this invention is a method of treating or preventing a disorder or condition characterized by defective retinal or brain angiogenesis and/or reduced endothelial cell barrier function and/or vascular leakage comprising administering to a person in need thereof a therapeutically effective amount of a FZD4/LRP5 tetravalent binding antibody molecule described herein. A further aspect of the invention is the use of a FZD4/LRP5 tetravalent binding antibody molecule for the manufacture of a medicament for the treatment or prevention of a disorder or condition characterized by defective retinal or brain angiogenesis and/or reduced endothelial cell barrier function and/or vascular leakage. Such disorders or conditions include ocular disorders, including but are not limited to disorders of the retina or macula. Such disorders of the retina or macula include, but are not limited to diabetic retinopathy, retinipathy of prematurity, Coats' disease, FEVR, Norrie disease, macular degeneration, diabetic macular edema, and pediatric vitreoretinopathies. Additional disorders or conditions

included in embodiments of this invention include but are not limited to Alzheimer's disease, epilepsy, multiple sclerosis, ischemia, and stroke.

An embodiment of this invention includes methods for producing vascularized cerebral organoids by promoting the barrier function of the vasculature network throughout the organoids, and thereby mimicking blood-brain-barrier function using an effective amount of a tetravalent FZD4 Agonist described herein.

Also, an embodiment of this invention is a method of treating a subject suffering from a gastrointestinal disorder, including a subject having inflammation of all or part of the intestines, also known as inflammatory bowel disease, by administering to such subject an effective amount of a pharmaceutical composition of this invention, e.g., a composition comprising a FZD5 Agonist. Examples of inflammatory bowel disease include, but are not limited to, Crohn's disease, and ulcerative colitis.

Also, an embodiment of this invention are methods for directing differentiation of iPS or other pluripotent stem cells (PSCs) towards various lineages by culturing these cells in the presence of an effective amount of a tetravalent binding antibody molecule of this invention.

Also described herein are methods for making the tetravalent binding antibody molecules of this invention.

The modular aspects of this invention allow for mixing and matching binding domains derived from FZD-binding antibodies and LRP5/6-binding antibodies on opposite termini of the Fc domain to generate a tetravalent binding antibody molecule that can engage a FZD-LRP5/6 co-receptor complexes to selectively activate Wnt signaling. The modularity and effectiveness of the tetravalent binding antibody molecules for activating Wnt signaling pathways described herein contrasts with the Wnt surrogates described in the prior art that consists of monovalent FZD and Wnt co-receptor binding ligands, or FZD and Wnt co-receptor binding ligands wherein the binding ligands are not attached to opposite ends of an Fc domain.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1A and Figure 1B. Single point ELISAs. FZD4-binding antibodies isolated from affinity matured libraries of the known FZD4-binding antibodies 5044 (Figure 1A) and 5027 (Figure 1B) bind to FZD4 sites that compete with their parental antibody. The reaction was

stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader; white=BSA; black and white stripe=Fc; gray=FZD4 + blocking antibody; and black=FZD4.

Figure 2. Epitope mapping of FZD4 antibodies. FZD4 and 5027 and 5044 have overlapping epitopes. The pan-FZD binder 5016 is a positive control showing that the antigens are functional, with the exception of "FZD4_Swap10". Both FZD4-specific antibodies 5027 and 5044 are unable to bind to "FZD4 Swap 7" suggesting that these molecules bind to this region of the FZD ECD.

Figure 3A. Size-exclusion chromatography (SEC). Analysis of FZD4 antibodies as compared to Trastuzumab. Protein elution was monitored using absorbance at 280 nM.

Figure 3B. ELISA specificity. Measurements of the FZD4 antibodies determined against FZD4 and against FZD1 and FZD10, two members of the FZD family most-closely related to FZD4. The reaction was stopped by adding 1M H3PO4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader.

Figure 4. Phage clonal ELISA of synthetic antibodies targeting LRP5. The results demonstrate that the synthetic antibodies bound to LRP5. The absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader; gray=BSA; light gray=his-Fc; dark gray=LRP5

Figures 5A and 5B. Phage clonal ELISA of synthetic antibodies targeting LRP6. The results demonstrate the synthetic antibodies bound to LRP6. The absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader; black=BSA; gray=Fc; light gray=LRP6-Fc.

Figure 6. Modalities of tetravalent binding antibody molecules. Illustrated are: a diabody-Fc-diabody format having an FZD-binding monospecific diabody on the N-terminal of the Fc domain and a LPR5/6-binding bispecific diabody on the C-terminal of the Fc domain; a Diabody-Fc-scFv format having an N-terminal LPR5/6-binding bispecific diabody and two C-terminal FZD binding scFv; an IgG-diabody format having two FZD-binding Fabs forming an N-terminal binding domain and a bispecific LRP5/6 binding diabody forming the C-terminal binding domain; an IgG-scFv format having two FZD-binding Fabs forming an N-terminal binding domain and two LRP5/6 binding scFvs forming the C-terminal binding

domain, and; a diabody-Fc-Fab format having a bispecific LRP5/6 binding diabody forming the N-terminal binding domain and two FZD-binding Fabs forming the C-terminal binding domain, wherein the Fabs are linked to the CH3 of the Fc domain via the Fab variable heavy region. It is specifically contemplated that in an alternate diabody-Fc-Fab format the Fabs are linked to the CH3 of the Fc domain via the Fab variable light region. The various domains of the tetravalent molecules, VL, VH, CH1, CH2, CH3, CL1 and Fc, are joined via linkers, e.g., peptide linkers. The Fc domain, is formed by the dimerization of the CH2 and CH3 domains of the Hole construct Fc region and Knob construct Fc region. The various domains of the tetravalent molecules, VL, VH, CH1, CH2, CH3, CL1 and Fc, are joined via linkers, e.g., peptide linkers.

Figure 7. FZD4 Agonist having a Diabody-Fc-Fab format. The Diabody-Fc-Fab format having an LRP5-binding bispecific diabody forming a bivalent bispecific N-terminal LRP5-binding domain and two FZD4-binding Fabs forming a bivalent monospecific C-terminal FZD4-binding domain and an Fc region with attenuated effector functions due to amino acid mutations, e.g., N297G (NG) and D265A, (DANG) variants. The various domains of the tetravalent molecules, VL, VH, CH1, CH2, CH3, CL1 and Fc, are joined via linkers, e.g., peptide linkers.

Figure 8. FZD4 Agonists having a Diabody-Fc-Fab format (ANT) bind FZD4 with high selectivity. Figure 8A depicts the apparent selectivity of the FZD4 Agonists for the recombinant extracellular domain (ECD) of 9 of the 10 FZD as determined by biolayer interferometry (BLI). Figure 8B demonstrates FZD agonists do not recognize common non-specific antigens. The FZD Agonists were tested at 100 nM for binding to a panel of antigens as described in Mouquet et al. Polyreactivity increases the apparent affinity of anti-HIV antibodies by heteroligation. Nature. 2010 Sep;467(7315):591-595. DOI: 10.1038/nature09385, PMC3699875, and Jain T. et al. Biophysical properties of the clinical-stage antibody landscape. Proceedings of the National Academy of Sciences of the United States of America. 2017 Jan;114(5):944-949. DOI: 10.1073/pnas.1616408114, PMC5293111.

Figure 9. FZD4 Agonists (ANT) having a Diabody-Fc-Fab format (having a LRP-binding bispecific diabody and two FZD4-binding Fabs) are stable and monomeric in solution. Figure 9A presents the results of an analytical SEC analysis of FZD agonists as compared to trastuzumab IgG. Figure 9B presents the results of differential scanning fluorimetry demonstrating that the FZD4 Agonists in the Diabody-Fc-Fab format have thermal

denaturation profiles similar to that of trastuzumab, whereas a first generation diabody-Fc-diabody FZD4 modality (CM0199) is less optimal.

Figure 10. FZD4-LRP5 specific FZD4 Agonists having the Diabody-Fc-Fab format (ANT). FZD4-LRP5 specific FZD4 Agonists in this format stimulate FZD4 in mouse endothelial cell line (bEND3.1) and lead to an increase in Axin2 (beta catenin target gene) gene transcription in a concentration-dependent manner.

Figure 11A and Figure 11B depicts a FZD4-LRP5 specific agonist having the diabody-fc-diabody format promotes endothelial cell barrier functions in a mechanism opposing VEGF-induced permeability. Figure 11A depicts Immunofluoresence of ZO-1/CLDN3 and ZO-1/CLDN5 localization on bEnd.3 cell junctions. bEnd.3 cells were treated or not with 30nM of F4L5.13 (aka CM0199) and Norrin (NDP) in the presence or absence of VEGF (100ng/ml) for 1h. Starting from the top row and working downward: NT (non-treated) show no change in permeability; VEGF treatment of bEND3.1 cells leads to junction disassembly as seen by loss of plasma membrane staining of CLDN3, CLDN5 and ZO-1; Co-treatment of cells with VEGF and the FZD4 agonist CM0199 (F4L5.13) leads to a near-complete rescue of the effect of VEGF alone; the last row of Figure 11A shows co-treatment of cells with VEGF and NDP and similarly leads to a near-complete rescue of the effect of VEGF alone, suggesting that the FZD4 Agonists described herein function as Norrin and Wnt7a/b mimetic molecules. Figure 11B shows a transendothelial permeability assay quantifying the passage of FITC-dextran through a monolayer of bEnd.3 cells. Passage of FITC-dextran was measured after exposure of bEnd.3 cells to 100 ng/ml VEGF, 30 nM F4L5.13 or both or pretreated with VEGF for 1 h before treating with F4L5.13 for 1 h. Data are presented as mean ± SD, n = 5 independent experiments. Significance was calculated by one-way ANOVA with Bonferroni's multiple comparisons test (*$P < 0.05$ as compared to VEGF treatment).

Figure 12. Single point ELISA. FZD5 antibodies that bind the extracellular domain of FZD5 at a site overlapping with 2919 identified from affinity maturation libraries. New FZD5 antibodies bind FZD5 at a site overlapping with 2919 identified from affinity maturation libraries. Single point ELISAs were performed on 96-well Maxisorp plates coated with the ECDs of human FZD5 protein in the presence or absence of a saturating concentration of 2919 IgG. The absorbance was measured spectrophotometrically at 450 nm in a microtiter

plate reader; white with black stripes=BSA; black with white stripes=Fc; gray=FZD5 + blocking antibody; black=FZD5.

Figure 13. Single point ELISA. demonstrates new FZD5 antibodies from 2928 affinity maturation library selectively bind FZD5. New FZD5 antibodies from 2928 affinity maturation library selectively bind FZD5. Single point ELISAs were performed on 96-well Maxisorp plates coated with the ECDs of human FZD2, FZD5, or FZD8 protein. The absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader; black with white stripes=Fc; white with black stripes=FZD2; gray=FZD8; black=FZD5.

Figure 14. Luciferase assay. Pan-FZD/LRP6 ANT9 and FZD5-specific/LRP6 ANT59 activate Wnt signaling in cells. TOPFLASH cells were treated overnight with varying concentrations of FZD agonist or a non-targeting control molecule (CM0156) and TCF/LEF-driven luciferase expression was measured using a standard luciferase assay. Both molecules are able to activate FZD-mediated luciferase expression in a concentration-responsive manner. ANT9, which is able to bind to 7 of the 10 FZD receptor subtypes produces a higher maximal activation signal than the FZD5-specific ANT59.

Figure 15. Original format ANT39 and inverted format ANT39i. The FZD4 Agonist ANT39 having a Diabody-Fc-Fab format and FZD4 Agonist ANT39i having an IgG-Diabody format (having two FZD-binding Fabs forming an N-terminal binding domain and a bispecific LRP5/6 binding diabody forming the C-terminal binding domain) and an Fc domain. The FZD binding domain of ANT39i comprises two Fab fragments attached to the N- terminus of the Fc domain and each Fab binds an FZD. The LRP5/6 co-receptor binding domain is attached to the C- terminus of the Fc domain and is composed of a diabody that binds two different sites on the co-receptor, e.g., a Wnt1 site (E1-E2) and a Wnt3 site (E3-E4) on LRP5/6. The Fabs may be specific for a particular FZD, e.g. FZD4, or may be pan-specific, binding to more than one FZD, e.g., to FZD4 and one or more other FZD. The Fc region may have attenuated effector functions due to amino acid mutations, e.g., N297G (NG) and D265A, (DANG) variants. The various domains of the tetravalent molecules, VL, VH, CH1, CH2, CH3, CL1 and Fc, are joined via linkers, e.g., peptide linkers.

Figure 16A depicts FZD4 Agonist ANT39 having a Diabody-Fc-Fab format (having an LRP5-binding bispecific diabody forming a bivalent bispecific N-terminal LRP5-binding domain and two FZD4-binding Fabs forming a bivalent monospecific C-terminal FZD4-

binding domain) with the Fc region having attenuated effector functions due amino acid mutations to N297G and D265A (DANG) variants or L234A, L235A, P331S (LALAPS) variants, and with the Fc region further comprising knob-in-hole heterodimerization variants Merrimack, Merchant or Merchant S:S (Merrimack CH3 mutations as described in WO2018/026942A1, Merchant CH3 mutations as described in Merchant A.M. et al Nature Biothechnology 1998 vol 16 p677-681). Figure 16A discloses SEQ ID NOS 886, 892, 891, 886, 892, 891, 886, 892, and 891, respectively, in order of appearance. Figure 16B depicts FZD4 Agonist ANT39i having an IgG-Fc-Diabody format (having two Fab fragments attached to the N- terminus of the Fc domain, each Fab binding to an FZD, and a LRP5/6 co-receptor binding domain attached to the C- terminus of the Fc domain that is composed of a diabody that binds two different sites on the co-receptor) and an Fc region with attenuated effector functions due to DANG or LALAPS variants, and Merrimack, Merchant or Merchant S:S heterodimerization variants. Figure 16B discloses SEQ ID NOS 891, 886, 891, 886, 891, 886, 891, and 886, respectively, in order of appearance.

Figure 17. Thermostability of ANT39 variants. Figure 17 presents the results of differential scanning fluorimetry experiments demonstrating that the LALA variant of FZD4 agonist ANT39 (ANT39 LALA) has improved thermal stability relative to the parental ANT39 (containing DANG mutations in the Fc). Specifically, the LALA variant showed an improved thermal stability that is closer to the profile of a variant of Trastuzumab that contains the same Knob/Hole Fc mutations as the ANT.

Figure 18. FZD4 Agonist ANT42 having a Diabody-Fc-Fab format. FZD4 Agonist ANT42 having an LRP5-binding bispecific diabody forming a bivalent bispecific N-terminal LRP5-binding domain and two FZD4-binding Fabs forming a bivalent monospecific C-terminal FZD4-binding domain with the Fc region having attenuated effector functions due amino acid mutations to N297G and D265A (DANG) variants or L234A, L235A, P331S (LALAPS) variants, and with the Fc region further comprising knob-in-hole heterodimerization variants Merrimack, Merchant or Merchant S:S (Merrimack CH3 mutations as described in WO2018/026942A1, Merchant CH3 mutations as described in Merchant A.M. et al Nature Biothechnology 1998 vol 16 p677-681). And FZD4 Agonist ANT42i having an IgG-Fc-Diabody format (having two Fab fragments attached to the N- terminus of the Fc domain, each Fab binding to an FZD, and a LRP5/6 co-receptor binding domain attached to the C-terminus of the Fc domain that is composed of a diabody that binds two different sites on the

co-receptor) and an Fc region with attenuated effector functions due to DANG or LALAPS variants, and Merrimack, Merchant or Merchant S:S heterodimerization variants. Figure 18 discloses SEQ ID NOS 886, 892, 891, 891, 886, 886, 892, 891, 891, 886, 886, 892, 891, 891, 886, 886, 892, 891, 891, and 886, respectively, in order of appearance.

Figure 19. Antibody modalities tested for FZD agonism. A) Diabody-Fc-Diabody, VH and VL were tested both FZD or LRP binding variable domains; B) Diabody-Fc-scFv; C) scFv-Fc-Diabody; D) scFv-Fc-scFv; E) IgG-Diabody; F) IgG-scFv; G) Diabody-Fc-Fab; H) Diabody-CH3-Diabody; I) Fab-Diabody. In figure 19, molecules B-F, H-I, comprise N-terminal variable domains that bind LRP and the C-terminal variable domains bind FZD. In figure 19, molecule G comprises a variable domain at the N-terminal that binds FZD and a variable domain at the C-terminal that binds LRP. These antibody formats marked with an * were tested using a Knobs-in-Holes Fc.

Figure 20. Multiple antibody architectures are able to elicit potent FZD agonism. Paratopes targeting pan-FZD and LRP6 were configured in various arrangements as described in table 14. Canonical Wnt pathway stimulation by each antibody was determined on wild-type HEK cells expressing the TOPFLASH reporter in a blinded manner by two different scientists. Data are presented as mean ± SD and are representative of 4 different experiments.

Figure 21. Expression Titers of various FZD agonist modalities. Various FZD agonist modalities were expressed in HEK cells, purified via protein A chromatography, and expression titer was determined based on the absorbance at 280 nm. EC50 for FZD activation was determined on wild-type HEK cells expressing the TOPFLASH reporter in a blinded manner by two different scientists.

Figure 22. Organoid viability Assay. Mouse small intestine organoids were grown in the presence of 1 μM LGK-974 to block endogenous Wnt secretion and treated with PBS, Wnt3a conditioned media or FLAg molecules as indicated. Left, representative images from n=3 independent experiments. Right, quantification of organoid viability via CellTiter-Glo luminescence assay. Bars represent mean +/- standard error from 3 independent experiments.

Figure 23. Mouse colon histology. Histological appearance of the mouse colon following DSS treatment cycle (7 days 2% DSS, 3 days 0.5% DSS) with intraperitoneal injection of either control IgG or ANT59 (10 mg/kg) on days 4 and 7. (A) Images captured at 20X

magnification showing overall architecture. (B) Images captured at 100X showing rescue of mucosal integrity with ANT59 treatment.

Figure 24. (A) Body weight changes in mice throughout DSS treatment cycle (7 days 2% DSS, 3 days 0.5% DSS) with intraperitoneal injection of either control CM0156, PanFZD agonist or ANT59 (10 mg/kg) on days 4 and 7. (B) Left: Representative images of dissected colons from 6-8 mice per treatment group with centimeter scale for comparison. Right: colon length from each treatment group with bar representing mean colon length +/- S.D. and individual data points displayed. *** indicates $p < 0.0001$ in one-way ANOVA, H2O indicates normal water (no DSS).

Figure 25. Characterization of FZD5/LRP6 ANTs. ANTs were expressed in HEK cells, purified via protein A chromatography, and expression titer was determined based on the absorbance at 280 nm. Using biolayer interferometry, the apparent affinity (avidity) of each molecule for recombinant Fc-fused human FZD5 was determined and selectivity against other human FZDs was measured. Dose–response curves for the activation of a LEF/TCF reporter gene in FZD-knockout (1,2,4,5,7) HEK293 cells overexpressing FZD5. Cells were seeded in 96-well dishes for 24 hours, then treated as indicated for 17 hours. Reporter activation was assessed using the Dual-Luciferase Reporter Assay System (Promega). Data are presented as mean ± SD for technical duplicates and representative of n=3 independent experiments.

DETAILED DESCRIPTION OF THE INVENTION

Described herein are tetravalent binding antibody molecules comprising an Fc domain, with or without effector function, a bivalent FZD binding domain and a bivalent LRP-binding domain, wherein the binding domains are attached to opposite ends of the Fc domain. In an embodiment, the FZD binding domain is attached to the carboxy terminus of the Fc region and the LRP co-receptor binding domain is attached to the amino terminus of the Fc domain. Alternatively, the FZD binding domain is attached to the amino terminus of the Fc region and the co-receptor binding domain is attached to the carboxy terminus of the Fc domain. The binding domains may be attached directly to the Fc domain or attached to the Fc domain via a linker. The FZD binding domain may bind to one or to more than one FZD receptor, i.e., one or more of FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, and FZD10.

In an embodiment of the invention the FZD binding domain is bivalent and comprises a diabody or comprises a scfv, a V_HH fragment, or an Fab fragment or combinations thereof

that bind FZD, and the co-receptor binding domain is bivalent and comprises a diabody or a V_HH fragment, an Fab, or a scFv or combinations thereof that bind the LRP5/6 co-receptor. In an embodiment of the invention the FZD binding domain is attached to the carboxy-terminus of the Fc domain and comprises two scfv, two V_HH fragments, two Fab fragments or a diabody that bind FZD, and the co-receptor binding domain attached to the amino terminus of the Fc domain comprises a diabody, two V_HH fragments or two scFvs that binds to the LRP5/6 co-receptor. When attached to the carboxy terminus of the Fc domain the FZD-binding Fabs are linked to the CH3 of the Fc domain via the Fab variable heavy region or variable light region. In other embodiments the FZD binding domain is attached to the amino terminus of the Fc domain and is comprised of two Fabs and the LRP5/6 co-receptor binding domain is attached to the carboxy terminus of the Fc domain and is comprised of a diabody or two scFvs that bind the co-receptor.

Figure 6 illustrates a tetravalent binding antibody molecule of this invention in the Diabody-Fc-scFv format having a LRP5/6 co-receptor binding domain, an Fc domain, and a FZD binding domain. The Diabody-Fc-sFv comprises (i) an Fc domain, (ii) a bispecific diabody attached to the N-terminal of the Fc domain that binds two different sites on the co-receptor, e.g., a Wnt1 (E1-E2) site on LRP5/6, and a Wnt3 site (E3-E4) on LRP5/6, and (iii) a FZD binding domain comprising two FZD-binding scFv fragments attached to the carboxy terminus of the Fc domain. The scFv may be specific for a particular FZD, e.g. FZD4, or may be pan-specific, binding to more than one FZD, e.g. to FZD4 and one or more other FZD.

An embodiment of this invention is a tetravalent binding antibody molecule in a Diabody-Fc-scFv format having (i) an Fc domain, (ii) a LRP5/6 co-receptor binding domain that comprises a bispecific diabody that binds two different sites on the co-receptor, e.g., a Wnt1 (E1-E2) site on LRP5/6, and a Wnt3 site (E3-E4) on LRP5/6, wherein the diabody is attached to the amino terminus of the Fc domain and (iii) a FZD binding domain, attached to the carboxy terminus of the Fc domain comprising two scFv fragments each binding FZD. The scFv may be specific for the FZD, or may be pan-specific, binding to the FZD and one or more other FZD.

Figure 6 also illustrates a tetravalent binding antibody molecule of this invention in the IgG-diabody format having (i) an Fc domain, (ii) a FZD binding domain that comprises of two Fab fragments attached to the N- terminus of the Fc domain, each Fab binding to an FZD,

and (iii) a LRP5/6 co-receptor binding domain attached to the C- terminus of the Fc domain that is composed of a diabody that binds two different sites on the co-receptor, e.g., a Wnt1 site (E1-E2) and a Wnt3 site (E3-E4) on LRP5/6. The Fabs may be specific for a particular FZD, e.g. FZD4, or may be pan-specific, binding to more than one FZD, e.g., to FZD4 and one or more other FZD.

An embodiment of this invention is a tetravalent binding antibody molecule in an IgG-Diabody format comprising (i) an Fc domain, (ii) an N-terminal binding domain for a FZD, comprising two FZD-binding Fabs and (ii) a C-terminal binding domain for a LRP5 and/or LRP6 co-receptor, comprising a LRP5/6 coreceptor-binding diabody. This FZD Agonist in the IgG-Diabody format comprises,

(1) a first and second heavy chain monomer, wherein each heavy chain monomer comprises a single-chain polypeptide comprising from N-terminus to C-terminus:

(a) a heavy chain variable domain (VH) that binds a FZD, linked to

(b) a heavy chain constant region domain 1 (CH1 domain), linked to

(c) an Fc region (or fragment thereof comprising a constant heavy chain domain 3 (CH3 domain)), linked to

(d) a peptide comprising a VH that binds a LRP5/6 co-receptor, linked to a light chain variable domain (VL) that binds a LRP5/6 co-receptor, and

(2) a first and second light chain monomer, each light chain monomer comprising from N terminus to C terminus a VL that binds the FZD, linked to a constant light chain domain 1 (CL1 domain).

The first and second heavy chain monomers dimerize via their Fc regions, or fragments thereof. The linker between the VH and VL that bind the LRP5/6 is of a length that promotes the pairing of the VH and VL of the first heavy chain monomer with the VL and VH of the second heavy chain monomer thereby forming a LRP5/6 co-receptor binding diabody. The FZD-binding Fabs are formed by the pairing of each heavy chain monomer with a light chain monomer such that the VH that binds FZD4 and CH1 of each of the heavy chain monomer, pairs with the VL that binds FZD4 and CL1 of the light chain monomers. In this IgG-Diabody format, the Fabs

form the FZD4-binding domain on the N-terminus of the Fc domain and the diabody forms the co-receptor-binding domain on the C-terminus of the Fc domain. The Fabs may be specific for one FZD, e.g., FZD4 or FZD5, or may be pan-specific, binding to more than one FZD, e.g., to FZD4 and/or FZD5, and in some cases more FZD. The Fc regions may dimerize via a knob-in-hole configuration. Methods for dimerizing peptides via a knob-in-hole configuration are described in WO2018/026942, inventors Van Dyk et al., Carter P. (2001) J. Immunol. Methods 248, 7–15; Ridgway et al. (1996) Protein Eng. 9, 617–621; Merchant, et al. (1998) Nat. Biotechnol. 16, 677–681, and; Atwell et al., (1997) J. Mol. Biol. 270, 26–35. The Fc regions may be Merrimack (knob chain: Q347M, Y349F, T350D, T366W and L368M; hole chain: S354I, E357L, T366S, L368A and Y407V), Merchant (knob chain: T366W; hole chain: T336S, L368A and Y407V) or Merchant S:S (Merchant mutations with additional S354C variant in the knob chain and Y349C in the hole chain). The Fc regions may also contain mutations that alter their effector function, e.g., the Fc region may have attenuated effector functions due to amino acid mutations, e.g., DANG variants and LALAPS variants.

Although in Figure 6 the peptides forming the diabody in the IgG-Diabody format are linked to the C-terminal of the Fc domain via their VH domain in a VH-VL orientation (N terminal to C terminal), in some embodiments, the peptides forming the diabody are linked to the C-terminal of the Fc domain via their VL domains in a VL-VH orientation (N-terminal to C-terminal). And, although the heavy chains are depicted as comprising a VH domain and a CH1 domain linked to the N-terminal of the Fc domain and the light chains are depicted as comprising a VL domain and CL1 domain to form the Fabs, in some embodiments (Diabody-Fc-Fab in Fig.6 and Fig. 7A) the diabodies are fused to the N-terminus of the Fc and the Fabs are fused to the C-terminus of the Fc. In order to do this, the CH3 domain of the Fc is fused directly to the heavy chain of the Fab via its VH domain (VH-CH1) or directly to the light chain via its VL domain (VL-CL) and where the light and heavy chains still associate to form the Fabs.

Figure 6 illustrates a tetravalent binding antibody molecule in a Diabody-Fc-Fab configuration having an LRP5/6-binding bispecific bivalent diabody forming the N-terminal binding domain, and two FZD-binding Fabs forming the C-terminal binding domain. The Fabs may be specific for a particular FZD, e.g. FZD4, or may be pan-specific, binding to

more than one FZD, e.g. FZD4 and one or more other FZD. See also Figure 7A, which illustrates a tetravalent binding antibody molecule in the Diabody-Fc-Fab format having an Fc in a knob-in-hole (KiH) configuration and an LRP5-binding bispecific bivalent diabody forming the N-terminal binding domain, and two FZD4-binding Fabs forming the C-terminal binding domain. Although Figures 6 and 7A illustrates the Fabs linked to the CH3 of the Fc domain (at the C-terminus) via the Fab variable heavy domain (VH), it is specifically contemplated that in an alternate diabody-Fc-Fab format the Fabs are linked to the CH3 of the Fc domain via the Fab variable light domain (VL). The various domains of the tetravalent molecules, VL, VH, CH1, CH2, CH3, CL1 and Fc, are joined via linkers, e.g., peptide linkers.

Also an embodiment of this invention is a tetravalent binding antibody molecule in the Diabody-Fc-Fab format comprising (i) an Fc domain, (ii) an N-terminal binding domain comprising a diabody that binds to the co-receptor, e.g., LRP5 and/or LRP6 co-receptor and (ii) a C-terminal binding domain comprising two Fab that bind to one or more FZD, e.g., FZD4 or FZD5. This FZD Agonist in the Diabody-Fc-Fab format comprises,

(1) a first and second heavy chain monomer, wherein each heavy chain monomer comprises a single-chain polypeptide comprising, from N-terminus to C-terminus:

(a) a peptide comprising a heavy chain variable (VH) domain that binds a LRP5/6 co-receptor and a light chain variable (VL) domain that binds a LRP5/6 co-receptor, linked to

(b) an Fc region (or fragment thereof comprising a constant heavy chain domain 3 (CH3 domain)), linked to

(c) a VH domain that binds a FZD, linked to

(d) a CH1 domain, and

(2) a first and second light chain monomer each light chain monomer comprising from N-terminus to C-terminus a VL domain that binds FZD, and a constant light chain domain 1 (CL1).

The first and second heavy chain monomers dimerize via the Fc regions or fragments thereof and a bivalent LRP5/6-binding diabody is formed by the pairing of the VH domain and VL

domain that bind LRP5/6 of the first heavy chain monomer with the VL domain and VH domain that bind LRP5/6 of the second heavy chain monomer. The two FZD-binding Fabs are formed by the pairing of each heavy chain monomer with a light chain monomer such that the VL that binds the FZD and the CL1 of a light chain monomer pairs with the VH that binds the FZD and the CH1 of each of the heavy chain monomers. In this Diabody-Fc-Fab format, the diabody forms the LRP5/6 co-receptor binding domain on the amino terminus of the tetravalent molecule and the two Fabs form the FZD binding domain on the C-terminus of the tetravalent binding antibody molecule. The Fc regions may dimerize via a knob-in-hole configuration.

Methods for dimerizing peptides via a knob-in-hole configuration are described in WO2018/026942, inventors Van Dyk et al., Carter P. (2001) J. Immunol. Methods 248, 7–15; Ridgway et al. (1996) Protein Eng. 9, 617–621; Merchant, et al. (1998) Nat. Biotechnol. 16, 677–681, and; Atwell et al., (1997) J. Mol. Biol. 270, 26–35. The Fc regions may be Merrimack (knob chain: Q347M, Y349F, T350D, T366W and L368M; hole chain: S354I, E357L, T366S, L368A and Y407V), Merchant (knob chain: T366W; hole chain: T336S, L368A and Y407V) or Merchant S:S (Merchant mutations with additional S354C variant in the knob chain and Y349C in the hole chain). The Fc regions may also contain mutations that alter their effector function, e.g., the Fc region may have attenuated effector functions due to amino acid mutations, e.g., DANG variants and LALAPS variants.

Although in Figures 6 and 7A the peptides forming the diabody in the Diabody-Fc-Fab format are linked to the Fc domain via their VL domains, thus in a VH -VL orientation (from N-terminal to C-terminal), in some embodiments the orientation can be switched such that the peptides forming the diabody are linked to the N-terminal of the Fc domain via their VH domains, thus in a VL-VH orientation (from N-terminal to C-terminal). Also, although the heavy chains in the Diabody-Fc-Fab format are depicted as comprising a VH domain and a CH1 domain, which pair with the light chain comprising a VL and CL1 domain to form the Fabs, it is also contemplated that in some embodiments the variable and constant domains are switched such that the heavy chains comprise a VL domain and a CL1 domain and the light chains comprises the VH domain and CH1 domain and the heavy and light chains still pair to form the Fabs.

In an embodiment of this invention the binding moiety of the FZD binding domain is derived from an antibody, or an antibody fragment, that binds specifically to one FZD, e.g. FZD4 or

FZD5, or is pan-specific interacting with a specific FZD, e.g. FZD4 or FZD5, and one or more additional FZD receptors (an FZD source antibody), and the co-receptor binding domain comprises a binding moiety that is derived from an antibody or antibody fragment that binds to a LPR5 and/or LRP6 (a LRP5/6 coreceptor source antibody). In an embodiment of the invention the FZD-binding antibodies bind to an extracellular cysteine rich domain (CRD) of the FZD receptor. The antibody that binds FZD may be an antibody that binds the FZD receptor and antagonizes Wnt signaling or inhibits binding of a Wnt ligand to the FZD receptor. The antibody that binds FZD may be an antibody that binds the FZD receptor without antagonizing or inhibiting binding of a Wnt ligand to the FZD receptor. The antibody that binds FZD may be an antibody that binds FZD and enhances Wnt signaling. The antibody that binds the LRP5/6 co-receptor may be an antibody that binds the LRP5/6 co-receptor and antagonizes Wnt signaling or inhibits binding of a Wnt ligand to the co-receptor, or the antibody that binds the LRP5/6 co-receptor may be an antibody that binds the co-receptor without antagonizing Wnt or Norrin signaling or inhibiting binding of a Wnt or Norrin ligand to the co-receptor.

In an embodiment of this invention the LRP5/6 co-receptor binding domain binds to a single epitope on a co-receptor, e.g., an epitope that binds to the Wnt1 (E1-E2) or Wnt3 (E3-E4) interacting domain of LRP5/6. In an embodiment of this invention the LRP5/6 co-receptor binding domain binds to two epitopes within the co-receptor, e.g., a paratope that binds to the Wnt1 (E1-E2) interacting epitope and a paratope that binds to Wnt3 (E3-E4) epitope of LRP5/6. In an embodiment of this invention the multivalent binding molecule comprises a Fc domain, wherein the Fc domain is the Fc domain of an immunoglobulin or a fragment thereof comprising the CH3 domain. In an embodiment of the invention the immunoglobulin is an IgG. In an embodiment of this invention the IgG is an IgG_1.

In an embodiment of this invention the LRP5/6 binding domain comprises a diabody comprising two peptides each comprising a heavy chain variable domain (VH) that binds to LRP5/6 linked to a light-chain variable domain (VL) that binds LRP5/6 wherein the binding domain is formed by pairing of the VH and the VL from one peptide to the VL and VH of the other peptide thereby forming the LRP5/6 binding domain.

In the tetravalent binding antibody molecules of this invention both of the binding domains are bivalent and one or both of the bivalent binding domains may be bispecific for the respective FZD receptor, e.g., FZD4 or FZD5, or LRP5/6 co-receptor. For example, the

binding molecule may comprise an FZD binding domain that is bivalent and monospecific (each binding site binding to the same epitope) and the LRP 5/6 binding domain is bivalent and bispecific, binding to two different epitopes (the Wnt1 (E1-E2) and Wnt3 (E3-E4) sites on the LRP5/6 ectodomain). In an embodiment of this invention both binding domains are bivalent and bispecific, each binding domain binding to two different epitopes on their respective target FZD receptor or LRP 5/6 co-receptor.

The VH and VL domains of the FZD binding domain of the tetravalent molecules of this invention may comprise the three light chain CDRs and three heavy chain CDRs of a FZD source antibody, e.g. the FZD4 or FZD5, binding antibodies of Table 1, Table 2 or Table 6, or three light chain CDRs and three heavy chain CDRs that are at least 50%, at least 55%, at least 60%, at least 75, at least. 80%, at least 85%, at least 90%, at least at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the CDRs of the FZD source antibody, e.g., the FZD4 antibodies of Table 1, Table 2 or Table 6, and still retain binding to the FZD or FZD5 receptor bound by the source antibody.

The VH and VL domains of the LRP5/6 co-receptor binding domain of the tetravalent molecules of this invention may comprise the three light chain CDRs and three heavy chain CDRs of an LRP5/6 co-receptor source antibody, e.g., the LRP5/6 binding antibodies of Table 3, Table 4 or Table 6, or three light chain CDRs and three heavy chain CDRs that are at least 50%, at least 55%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the VH and VL of the Wnt co-receptor source antibody, e.g., the LRP5/6 binding antibodies of Table 3, Table 4 or Table 6, and still bind to the LRP5/6 co-receptor.

In an embodiment of this invention the FZD binding domain of the tetravalent binding molecule of this invention binds FZD4 (an FZD4 Agonist) or FZD5 (FZD5 Agonist) or FZD4 and/or FZD5 and one or more other FZDs (a pan-FZD Agonist) and comprises the CDR-H1, CDR-H2 and CDR-H3 and the CDR-L1, CDR-L2 and CDR-L3 of the antibodies of Table 1, Table 2 or Table 6, or CDRs that are at least 50%, at least 55%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the CDR-H1, CDR-H2 and CDR-H3 and CDR-L1, CDR-L2 and CDR-L3 of the antibodies of Table 1, Table 2 or Table 6, and still bind to FZD4 or FZD5,

and the LRP5/6 binding domain of the FZD4 Agonist or FZD5 Agonist or pan-FZD Agonist comprises

the CDR-H1, CDR-H2 and CDR-H3 and CDR-L1, CDR-L2 and CDR-L3 of the antibodies of Table 3, Table 4 or Table 6 or the CDRs are at least 50%, at least 55%, at least 60%, at least 75%. at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the CDR-H1, CDR-H2 and CDR-H3 and CDR-L1, CDR-L2 and CDR-L3 of the antibodies in Table 3, Table 4 or Table 6, and still bind to LRP5 or LRP6.

In an embodiment, the tetravalent binding antibody molecule's FZD binding domain does not comprise a diabody, scFv, or Fab comprising the three heavy chain CDRs or three light chain CDRs of the FZD4-binding antibody 5044 in combination with a Wnt co-receptor binding domain comprising a diabody, scFv, or Fab comprising the three heavy chain CDRs and three light chain CDRs of LRP6-binding antibody 2542 and/or antibody 2539. In an embodiment, the tetravalent binding molecule does not comprise a diabody, scFv, or Fab, comprising the three heavy chain CDRs and three light chain CDRs of the FZD4-binding antibody 5027 in combination with a Wnt co-receptor binding domain comprising a diabody, scFv, or Fab comprising the three heavy chain CDRs and three light chain CDRs of LRP6-binding antibody 2542 and/or antibody 2539.

Also, an embodiment of this invention are the nucleic acid molecules encoding the tetravalent binding molecules described herein. An embodiment of this invention are the nucleic acid molecules encoding the polypeptides of the tetravalent binding molecules described herein comprising the heavy chain and light chain CDRs set forth in Tables 1, 2, 3, 4, 6. Also an embodiment of this invention are the nucleic acid molecules that encode the polypeptides of the tetravalent binding molecules, e.g., FZD5 Agonists or FZD4 Agonists, of Figure 7A and 7B that comprise the CDRs of Table 6. Also, an embodiment of this invention are the nucleic acid molecules that encode VH and VL domains comprising respectively the heavy chain and light chain CDRs set forth in Tables 1, 2, 3, 4, and 6. The nucleic acid molecules can be inserted into a vector and expressed in an appropriate host cell and then the tetravalent binding antibody molecules may be isolated from the cells using methods well known in the art. As such, also an aspect of this invention are expression cassettes and vectors comprising the nucleic acid molecules that encode the polypeptides of the tetravalent binding molecules, e.g., FZD4 or FZD5 Agonists, described herein, the VL and VH domains, the Fabs and the

diabodies comprising the CDRs of set forth in Tables 1, 2, 3, 4, and 6, and the Fc domains described herein. An aspect of this invention are the host cells expressing these expression cassettes and vectors.

As used in this invention, the term "vector" refers to a nucleic acid delivery vehicle or plasmid that can be engineered to contain a nucleic acid molecule, e.g., a nucleic acid sequence encoding the tetravalent binding antibody molecules described herein. The vector that can express protein when inserted with a polynucleotide is called an expression vector. Vectors can be inserted into the host cell by transformation, transduction, or transfection, so that the carried genetic substances can be expressed in the host cell. Vectors are well known to the technical personnel in the field, including but not limited to: plasmid; phagemid; cosmid; artificial chromosome such as yeast artificial chromosome (YAC), bacterial artificial chromosome (BAC), or P1 derived artificial chromosome (PAC); phage such as λphage or M13 phage and animal viruses etc. Animal viruses may include but not limited to, reverse transcriptase virus (including lentivirus), adenovirus, adeno-associated virus, herpes virus (e. g. herpes simplex virus), chicken pox virus, baculovirus, papilloma virus, and papova virus (such as SV40). A vector can contain multiple components that control expression of the tetravalent binding antibody molecules described herein, including but not limited to, promoters, e.g., viral or eukaryotic promoters, e.g., a CMV promoter, signal peptides, e.g., TRYP2 signal peptide, transcription initiation factor, enhancer, selection element, and reporter gene. In addition, the vector may also contain replication initiation site(s).

As used in this invention, the term "host cell" refers to cells that can import expression cassettes and vectors, including but not limited to, prokaryotic cells such as Escherichia coli and Bacillus subtilis, fungal cells such as yeast and Aspergillus, insect cells such as S2 drosophila cells and Sf9, or animal cells, including human cells, e.g., fibroblast cells, CHO cells, COS cells, NSO cells, HeLa cells, BHK cells, or HEK293 cells.

An embodiment of this invention is a pharmaceutical composition comprising a FZD Agonist or a nucleic acid molecule, expression cassette and vector encoding a FZD Agonist described herein and a pharmaceutically acceptable carrier, diluent or excipient. The pharmaceutical composition may further comprise an additional agent, e.g., a second therapeutic antibody e.g. an anti-VEGF antibody (aflibercept, ranibizumab and bevacizumab), a growth factor, e.g., VEGF, or an agent that activates a Wnt pathway, e.g., the small molecule CHIR99021, a Norrin or R-Spondin, or a nucleic acid molecule, expression cassettes and vectors that encode

the agent. The pharmaceutical composition may consist of or consist essentially of a FZD Agonist, or a nucleic acid molecule, an expression cassette or vector encoding an FZD Agonist described herein, and a pharmaceutically acceptable diluent, carrier or excipient. Suitable carriers, diluents and excipients, and their formulations are described in Remington: The Science and Practice of Pharmacy (19th ed.) ed. A. R. Gennaro, Mack Publishing Company, Easton, Pa. 1995. Typically, an appropriate amount of a pharmaceutically-acceptable salt is used in the formulation to render the formulation isotonic. Examples of the pharmaceutically-acceptable carrier include, but are not limited to, saline, Ringer's solution and dextrose solution. The pH of the solution may be e.g., from about 5 to about 8, from about 5 to 7.5 or from about 6 to 7. Further carriers include sustained release preparations such as semipermeable matrices of solid hydrophobic polymers containing the agonist, which matrices are in the form of shaped articles, e.g., films, liposomes or microparticles. It will be apparent to those persons skilled in the art that certain carriers may be more preferable depending upon, for instance, the route of administration and concentration of the FZD Agonists being administered.

This invention also includes methods for using the FZD Agonists, described herein. An embodiment of this invention is a method for activating a Wnt signaling pathway in a cell, comprising contacting a cell having an FZD receptor and a LRP5/6 co-receptor, with a tetravalent binding antibody molecule of this invention that binds the FZD, e.g., FZD4, and the LRP5/6 in an amount effective to activate Wnt signaling. It has been reported that the Norrin-FZD4 pathway plays a role in retinal angiogenesis (see Wang et al. Cell. 2012;151(6):1332–1344.; Braunger BM, Tamm ER. Adv Exp Med Biol. 2012; 723:679–683; Ohlmann A, Tamm ER. Prog Retin Eye Res. 2012;31(3):243–257 and; Ye et al. Trends Mol Med. 2010;16(9):417–425). Signaling through Norrin-FZD4 pathway is necessary for development and maintenance of retinal vasculature. Mutations affecting genes of this pathway may result in several vitreoretinopathies, such as Norrie Disease, Familial Exudative Vitreoretinopathy (FEVR), and Pseudoglioma and Osteoporosis Syndrome. Additionally, Retinopathy of Prematurity (ROP) has been associated with mutations in this Norrin-FZD4 pathway, and Wnt-pathway mutations have been reported in Coats Disease and Persistent Fetal Vasculature (PFV). FZD4 signaling activated by Norrin and/or WNT7A/B pathway is also associated with CNS blood brain barrier development and homeostasis. Genetic ablation of the Norrin, *FZD4*, *LRP5*, *LRP6* and the co-receptor Tetraspanin-12 (Tspan-12) result in defective angiogenesis and barrier disruption in the retinal and/or cerebellar vessels (Cho et

al. (2017) Neuron 95, 1056-1073; Zhou et al., (2014) J Clin Invest 124:3825–3846). Thus, a functional Wnt signaling system plays a key fundamental role in the development of a sufficient vascular and neural network in the eye and retina to support vision and in the CNS to support BBB development and homeostasis.

An aspect of this invention is a method for promoting and/or maintaining retinal vasculature by treating eye tissue, e.g., retinal tissue, with an effective amount of a pharmaceutical compositions comprising the tetravalent antibody molecules of this invention, e.g., tetravalent antibody molecules that binds FZD4 and LRP5/6, a FZD4 Agonists, having the structures illustrated in Figure 6 through local or systemic administration. Also, an aspect of this invention is a method for promoting and/or maintaining BBB vasculature by treating a subject in need thereof with an effective amount of a pharmaceutical compositions of this invention, e.g., a composition comprising a FZD4 Agonists having the structures depicted in Figure 6. The BBB is initiated during development and its integrity remains vital for homeostasis and neural protection throughout life. A subject in need thereof includes a subject having a neurological condition associated with BBB dysfunction, e.g., neurodegenerative diseases such as Alzheimer's disease, as well epilepsy, multiple sclerosis, and stroke.

A further aspect of this invention is a method for treating a subject having a disorder characterized by vascular leakage, particularly retinal vascular leakage, and/or endothelial cell leakage, and disorders characterized by reduced retinal or brain endothelial cell barrier functions or a compromised BBB or BRB, e.g., diabetic retinopathy, retinipathy of prematurity, Coat's disease, FEVR, Norrie disease, macular degeneration, diabetic macular edema, and pediatric vitreoretinopathies, by administering to such subject an effective amount of a pharmaceutical compositions of this invention, e.g., a composition comprising a FZD4 Agonist having the structures depicted in Figure 6. An effective amount of such composition is an amount sufficient, e.g., to increase or restore endothelial cell barrier functions and thereby reducing vascular leakage in such subject. The subject may be a fetus. The FZD4 Agonists of this invention particularly the FZD4 Agonist in the diabody-Fc-Fab format comprising two Fab fragments forming the FZD4 binding domain on the carboxy terminal of the Fc receptor and a binding domain for LRP5 and/or LRP6 composed of a diabody on the amino terminal of the Fc domain, e.g., as illustrated in Figure 6, activates FZD4 and β-catenin signaling in endothelial cells, promotes barrier functions and thereby

reduces endothelial cell permeability and significantly enhance angiogenesis. In particular, treatment of endothelial cells, in vivo, ex vivo or in vitro, with these FZD4 Agonists, preferably those with the diabody-Fc-Fab format, enhance the development and maintenance of retinal vasculature and/or the BRB and the BBB far more effectively than other molecules that do not have this structure.

A further aspect of the invention is a method for treating a subject having inflammation of all or part of the intestines, also known as inflammatory bowel disease, by administering to such subject an effective amount of a pharmaceutical composition of this invention, e.g., a composition comprising a FZD5 Agonist. Examples of inflammatory bowel disease include, but are not limited to, Crohn's disease, and ulcerative colitis. An effective amount of such composition is an amount sufficient to reduce, ameliorate, eliminate, or treat the inflammation. A subject in need thereof includes a subject having inflammation of the mucosal of the gastrointestinal tract. The methods disclosed herein may be practiced to reduce inflammation (e.g., inflammation associated with IBD or in a tissue affected by IBD, such as gastrointenstinal tract tissue, e.g., small intestine, large intestine, or colon), activate WNT signaling, or reduce any of the histological symptoms of IBD (e.g., those disclosed herein).

The FZD Agonists of the present invention may be administered systemically or locally, e.g., by injection (e.g. subcutaneous, intravenous, intraperitoneal, intrathecal, intraocular, intravitreal, etc.), implantation, topically, or orally. Depending on the route of administration, the FZD Agonists may be coated in a material to protect the agonists from conditions that may inactivate the agonists. The tetravalent binding antibody molecules described herein may be dissolved or suspended in a pharmaceutically acceptable, preferably aqueous carrier. In addition, the composition comprising the FZD Agonists can contain excipients, such as buffers, binding agents, blasting agents, diluents, flavors, lubricants, etc. An extensive listing of excipients that can be used in such a composition, can be, for example, taken from A. Kibbe, Handbook of Pharmaceutical Excipients (Kibbe, 2000). The tetravalent binding antibody molecules can also be administered together with immune stimulating substances, such as cytokines.

An embodiment of this invention includes a method for deriving cerebral organoids with a vascular network exhibiting barrier functions by using the tetravalent antibody molecules described herein. The tetravalent binding antibody molecules described herein that activate

FZD4 signaling are envisioned to promote barrier function within endothelial cells cultured with cerebral organoids and thereby promoting angiogenesis.

An embodiment of this invention includes a method for directed differentiation of multipotent or pluripotent stem cells (PSC) or induced pluripotent stem (iPS) cells comprising culturing the cells under conditions suitable for directed differentiation wherein said culturing conditions further comprise an effective amount of a tetravalent binding antibody molecule described herein. Studies in mouse and human PSCs have identified specific approaches to the addition of growth factors, including Wnt, which can induce PSC differentiation into different lineages. Methods for directed differentiation of PSCs comprising the activation of Wnt signaling are known in the art see e.g. Lam et al. (2014) Semin Nephol 34(4); 445-461; Yucer et al. (September 6, 2017) Scientific Reports 7, Article number 10741. It is contemplated that the FZD Agonists, e.g. FZD4 Agonists, described herein can be used in an amount sufficient to effect activation of Wnt signaling pathways to direct differentiation of the PSCs to certain mesodermal lineages such as cardiomyocytes (cite Yoon et al. FZD4 Marks Lateral Plate Mesoderm and Signals with NORRIN to Increase Cardiomyocyte Induction from Pluripotent Stem Cell-Derived Cardiac Progenitors. Stem Cell Reports. 2018 Jan;10(1):87-100. DOI: 10.1016/j.stemcr.2017.11.008.PMID: 29249665).

An embodiment of this invention is a method for enhancing tissue regeneration in a subject in need thereof by activating Wnt signaling in such subject by administering to the subject in need thereof an effective amount of a FZD Agonists described herein.

An embodiment of this invention includes a method for promoting endothelial cell barrier functions in eye tissue, e.g., retinal tissue, in a subject in need thereof, by administering an effective amount of a tetravalent binding molecule of this invention that binds FZD4 and LPR5/6, an FZD4 Agonist. In a particular embodiment the FZD4 Agonist of this invention that binds to FZD4 and a binding domain that binds to LRP5 or/and LRP6 has a diabody-Fc-Fab structure depicted in Figure 6 and 7. In an embodiment of this invention the FZD4 Agonists for enhancing retinal angiogenesis comprise the light chain CDRs, i.e., CDR-L1, CDR-L2, and CDR-L3 and heavy chain CDRs, i.e., CDR-H1, CDR-H2 and CDR-H3 of the

FZD4-binding antibodies set forth in Tables 1, 2, and 6 and the LRP5/6-binding antibodies set forth in Tables 3, 4, and 6.

A subject as used herein may be any animal (e.g., a mammal), including, but not limited to, humans, non-human primates, horses, cows, dogs, cats, rodents, and the like. The subject may be a fetus. Typically, the subject is human.

Effective dosages and schedules for administering the FZD Agonists and nucleic acids that encode them described herein may be determined empirically, and making such determinations is within the skill in the art. Those skilled in the art will understand that the dosage of such FZD Agonists that must be administered will vary depending on, for example, the subject who will receive the antibody, the route of administration, the particular type of FZD Agonists used and other drugs being administered. Guidance in selecting appropriate doses for FZD Agonists is found in the literature on therapeutic uses of antibodies, e.g., Handbook of Monoclonal Antibodies, Ferrone, eds., Noges Publications, Park Ridge, N.J., (1985) ch. 22 and pp. 303-357; Smith, Antibodies in Human Diagnosis and Therapy, Haber, eds., Raven Press, New York (1977) pp. 365-389. The dosage ranges for the administration of the compositions are those large enough to produce the desired effect, e.g., promote endothelial cell barrier functions, vascular homeostasis, or enhance Wnt signaling. The dosage should not be so large as to cause adverse side effects, such as unwanted cross-reactions, anaphylactic reactions, and the like. Generally, the dosage will vary with the age, condition, gender and the extent of the disease or disorder, in the patient and can be determined by one of skill in the art. The dosage can be adjusted by the individual physician in the event of any contraindications. Dosage can vary, and can be administered in one or more dose administrations daily, for one or several days. While individual needs vary, determination of optimal ranges of effective amounts of the vector is within the skill of the art.

Also, an aspect of this invention is a method for making the tetravalent binding antibody molecules described herein. The amino acid sequences of FZD receptors, e.g. FZD4, and the Wnt co-receptors LRP5/6, and nucleotide sequences encoding FZD receptors and the Wnt co-receptors LRP5/6, as well as antibodies and libraries of antibodies that bind FZD, e.g., FZD4, or the Wnt co-receptors LRP5/6, are readily available or can be generated using methods well known in the art (see e.g., U.S. publication no. 2015/0232554, inventors Gurney et al. and US publication no. 2016/0194394, inventors Sidhu et al. and US 20190040144, inventors Pan et

al.; U.S. publication no. 2017/0166636, inventors Wu et al.; U.S. publication no. 2016/0208018, inventors Chen et al.; U.S. publication no. 2016/0053022, inventors Macheda et al.; U.S. publication no. 2015/031293, inventors Damelin et al.). And a variety of methods are known in the art for generating and screening such phage display libraries for antibodies, and antibody fragments, scFv, Fab, VL, and VH possessing the desired binding characteristics. Such methods are reviewed, e.g., in Hoogenboom et al. in Methods in Molecular Biology 178:1-37 (O'Brien et al., ed., Human Press, Totowa, N.J., 2001) and further described, e.g., in the McCafferty et al., Nature 348:552-554; Clackson et al., Nature 352: 624-628 (1991); Marks et al., J. Mol. Biol. 222: 581-597 (1992); Marks and Bradbury, in Methods in Molecular Biology 248:161-175 (Lo, ed., Human Press, Totowa, N.J., 2003); Sidhu et al., J. Mol. Biol. 338(2): 299-310 (2004); Lee et al., J. Mol. Biol. 340(5): 1073-1093 (2004); Fellouse, Proc. Natl. Acad. Sci. USA 101(34): 12467-12472 (2004); and Lee et al., J. Immunol. Methods 284(1-2): 119-132(2004), all incorporated herein by reference. In certain phage display methods, repertoires of VH and VL genes are separately cloned by polymerase chain reaction (PCR) and recombined randomly in phage libraries, which can then be screened for antigen-binding phage as described in Winter et al., Ann. Rev. Immunol., 12: 433-455 (1994). Phage typically display antibody fragments, either as single-chain Fv (scFv) fragments or as Fab fragments. Libraries from immunized sources provide high-affinity antibodies to the immunogen without the requirement of constructing hybridomas. Alternatively, the naive repertoire can be cloned (e.g., from human) to provide a single source of antibodies to a wide range of non-self and also self antigens without any immunization as described by Griffiths et al., EMBO J, 12: 725-734 (1993). Finally, naive libraries can also be made synthetically by cloning unrearranged V-gene segments from stem cells, and using PCR primers containing random sequence to encode the highly variable CDR3 regions and to accomplish rearrangement in vitro, as described by Hoogenboom and Winter, J. Mol. Biol., 227: 381-388 (1992). Patent publications describing human antibody phage libraries include, for example: U.S. Pat. No. 5,750,373, and US Patent Publication Nos. 2005/0079574, 2005/0119455, 2005/0266000, 2007/0117126, 2007/0160598, 2007/0237764, 2007/0292936, and 2009/0002360, all incorporated herein by reference. Antibodies or antibody fragments

isolated from human antibody libraries are considered human antibodies or human antibody fragments herein.

In an embodiment of this invention a tetravalent binding antibody molecule in a diabody-Fc-scFv format comprising a LRP5/6 coreceptor binding domain comprising LRP5/6 -binding diabody and an FZD-binding domain comprising two FZD-binding scFvs is generated by,

(a) selecting an Fc domain having a C-terminus and an N-terminus

(b) identifying an antibody that binds to an FZD receptor (the "FZD source antibody"), and

(c) identifying an antibody that binds LRP 5/6 co-receptor ("coreceptor source antibody" or "LRP 5/6 source antibody"),

(d) generating a nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide monomer comprising

(i) a peptide comprising a VL domain linked to a VH domain, the domains comprising the heavy chain and/or light chain CDRs of the antibody of step b that bind the FZD receptor, or comprising heavy chain and/or light chain CDRs derived from the antibody of step b that still bind the FZD, linked to

(ii) an Fc domain of step a, linked to

(iii) a peptide comprising VL domain linked to a VH domain comprising the light chain and/or heavy chain CDRs of the antibody of step c, or comprising CDRs derived from the antibody of step c and that still bind LRP 5/6 co-receptor,

(e) expressing the nucleic acid molecule of step d to produce the polypeptide monomer and then dimerizing the polypeptide,

wherein the VH and VL that bind the FZD of each monomer form a scFv that binds FZD, and the VH and VL domains that bind the LRP 5/6 coreceptor of one monomer bind the VL and VH that binds the Wnt coreceptor of another monomer forming a LRP5/6 co-receptor-binding diabody, and

wherein the polypeptide monomer dimerizes via the Fc regions to form a tetravalent binding antibody molecule comprising an Fc domain, a FZD-binding domain comprised of two FZD-binding scFvs, and a LRP5/6 coreceptor binding domain comprised of the diabody,

wherein the FZD binding domain and the LRP5/6 co-receptor binding domain are on opposite termini of Fc domain. It is contemplated that the peptides comprising the VL and VH domains that bind the FZD or the LRP may be linked to either the N or C terminus of the Fc domain via the VL domain or the VH domain provided the FZD binding domain and LRP binding domain are on opposite termini of the Fc domain. The FZD may be one or more of FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, and FZD10.

In an embodiment of this invention, the tetravalent binding antibody molecule has two FZD-binding Fabs, e.g., FZD4-binding Fabs, linked to one terminus of the Fc domain and two LRP5/6-binding scFvs or a LRP5/6-binding diabody linked to the other terminus of the Fc domain and is generated by,

(a) identifying the light chain complementary determining regions (CDR-L1, CDR-L2, and CDR-L3) and/or heavy chains complementary determining regions (CDR-H1, CDR-H2, and CDR-H3) of an antibody that binds to the FZD, e.g., FZD4 or FZD5, (the "FZD source antibody") and

(b) identifying the CDR-L1, CDR-L2, and CDR-L3 and/or the CDR-H1, CDR-H2, and CDR-H3 of one or more antibodies that binds to LRP5 or LRP6, (the "LRP5/6 source antibody"),

(c) generating a nucleic acid molecule encoding a "heavy chain" polypeptide comprising

(i) a peptide comprising an immunoglobulin constant heavy chain region 1 (CH1 domain) linked to a VH domain comprising the CDR-H1, H2 and H3 of the antibody of step a), or a CDR-H1, CDR-H2 and CDR-H3 derived from the antibody of step a) that still binds the FZD4, linked to

(ii) an Fc region, linked to

(iii) a peptide comprising a VL domain comprising the CDR-L1, CDR-L2 and CDR-L3 of an antibody of step b) linked to a VH domain comprising

the CDR-H1, CDR-H2 and CDR-H3 of an antibody of step b), or CDR-H1, CDR-H2 and CDR-H3 derived from the antibody of step b) that binds to LRP5 or LRP6,

(d) generating a nucleic acid molecule comprising a nucleic acid sequence that encodes a "light chain" polypeptide comprising an immunoglobulin constant light region 1 (CL1) linked to a VL domain wherein the VL domain comprises the FZD light chain CDR-L1, CDR-L2 and CDR-L3 of the antibody in step a),

(e) expressing the nucleic acid molecules of (c) and (d) to produce the heavy chain polypeptide and the light chain polypeptide,

wherein two heavy chain polypeptides dimerize via their Fc regions and the VH that binds the FZD and CH1 domains of the heavy chain polypeptide pair with the VL that binds the FZD and CL1 domains of the light chain polypeptide forming two FZD Fabs and

wherein the VH and VL that binds LRP5/6 in each heavy chain polypeptide pair to form an scFv that binds LRP5/6, or the VH and VL that bind LRP5/6 of one heavy chain polypeptide in the dimer pair with the VL and VH that bind the LRP5/6 of the other heavy chain polypeptide in the dimer to form a diabody, thereby forming the tetravalent binding antibody molecule comprising an Fc domain, two FZD Fabs linked to either the N or C terminus of the Fc domain and two LRP5/6-binding scFvs or a LRP5/6-binding diabody linked to the other terminus of the Fc domain.

The FZD source antibody may be an antibody that binds specifically to one FZD, e.g., FZD4, or is a pan-specific antibody binding FZD, e.g., FZD4 or FZD5, and one or more other FZD receptors and antagonizes Wnt signaling or inhibits Wnt binding to the receptor. Alternatively, the FZD source antibody may be an antibody that binds specifically to one FZD, e.g., FZD4 or FZD5, or is a pan-specific antibody binding one FZD, e.g., FZD4 or FZD5, and one or more other FZD receptors without antagonizing Wnt signaling or inhibiting Wnt binding to the receptor. The LRP source antibody may be an antibody that binds specifically to LRP5/6, or is panspecific binding to LRP5/6 and to one or more of the Wnt co-receptors, and antagonizes Wnt signaling or inhibits Wnt binding to the co-receptor. Alternatively, the LRP5/6 source antibody may be an antibody that binds to the LRP 5/6 co-

receptor, or is panspecific binding to LRP5/6 and to one or more of the Wnt co-receptors, without antagonizing Wnt signaling or inhibiting Wnt binding to the LRP5/6 co-receptor.

The FZD source antibody may be an antibody fragment that binds the FZD receptor, e.g., an Fab, a VL or VH. The light chain and heavy chain CDRs, the VH and/or VL in the FZD binding domain of the FZD Agonists may be identical to the CDRs, the VH and/or VL of the FZD source antibody or may be at least 50%, at least 55%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the CDRs, VH or VL of the source antibody and still retain binding to the FZD receptor. The CDRs, the VH and/or VL in the FZD binding domain of the FZD Agonists may be identical to the CDRs, the VH and/or VL of a FZD4-binding or FZD5-binding antibody of Table 1, Table 2 or Table 6, or may be at least 50%, at least 55%, at least 60%, 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the CDRs, VH or VL of a FZD4-binding or FZD5-binding antibody of Table 1 or Table 2 or Table 6 and still retain binding to the FZD receptor.

Likewise, the Wnt co-receptor source antibody may be an antibody fragment, e.g. an Fab, a VL or a VH, that binds the LRP co-receptor, e.g., LRP5/6. The light chain CDRs and heavy chain CDRs, the VH and/or VL in the Wnt co-receptor binding domain of the FZD4 Agonists may be identical to the CDRs, the VH and/or VL of the Wnt co-receptor source antibody or may be at least at least 50%, at least 55%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the CDRs, VHs or VLs of the source antibody and still retain binding to the LRP co-receptor. The light chain CDRs and heavy chain CDRs, the VH and/or VL in the LRP5/6 binding domain of the FZD Agonists may be identical to the light chain CDRs and heavy chain CDRs, the VH and/or VL of a LRP-binding antibody of Table 3, Table 4 or Table 6 or may be at least at least 50%, at least 55%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to the light chain CDRs and heavy chain CDRs, VH or VL of a LRP-binding antibody of Table 3, Table 4 or Table 6 and still retain binding to the LRP co- receptor.

In an embodiment of this invention, two polypeptides of the tetravalent binding antibody molecule dimerize via knob-in-hole configuration of their Fc sequences. The tetravalent binding antibody molecules of this invention may be generated by dimerizing two

polypeptides in a "knob-in-hole" configuration. The knob-in-hole configuration increases the modularity of this invention by facilitating the association of peptides that comprise binding moieties that bind different epitopes on a FZD receptor or LRP5/6 co-receptor or to epitopes on different members of the FZD receptor or co-receptor family, see e.g., Figure 6. Methods for engineering Fc molecules via the knobs into holes design are well known in the art, see e.g., WO2018/026942, inventors Van Dyk et al., Carter P. (2001) J. Immunol. Methods 248, 7–15; Ridgway et al. (1996) Protein Eng. 9, 617–621; Merchant, et al. (1998) Nat. Biotechnol. 16, 677–681, and; Atwell et al., (1997) J. Mol. Biol. 270, 26–35.

Without wishing to be bound by theory, it is contemplated that the tetravalent binding antibody molecules of this invention facilitate the interaction of a FZD receptor and an LRP5/6 co-receptor on a cell by promoting their proximity and stabilizing conformations of the receptor proteins that are favorable for activating Wnt signaling pathways. Another embodiment of this invention is a method for facilitating the interaction of a FZD receptor and an LRP5/6 co-receptor on a cell thereby activating a Wnt signaling pathway in the cell comprising, a) selecting an Fc domain, or fragment thereof comprising a CH3 domain, having a C-terminus and an N-terminus b) linking a first bivalent binding domain, which binds the FZD receptor, on one terminus of the Fc domain and linking a second bivalent binding domain, which binds to the Wnt co-receptor, on the other terminus of the Fc domain thereby forming a tetravalent binding antibody molecule; c) contacting said tetravalent binding antibody molecule with the cell expressing said FZD receptor and Wnt co-receptor under conditions wherein the FZD receptor and co-receptor both bind to the tetravalent binding antibody molecule thereby activating the Wnt signaling pathway. The Wnt co-receptor binding domain and FZD binding domain are bivalent and each comprise a VL and/or a VH, or V_HH domain and one or both of the binding domains may be monospecific. In an embodiment of the invention one or both the Wnt co-receptor binding domain and FZD binding domain are bispecific. In an embodiment of the invention the Wnt co-receptor binding domain is bivalent and bispecific. The FZD binding domain may comprise a scFV that binds FZD, a V_HH that binds FZD, or an Fab that binds FZD, or combinations thereof, or a diabody that binds FZD. The Wnt co-receptor binding domain may comprise a scFV that binds the LRP5/6 co-receptor, a V_HH that binds LRP5/6, an Fab that binds the LRP5/6 co-receptor, or combinations thereof, or a diabody that binds the LRP5/6 co-receptor. In an embodiment of the invention the FZD binding domain comprises two FZD-binding Fabs and

the Wnt co-receptor binding domain comprises a bispecific bivalent diabody that binds LRP5/6 on two different epitopes.

The tetravalent binding antibody molecules of this invention initiate the Wnt signaling pathway(s) that are stimulated by the FZD-co-receptor complexes, e.g., the β-catenin pathway stimulated by FZD-LRP5/6 complexes. Wnt ligands function by promoting the clustering of FZD receptors with co- receptors. Without wishing to be bound by theory, it is contemplated that the FZD Agonists described herein bind both the FZD receptor and its LRP5/6 co-receptor thereby forming a complex that mimics the binding of a Wnt molecule to the FZD receptor and LRP 5/6 co-receptor(s), which in turn activates Wnt signaling pathways, the Wnt β-catenin pathway.

An embodiment of this invention is a method for activating a Wnt signaling pathway comprising contacting a cell expressing a FZD receptor and its LRP5/6 co-receptor with an effective amount of the FZD Agonists of this invention comprising a FZD binding domain and a LRP5/6 co-receptor binding domain.

The FZD Agonists of this invention may be made recombinantly, e.g., by Gibson assembly (see Gibson et al. (2009) Nature Methods 6 (5): 343–345 and Gibson DG. (2011) Methods in Enzymology 498: 349–361), or the molecules may be made synthetically e.g., using commercial synthetic apparatuses, for example, automated synthesizers by Applied Biosystems, Inc., Beckman, etc. By using synthesizers, naturally occurring amino acids may be substituted with unnatural amino acids. The particular sequence and the manner of preparation will be determined by convenience, economics, purity required, and the like. If desired, various groups may be introduced into the peptide during synthesis or during expression, which allow for linking to other molecules or to a surface.

The binding domains of the FZD Agonists may be linked to the Fc domain via a linker. In some embodiments, adjacent VH and VL domains may be attached to each other via a peptide linker. In some embodiements adjacent constant domains and variable domains are attached via a peptide linker. The linker may be, e.g. a polypeptide linker, or a non-peptidic linker. In some embodiments the constant domains and variable domains of the FZD Agonists are attached to the Fc domain via a peptide linker. Suitable linkers are well known in the art, e.g., an XTEN linker (see WO2013120683, inventors Schellenberger et al.) In some embodiments, the peptide linker comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13,

14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or at least 100 amino acids. In some embodiments, the peptide linker is between 1 to 100, 5 to 75, 1 to 50, 5 to 50, 1 to 30, 1 to 25, 5 to 25, 5 to 20, 5 to 15, 5 to 10, 1-10 or 1-5 amino acids in length. The modular aspects of this invention allow for mixing and matching of binding domains derived from antibodies that bind to FZD receptor or antibodies that bind LRP5/6 co-receptor on the opposite termini of the Fc domain to generate a tetravalent binding antibody molecule that can engage FZD receptor – LRP5/6 co-receptor complexes to activate Wnt signaling.

The Fc domain of the FZD Agonists, with or without the linker, is of a length and flexibility that allows for the tetravalent binding antibody molecule of this invention to bind both the FZD receptor and its LRP5/6 co-receptor thereby stabilizing receptor conformations that are compatible with activation of downstream Wnt signaling pathways. In an embodiment of this invention the Fc domain, or fragment thereof comprising the CH3 domain, with or without the linker is greater than 100 amino acids spanning up to 300Å, greater than 125 amino acids spanning up to 375Å, greater than 150 amino acids spanning up to 450Å, greater than 175 amino acids spanning up to 525Å, or greater than 300 amino acids spanning up to 900Å. Preferably the Fc domain is about 200 amino acids to about 300 amino acids in length.

As used herein and in the appended claims, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a cell" includes a plurality of such cells and reference to "the peptide" includes reference to one or more peptides and equivalents thereof, e.g. polypeptides, known to those skilled in the art, and so forth.

An "affinity matured" antibody or “maturation of an antibody” refers to an antibody with one or more alterations in one or more hypervariable regions (HVRs), compared to a parent or source antibody which does not possess such alterations, such alterations resulting in an improvement in the affinity of the antibody for antigen or to other desired properties of the molecule.

By "comprising" it is meant that the recited elements are required in the composition/method/kit, but other elements may be included to form the

composition/method/kit etc. within the scope of the claim. For example, a composition comprising tetravalent binding antibody molecules is a composition that may comprise other elements in addition to the tetravalent binding antibody molecules, e.g. functional moieties such as polypeptides, small molecules, or nucleic acids bound, e.g. covalently bound, to the tetravalent binding antibody molecules; agents that promote the stability of the tetravalent binding antibody molecule composition, agents that promote the solubility of the tetravalent binding antibody molecule composition, adjuvants, etc. as will be readily understood in the art, with the exception of elements that are encompassed by any negative provisos.

By "consisting essentially of", it is meant a limitation of the scope of composition or method described to the specified materials or steps that do not materially affect the basic and novel characteristic(s) of the subject invention. For example, a tetravalent binding antibody molecule "consisting essentially of" a disclosed sequence has the amino acid sequence of the disclosed sequence plus or minus about 5 amino acid residues at the boundaries of the sequence based upon the sequence from which it was derived, e.g. about 5 residues, 4 residues, 3 residues, 2 residues or about 1 residue less than the recited bounding amino acid residue, or about 1 residue, 2 residues, 3 residues, 4 residues, or 5 residues more than the recited bounding amino acid residue.

By "consisting of", it is meant the exclusion from the composition, method, or kit of any element, step, or ingredient not specified in the claim. For example, a tetravalent binding antibody molecule "consisting of" a disclosed sequence consists only of the disclosed amino acid sequence.

Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limits of that range is also specifically disclosed. Each smaller range between any stated value or intervening value in a stated range and any other stated or intervening value in that stated range is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included or excluded in the range, and each range where either, neither or both limits are included in the smaller ranges is also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the

stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

The basic antibody structural unit is known to comprise a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector functions, e.g., binding Fc receptors and activation of antibody-dependent cellular cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC). Methods for dimerizing peptides via a knob-in-hole configuration are described in WO2018/026942, inventors Van Dyk et al., Carter P. (2001) J. Immunol. Methods 248, 7–15; Ridgway et al. (1996) Protein Eng. 9, 617–621; Merchant, et al. (1998) Nat. Biotechnol. 16, 677–681, and; Atwell et al., (1997) J. Mol. Biol. 270, 26–35. The Fc regions may be Merrimack (knob chain: Q347M, Y349F, T350D, T366W and L368M; hole chain: S354I, E357L, T366S, L368A and Y407V), Merchant (knob chain: T366W; hole chain: T336S, L368A and Y407V) or Merchant S:S (Merchant mutations with additional S354C variant in the knob chain and Y349C in the hole chain). The Fc regions may also contain mutations that alter their effector function, e.g., the Fc region may have attenuated effector functions due to amino acid mutations, e.g., DANG variants and LALAPS variants. Methods are well known in the art for mitigating antibody effector function, including for example amino acid substitutions in the Fc regions, e.g., the N297G and D265A, N297G (DANG) variants, L234A, L235A, P331S (LALAPS), LALAPS Merchant, LALAPS Merchant S-S (Merchant A.M. et al Nature Biothechnol 1998 vol 16 p677-681) variants, or L234A, L235A, P329G (LALA-PG) substitutions, see e.g., Lo et al. “Effector Attenuating Substitutions that Maintain Antibody Stability and Reduce Toxicity in Mice. The Journal of Biological Chemistry Vol. 292, No. 9, pp. 3900 –3908, March 3, 2017, incorporated herein by reference. In general, antibody molecules obtained from humans relate to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG_1, IgG_2, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain.

Three highly divergent stretches within each of the heavy chain variable domain, VH or VH domain, and light chain variable domain, VL or VL domain, referred to as complementarity

determining regions (CDRs), are interposed between more conserved flanking stretches known as "framework regions", or "FRs". Thus, the term "FR" refers to amino acid sequences which are naturally found between, and adjacent to, CDRs in immunoglobulins. A VH domain typically has four FRs, referred to herein as VH framework region 1 (FR1), VH framework region 2 (FR2), VH framework region 3 (FR3), and VH framework region 4 (FR4). Similarly, a VL domain typically has four FRs, referred to herein as VL framework region 1 (FR1), VL framework region 2 (FR2), VL framework region 3 (FR3), and VL framework region 4 (FR4). In an antibody molecule, the three CDRs of a VL domain (CDR-L1, CDR-L2 and CDR-L3) and the three CDRs of a VH domain (CDR-H1, CDR-H2 and CDR-H3) are disposed relative to each other in three-dimensional space to form an antigen-binding site within the antibody variable region. The surface of the antigen-binding site is complementary to a three-dimensional surface of a bound antigen. The amino acid sequences of VL and VH domains may be numbered, and CDRs and FRs therein identified/defined, according to the Kabat numbering system (Kabat et al., 1991, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md.) or the INTERNATIONAL IMMUNOGENETICS INFORMATION SYSTEM (IMGT numbering system; Lefranc et al., 2003, Development and Comparative Immunology 27:55-77), both incorporated herein by reference. One of ordinary skill in the art would possess the knowledge for numbering amino acid residues of a VL domain and of a VH domain, and identifying CDRs and FRs therein, according to a routinely employed numbering system such as the IMGT numbering system, the Kabat numbering system, and the like.

The term “antibody” as referred to herein includes whole antibodies and any antigen binding fragment (i.e., “antigen-binding portion”) or single chain thereof. A “whole antibody” or full-length refers to a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, or an antigen binding portion thereof. Each heavy chain is comprised of a heavy chain variable region or domain (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region or domain (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL or CL1. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions

(FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (Clq) of the classical complement system.

The term "antigen-binding portion" or "antigen-binding fragment" of an antibody (or simply "antibody portion" or "antibody fragment"), as used herein, refers to one or more fragments, portions or domains of an antibody that retain the ability to specifically bind to an antigen. It has been shown that fragments of a full-length antibody can perform the antigen-binding function of an antibody. Examples of binding fragments encompassed within the term "antigen-binding portion" of an antibody include (i) an Fab fragment, a monovalent fragment consisting of the VL, VH, CL1 and CH1 domains; (ii) an $F(ab')_2$ fragment, a bivalent fragment comprising two F(ab)' fragments linked by a disulfide bridge at the hinge region; (iii) an Fd fragment consisting of the VH and CH1 domains; (iv) an Fv fragment consisting of the VL and VH domains of a single arm of an antibody; (v) a dAb fragment (Ward et al. (1989) Nature 241:544-546), which consists of a VH domain; and (vi) an isolated complementary determining region (CDR). Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single contiguous chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Bird et al. (1988) Science 242:423-426; and Huston et al. (1988) Proc. Natl. Acad. Sci. USA 85:5879-5883). Such single chain antibodies are also intended to be encompassed within the term "antigen-binding portion" of an antibody. Other forms of single chain antibodies, such as diabodies, are also encompassed (see e.g., Holliger et al. (1993) PNAS. USA 90:6444-6448).

“Diabodies,” or sometimes referred to herein as “Dia,” as used herein are dimeric antibody fragments. In each polypeptide of the diabody, a heavy-chain variable domain (VH) is linked to a light-chain variable domain (VL) but unlike single-chain Fv fragments, the linker between the VL and VH is too short for intramolecular pairing and as such each antigen-binding site is formed by pairing of the VH and VL of one polypeptide with the VH and VL of the other polypeptide. Diabodies thus have two antigen-binding sites, and can be

monospecific or bispecific. (see, e.g., Holliger, P., et al. (1993) Proc. Natl. Acad. Sci. USA 90:6444-6448; Poljak, R. J., et al. (1994) Structure 2:1121-1123; Kontermann and Dubel eds., Antibody Engineering (2001) Springer-Verlag. New York. 790 pp. (ISBN 3-540-41354-5) incorporated herein by reference.

As used herein an "effective amount" of an agent, e.g., the tetravalent binding antibody molecules or a pharmaceutical composition comprising the molecules, refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired result. In some embodiments, a therapeutically effective amount is one that reduces the incidence and/or severity of, stabilizes one or more characteristics of, and/or delays onset of, one or more symptoms of the disease, disorder, and/or condition. In some embodiments, the amount of a FZD Agonists administered to the subject is in the range of about 0.001mg/kg to 10mg/kg, 0.5 mg/kg to about 10 mg/kg, or about 0.5 mg/kg to about 1mg/kg of the subject's body weight. For example, in some embodiments the FZD4 Agonist may be applied to the eye in an amount of, e.g., about 0.02 -1.5 mg, about 0.05-1.0mg, or about 0.1-0.5 mg per eye.

As used herein, the term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or fragment thereof, or a T-cell receptor. The term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or T-cell receptor. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three-dimensional structural characteristics, as well as specific charge characteristics. An antibody is said to specifically bind an antigen when the dissociation constant is $\leq 10\mu M$; e.g., ≤ 100 nM, preferably ≤ 10 nM and more preferably ≤ 1 nM.

The constant region of immunoglobulin molecules is also called the fragment crystallizable region, the “Fc region” or “Fc domain.” The Fc domain is composed of two identical protein fragments, derived from the second and third constant domains of the antibody's two heavy chains and the Fc domains of IgGs bear a highly conserved N-glycosylation site. Glycosylation of the Fc fragment is essential for Fc receptor-mediated activity. In an embodiment of the invention the Fc domain of the tetravalent binding antibody molecule is engineered such that it does not target the cell that binds the tetravalent binding antibody molecule for ADCC or CDC-dependent death. In an embodiment of the invention the Fc

domain of the tetravalent binding antibody molecule is a peptide dimer in a knob-in-hole configuration. The peptide dimer may be a heterodimer.

The terms "individual," "subject," "host," and "patient," are used interchangeably herein and refer to any mammalian subject for whom diagnosis, treatment, or therapy is desired, particularly humans.

"LRP", "LRP proteins" and "LRP receptors" is used herein to refer to members of the low density lipoprotein receptor-related protein family. These receptors are single-pass transmembrane proteins that bind and internalize ligands in the process of receptor-mediated endocytosis. LRP proteins LRP5 (e.g., LRP5: NP_002326.2) and LRP6 (e.g., LRP6: NP_002327.2) are included in a Wnt receptor complex required for activation on the Wnt-ßcatenin signaling pathway. See also, for human/mouse LRP5 and LRP6: https :// www.uniprot. org/uniprot/O75197, https :// www.uniprot. org/uniprot/Q91VN0, https :// www.uniprot. org/uniprot/O75581, https :// www.uniprot .org/uniprot/O88572.

The term "polypeptide fragment" as used herein refers to a polypeptide that has an amino terminal and/or carboxy-terminal deletion, but where the remaining amino acid sequence is identical to the corresponding positions in the naturally-occurring sequence deduced, for example, from a full-length cDNA sequence.

As used herein the term “paratope” includes the antigen binding site in the variable region of an antibody that binds to an epitope.

"Single-chain Fv" or "scFv" antibody fragments comprise the VH and VL domains of an antibody, wherein these domains are present in a single polypeptide chain. Generally, the Fv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen binding. For a review of scFv and other antibody fragments, see James D. Marks, Antibody Engineering, Chapter 2, Oxford University Press (1995) (Carl K. Borrebaeck, Ed.).

“Single-domain antibody” (sdAb), or “nanobody”, is an antibody fragment consisting of a single monomeric variable antibody domain. “VHH” or “VHH fragment” as used herein refers to a human VH that has been engineered to be independent of the light chain

(Nilvebrant et al. Curr Pharm Des. (2016) 22(43):6527-6537; Barthelemy et al., Journal of Biological Chemistry (2007) 283:3639-3654).

The terms "treatment", "treating" and the like are used herein to generally mean obtaining a desired pharmacologic and/or physiologic effect. The effect may be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or may be therapeutic in terms of a partial or complete cure for a disease and/or adverse effect attributable to the disease. "Treatment" as used herein covers any treatment of a disease in a mammal, and includes: (a) preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it; (b) inhibiting the disease, i.e., slowing or arresting its development; or (c) relieving the disease, i.e., causing regression of the disease. The therapeutic agent may be administered before, during or after the onset of disease or injury. The treatment of ongoing disease, where the treatment stabilizes or reduces the undesirable clinical symptoms of the patient, is of particular interest. Such treatment is desirably performed prior to complete loss of function in the affected tissues. The subject therapy may be administered during the symptomatic stage of the disease, and in some cases after the symptomatic stage of the disease.

The ability of the tetravalent binding antibody molecules of this invention to activate Wnt signaling can be confirmed by a number of assays. The tetravalent binding antibody molecules of this invention typically initiate a reaction or activity that is similar to or the same as that initiated by the FZD receptor's natural ligand. The tetravalent binding antibody molecules of this invention activates the Wnt signaling pathways, e.g., the canonical Wnt-βcatenin signaling pathway. As used herein, the term "activates" refers to a measurable increase in the intracellular level of a Wnt signaling pathway, e.g., the Wnt-βcatenin signaling pathway, compared with the level in the absence of a FZD Agonist of the invention.

Various methods are known in the art for measuring the level of Wnt-βcatenin activation. These include but are not limited to assays that measure: Wnt-βcatenin target gene expression; LEF/TCF reporter gene expression (such as TopFLASH, superTopFLASH, pBAR); βcatenin stabilization; LRP5/6 phosphorylation; Dishevelled phosphorylation; Axin translocation from cytoplasm to cell membrane and binding to LRP5/6. The canonical Wnt-βcatenin signaling pathway ultimately leads to changes in gene expression through the transcription factors TCF1, TCF7L1, TCF7L2 and LEF1. The transcriptional response to Wnt

activation has been characterized in a number of cells and tissues. As such, global transcriptional profiling by methods well known in the art can be used to assess Wnt-βcatenin signaling activation.

Changes in Wnt-responsive gene expression are generally mediated by TCF and LEF transcription factors. A TCF reporter assay assesses changes in the transcription of TCF/LEF controlled genes to determine the level of Wnt-βcatenin signaling. A TCF reporter assay was first described by Korinek, V. et al., 1997. Also known as TOP/FOP this method involves the use of three copies of the optimal TCF motif CCTTTGATC, or three copies of the mutant motif CCTTTGGCC, upstream of a minimal c-Fos promoter driving luciferase expression (pTOPFLASH and pFOPFLASH, respectively) to determine the transactivational activity of endogenous βcatenin/TCF. A higher ratio of these two reporter activities (TOP/FOP) indicates higher βcatenin/TCF activity. A newer and more sensitive version of this reporter is called pBAR and contains 12 repeats of the TCF motifs (Biechele and Moon, Methods Mol Biol. 2008;468:99-110, PMID: 19099249).

General methods in molecular and cellular biochemistry can be found in such standard textbooks as Molecular Cloning: A Laboratory Manual, 3rd Ed. (Sambrook et al., CSH Laboratory Press 2001); Short Protocols in Molecular Biology, 4th Ed. (Ausubel et al. eds., John Wiley & Sons 1999); Protein Methods (Bollag et al., John Wiley & Sons 1996); Nonviral Vectors for Gene Therapy (Wagner et al. eds., Academic Press 1999); Viral Vectors (Kaplift & Loewy eds., Academic Press 1995); Immunology Methods Manual (I. Lefkovits ed., Academic Press 1997); and Cell and Tissue Culture: Laboratory Procedures in Biotechnology (Doyle & Griffiths, John Wiley & Sons 1998).

Unless otherwise defined, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally, nomenclatures utilized in connection with, and techniques of, cell and tissue culture, molecular biology, and protein and oligo- or polynucleotide chemistry and hybridization described herein are those well-known and commonly used in the art. Standard techniques are used for recombinant DNA, oligonucleotide synthesis, and tissue culture and transformation (e.g., electroporation, lipofection). Enzymatic reactions and purification techniques are performed according to manufacturer's specifications or as commonly accomplished in the art or as described herein. The foregoing techniques and procedures are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification. See e.g., Sambrook et al. Molecular Cloning: A Laboratory Manual (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). The nomenclatures utilized in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well-known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

EXAMPLES

EXAMPLE I Identification and characterization of FZD4 binding or FZD5 binding Fab-phage.

A. FZD4 antibodies from affinity matured libraries of FZD4-binding antibody 5027 and 5044; FZD5 antibodies from affinity matured libraries of FZD5-binding antibody 2919 and 2928.

Affinity matured libraries of known FZD4-binding antibodies 5027 and 5044 and known FZD5-binding antibodies 2919 and 2928 were prepared using routine methods, essentially as described in US publication no. 2016/0194394, inventors Sidhu et al., see also Persson et al.

J. Mol. Biol., 2013 Feb 22; 425(4):803-11 https ://pubmed. ncbi.nlm.nih. gov/23219464/, both incorporated herein in their entirety by reference.

The 6 CDRs of the heavy chain (CDR-H1, CDR-H2 and CDR-H3) and light chains (CDR-L1, CDR-L2 and CDR-L3) of antibodies 5044, 5027, 2919, and 2928 antibodies isolated from the affinity matured libraries are set forth in Table 1 and Table 2.

Single point ELISAs were performed on 96-well Maxisorp plates coated with the extracellular domains (ECDs) of human FZD4 protein in the presence or absence of a saturating concentration of 5027 diabody-Fc (a diabody comprising the VL and VH of 5027 linked to an Fc domain). The plates were incubated with monoclonal Fab-phage followed by incubation with horseradish peroxidase (HRP)-conjugated anti-M13 antibody. Wells were subsequently washed 8 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 5-10 min. The reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader. The results of the assay are depicted in Figure 1 and Figure 2 and demonstrate that the newly identified FZD4 antibodies bind FZD4 at a site overlapping with the site recognized by antibody 5027. FZD4 binding antibodies 5027 and 5044 are described in US provisional application no. 62/885,781, incorporated herein by reference.

B. Epitope mapping of Lead FZD4 antibodies.

ELISA assays were performed in 384-well Maxisorp plates coated with FZD4 ECD wild-type (FZD4) or mutant FZD4 proteins (FZD_swap1-18) that replace segments of the FZD4 ECD with corresponding regions from FZD5. The plates were incubated with 10 nM IgG known to bind specifically to FZD4, i.e., 5044 and 5027, or to be panspecific, i.e., 5016 (binds FZD4, FZD5, and other FZD receptors), followed by incubation with horseradish peroxidase (HRP)-conjugated anti-Kappa light chain antibody. Phosphate buffered saline (PBS) and IgG 4275 which does not bind FZD4 or FZD5 were used as controls. The wells were washed 6 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 3-5 min. The reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader, see Figure 2. The pan-FZD binder 5016 is a positive control showing that the antigens are functional, with the exception of "FZD4_Swap10". Both FZD4-specific antibodies 5027 and 5044 are unable

to bind to "FZD4 Swap 7", suggesting that these molecules bind to this region of the FZD ECD.

C. Characterization of FZD4 IgG.

FZD4-binding full length IgGs were expressed via transient transfection in an Expi293 cell culture system, essentially as described in Tao et al., Tailored tetravalent antibodies potently and specifically activate Wnt/Frizzled pathways in cells, organoids and mice. Elife. 2019 Aug 27;8:e46134. doi: 10.7554/eLife.46134; PMID: 31452509. and purified via Protein A affinity chromatography. Briefly, cells were grown to a density of approximately 2.5 x 10^6 cells/ml in Expi293 Expression Media (Gibco) in baffled cell culture flasks and transfected with the appropriate vectors using FectoPRO transfection reagent (Polyplus-transfection) using standard manufacture protocols (ThermoFisher). Expression was allowed to proceed for 5 days at 37 °C and 8% CO_2 with shaking at 125 rpm. After expression, cells were removed by centrifugation and protein was purified from the conditioned media using rProtein A Sepharose (GE Healthcare). Purified protein was buffer exchanged into either PBS or a formulated stabilization buffer (36.8 mM citric acid, 63.2 mM Na_2HPO_4, 10% trehalose, 0.2 M L-arginine, 0.01% Tween-80, pH 6.0) for storage. Proteins concentrations were determined by absorbance at 280 nm and purity was confirmed by SDS-PAGE analysis.

Expression titers were determined as mg of purified protein per liter of mammalian cell culture. Size exclusion chromatography (SEC) results in Table A below are defined as "-": evidence of multiple peaks on SEC trace, <50% monomeric species; "+": >50% monomeric species, delayed retention time (>14 min.); "++": >90% of major peak at/near expected retention time for a monomeric IgG. Standard retention time was determined by comparison to Trastuzumab.

Table A

TRAC ID	Expression Titer (mg/l)	SEC Result
13980	58	-
13981	40	-
13982	43	-
13983	65	++
13984	52	-
13985	61	++
13956	47	+
13957	52	+
13958	58	-
13959	46	+
13962	38	-
13963	56	-
13964	47	-
13965	74	++
13966	86	-
13967	87	-
13968	89	+
13969	72	-
13970	36	-
13971	46	++
13972	27	+
13973	41	+
13974	41	+
13975	41	++
13979	49	-

Trac ID corresponds to the antibody number in Table 1 and Table 2.

D. Size-exclusion chromatography analysis and ELISA specificity measurements of the FZD4 IgGs.

Twenty micrograms of the FZD4 binding IgGs were separated over an AdvanceBio SEC, 300Å, 2.7 μm, 4.6 x 300 mm column in a mobile phase of PBS using an Agilent Bio-Inert HPLC. Protein elution was monitored using absorbance at 280 nM. The results are presented in Figure 3A.

ELISA specificity measurements of the FZD4 antibodies were determined against FZD1 and FZD10, the two FZD family member most closely related to FZD4. ELISA assays were performed in 384-well Maxisorp plates coated with FZD ECD wild-type or mutant proteins at a concentration of 1 μg/ml and excess binding sites were blocked with 0.5% BSA. The plates

were incubated with 10 nM of the FZD4 binding IgGs followed by incubation with horseradish peroxidase (HRP)-conjugated anti-Kappa light chain antibody. The wells were washed 6 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 3-5 min. The reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader. The results are presented in Figure 3B.

E. Identification of the CDRs of the FZD4 or FZD5 binding antibodies.

The amino acid sequences of the CDRs of the FZD4-binding and FZD5-binding immunoglobulins are set forth in Tables 1 and 2. The CDRs were identified according to the INTERNATIONAL IMMUNOGENETICS INFORMATION SYSTEM (IMGT numbering system; Lefranc et al., 2003, Development and Comparative Immunology 27:55-77), and annotated as described in Persson et al. J Mol Biol. 2013 Feb 22;425(4):803-11, both incorporated herein by reference.

Table 1		FZD4 binding antibodies CDRs											
Antibody ID	Library	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
5044	F	SVSSA	1	SASSLYS	2	WYYAPI	3	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79
13953	5044AM	SVSSA	1	SASSLYS	2	GNYGPI	4	IAFYSI	25	YISPFSGITH	52	PAVGHLAM	80
13954	5044AM	SVSSA	1	SASSLYS	2	GYYAPI	5	IYSYSI	26	YISSYYGYTY	51	STVGHGGM	81
13955	5044AM	SVSSA	1	SASSLYS	2	WYYAPI	3	ISSYSI	27	YISPYYSYTY	53	PAPAHWGF	82
13956	5044AM	SVSSA	1	SASSLYS	2	GYYALI	6	LSSYSM	24	YISSYAGYTS	54	PALGHAGM	83
13957	5044AM	SVSSA	1	SASSLYS	2	WYFAPI	7	ISAYSI	28	YISPYFGLTG	55	PAPGHWGM	84
13958	5044AM	SVSSA	1	SASSLYS	2	WYYAPI	3	LSSYSI	29	YISSYYGYTY	51	PVAGHGGM	85
13959	5044AM	SVSSA	1	SASSLYS	2	GYNAPI	8	LYSYSM	30	FISSFYGYTD	56	PAVGHLAL	86
13960	5044AM	SVSSA	1	SASSLYS	2	WYYAPI	3	LTSYSM	31	YISSYYGSTY	57	PAPGHWGM	84
13961	5044AM	SVSSA	1	SASSLYS	2	WYYAPI	3	ISSYSM	32	YISSYYSYTY	58	PAPGYGAL	87
13962	5044AM	SVSSA	1	SASSLYS	2	GYFAPI	9	LFSYPM	33	YISPYYGYTN	59	QTAGHAGM	88
13963	5044AM	SVSSA	1	SASSLYS	2	WFNAPI	10	LSAYSM	34	YISSYYGYTY	51	PAPGHWGF	79
13964	5044AM	SVSSA	1	SASSLYS	2	SNYAPI	11	ISSHSM	35	YISPFFSFTH	60	QAPGVSGI	89
13965	5044AM	SVSSA	1	SASSLYS	2	WYNAPI	12	LSSYSM	24	YISSYDSITD	61	PAVGHMAF	90
13966	5044AM	SVSSA	1	SASSLYS	2	GFYAPI	13	LSSYSM	24	YISSYYSYTA	62	PTPGHGGL	91
13967	5044AM	SVSSA	1	SASSLYS	2	WYYAPI	3	ISAYAM	36	YISPYYGYTF	63	PAPGHGGM	92
13968	5044AM	SVSSA	1	SASSLYS	2	GYSAPI	14	ISTYSM	37	YISPHYGFTS	64	PAVGHLGM	93
13969	5044AM	SVSSA	1	SASSLYS	2	WYFAPI	7	LHAFSM	38	YISPYYGYTY	65	PAPGHWGL	94
13970	5044AM	SVSSA	1	SASSLYS	2	GFYAPI	13	ISGYSI	39	YISSYYGYTF	66	TAPGHGAF	95
13971	5044AM	SVSSA	1	SASSLYS	2	GFYAPI	13	ISNYSI	40	IISSNFGYTS	67	PALGHLAM	96
13972	5044AM	SVSSA	1	SASSLYS	2	GYAGLI	15	ISAYSM	41	SISSYYGFTS	68	LAPGHPAL	97
13973	5044AM	SVSSA	1	SASSLYS	2	GFSSPI	16	LTSYAM	42	YISPYYGYTY	65	PAAGHLAL	98
13974	5044AM	SVSSA	1	SASSLYS	2	GYYAPI	5	LYSYSI	43	YISPSYGSTY	69	PIPGHLAF	99
13975	5044AM	SVSSA	1	SASSLYS	2	GHYAPI	17	LSSFSM	44	YISSFNGSTF	70	PTWAHGAF	100
13976	5044AM	SVSSA	1	SASSLYS	2	SFYAPI	18	IASYSI	45	YISSYYGSTY	57	PVLAHSAF	101
13977	5044AM	SVSSA	1	SASSLYS	2	GYRAPI	19	IHSNSM	46	YISPYYSFTS	71	QTPGHSGM	102
13978	5044AM	SVSSA	1	SASSLYS	2	WHRAPI	20	LSTNSM	47	YISPYYSFTY	72	QAPGPWGM	103
13979	5044AM	SVSSA	1	SASSLYS	2	SFYAPI	18	LHSFSM	48	FISSYYGYTY	73	PAPGHGAF	104

Table 1 cont'		FZD4 binding antibodies CDRs											
Antibody ID	Library	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
13980	5044AM	SVSSA	1	SASSLYS	2	GYYAPI	5	LTSYSM	31	SISPYYSYTN	74	PTTAHMAL	105
13981	5044AM	SVSSA	1	SASSLYS	2	WYYAPI	3	ISSFSI	49	FINPYYSYTY	75	PAPGHWGM	84
13982	5044AM	SVSSA	1	SASSLYS	2	GYYAPI	5	ISSYSM	32	YISSYYDYTY	76	PTPGHSGF	106
13983	5044AM	SVSSA	1	SASSLYS	2	GDFAPF	21	LPYYSM	50	IISSYFGFTY	77	PAVGHGAL	107
13984	5044AM	SVSSA	1	SASSLYS	2	GYSSPI	22	ISSHSM	35	YISPYYSYTY	53	TAPGHPAM	108
13985	5044AM	SVSSA	1	SASSLYS	2	WFYAPI	23	ISSYSI	27	YISSNFGSTY	78	PVPAHGAF	109

Table 2A		FZD4 binding antibodies CDRs											
Antibody ID	Library	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
5027	**F**	**SVSSA**	**1**	**SASSLYS**	**2**	**SSYSLI**	**130**	**SSFYFM**	**148**	**TVYPYLDYTY**	**985**	**AFPGSYHPM**	**199**
13986	5027AM	SVSSA	1	SASSLYS	2	ASYYLI	110	STYFFI	139	TIYPYLNSTY	166	AYPGSYHPL	198
13987	5027AM	SVSSA	1	SASSLYS	2	SNYALI	111	TSFYFM	140	SVYPYLDNTY	167	AFPGSYHPM	199
13988	5027AM	SVSSA	1	SASSLYS	2	SSSFLI	112	SSFYFI	141	TVYSYIDITY	168	AFPFSYHPM	200
13989	5027AM	SVSSA	1	SASSLYS	2	SSDSLI	113	SAYYFI	142	TVYPYRGYTY	169	GYPLAYTPL	201
13990	5027AM	SVSSA	1	SASSLYS	2	STHFLI	114	SYFYFM	143	SVYPYLSYTY	170	AFPGSYHPM	199
13991	5027AM	SVSSA	1	SASSLYS	2	ASYSLI	115	SSFYFI	141	SVYPYLDFTY	171	ALQGHYHPM	202
13992	5027AM	SVSSA	1	SASSLYS	2	SAYTLI	116	TSFYYM	144	AIYPYLDYTY	172	AFPGSYLPM	203
13993	5027AM	SVSSA	1	SASSLYS	2	SSVSLI	117	FTFYFM	145	SIYPYLNYTF	173	AFPGSYHPM	199
13994	5027AM	SVSSA	1	SASSLYS	2	SYYSLI	118	SSYYFI	146	TIYPYSDNTY	174	GFPGRYHPL	204
13995	5027AM	SVSSA	1	SASSLYS	2	SSYYLI	119	SSFYVM	147	SIYSYGNITY	175	AFPLSYHPM	205
13996	5027AM	SVSSA	1	SASSLYS	2	ASYYLI	110	SSFYFM	148	AIYPYLSYTY	176	AFPGRYHGM	206
13997	5027AM	SVSSA	1	SASSLYS	2	AYYFLI	120	SSFYYI	149	TVFPYLGRTY	177	AFPFSYTPL	207

Table 2A – cont'		FZD4 binding antibodies CDRs											
Antibody ID	Library	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
13998	5027AM	SVSSA	1	SASSLYS	2	SSFSLI	121	STFYFM	150	SVYPYLNYTY	178	AFPGAYSPM	208
13999	5027AM	SVSSA	1	SASSLYS	2	SAYSLI	122	SAFYYM	151	TVYPYLSYTY	179	AFPGAYHPM	209
14000	5027AM	SVSSA	1	SASSLYS	2	SSYALI	123	ASFYFM	152	TVYPYLNHTY	180	AFPGAYHPF	210
14001	5027AM	SVSSA	1	SASSLYS	2	SYFSLI	124	SAFYFI	153	SIYPYLSYTY	181	AFPGAYHPM	209
14002	5027AM	SVSSA	1	SASSLYS	2	SRFTLI	125	FPFYFM	154	SVYPYLNDTY	182	AYPGFYHPI	211
14003	5027AM	SVSSA	1	SASSLYS	2	SSNTLI	126	SAFYFM	155	SVYSSLSHTY	183	AYPLSYHPM	212
14004	5027AM	SVSSA	1	SASSLYS	2	SSFSLI	121	ASYYFM	156	SVYPYLDFTY	171	ALPGFYHPF	213
14005	5027AM	SVSSA	1	SASSLYS	2	SSFALI	127	SVFYFM	157	SVYPYNDITY	184	GFPGTYHPL	214
14006	5027AM	SVSSA	1	SASSLYS	2	ANYALI	128	SSLYYM	158	SVYPYLDNTH	185	AIPGFYHPI	215
14008	5027AM	SVSSA	1	SASSLYS	2	ASYSLI	115	SNFYLM	159	SIYSYLNYTF	186	AFPGSYHPM	199
14009	5027AM	SVSSA	1	SASSLYS	2	SSASLI	129	FSFYFI	160	SIYPYLDFTH	187	AFPGSYHPL	216
14010	5027AM	SVSSA	1	SASSLYS	2	SSYSLI	130	SAFYFM	155	AIYPYIGYTY	188	PFPASYHPL	217
14011	5027AM	SVSSA	1	SASSLYS	2	SSYSLI	130	SSLYFM	161	TIYPFRGTTY	189	AYPGRYHPL	218
14012	5027AM	SVSSA	1	SASSLYS	2	SAFYLI	131	YYFYYM	162	AIYPYLGYTY	190	AFPGSYHPL	216
14013	5027AM	SVSSA	1	SASSLYS	2	SAYFLI	132	SSFYFI	141	SVYPYLGDTY	191	AFPGFYHPF	219
14015	5027AM	SVSSA	1	SASSLYS	2	ASSSLI	133	TSYYFI	163	SVYSYLGYTF	192	AFPGSYHPL	216
14016	5027AM	SVSSA	1	SASSLYS	2	SIYSLI	134	SYFYFM	143	AIYPYLSYTY	176	AFPGSYHPM	199
14018	5027AM	SVSSA	1	SASSLYS	2	ASYYLI	110	FSFYFI	160	TVYPYLSHTY	193	AFPGSYHPM	199
14019	5027AM	SVSSA	1	SASSLYS	2	STGSLI	135	SDFYFI	164	TIYPFIGNTY	194	AFPGSYHPF	220
14020	5027AM	SVSSA	1	SASSLYS	2	SSHSLI	136	SSFYFM	148	SVYPYVDYTY	195	AFPGFYHPM	221
14021	5027AM	SVSSA	1	SASSLYS	2	SSYTLI	137	SSFYYM	165	TVYPYLSFTY	196	ALPGSYHPF	222
14022	5027AM	SVSSA	1	SASSLYS	2	SYHYLI	138	STFYFM	150	SVYPYLDDTY	197	AYPGSYHPL	198

Table 2B	**FZD5 binding antibodies CDRs**													
Antibody ID	Antigen Name	Selection ID	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
14023	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSGVHGLI	223	LIYTYI	308	TIYPASSSTS	381	GAM	
14024	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSSAHVPF	224	ITYPGM	309	TIFSSHGSTS	382	FGM	
14025	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSYGHHLI	225	ISYSYM	310	SIYSSSSSTS	383	GAL	
14026	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYTSGHVLI	226	ISFFYM	311	TIDSSTGSTT	384	GAL	
14027	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYASDHGLI	227	IPYFYM	312	SIYSSSGSTS	385	GAM	
14028	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSPGNVLI	228	ISYYYI	313	SIYPSSSSTT	386	AAF	
14029	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSTRNILI	229	ISYAYM	314	SIYPSSSSTA	387	YAF	
14030	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYFSDHDLF	230	ITYFYM	315	SIYPSFGSTS	388	GGM	
14031	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGDVLI	231	IYYSYI	316	SIYSSNGGTS	389	GAM	
14032	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSADVLF	232	ILNTYM	317	SIYPSSSSTA	387	GGL	
14033	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGHGLI	233	ISFYYI	318	SIYPASSSTS	390	GGI	
14034	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGHALI	234	LAYSYM	319	SIYPSSGDTS	391	GAM	
14035	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSNHIPI	235	IRYSYI	320	AIYSSSSSTS	392	GAM	
14036	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSSNVLI	236	ITYSYM	321	TIYPSSGSTA	393	FAM	
14037	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYFSDRVLI	237	IINTYM	322	SIYSAPSSTA	394	GAI	
14038	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYPSSHVLI	238	ISYSYM	310	TIYPSSGSTA	393	GGM	
14039	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSRHHLI	239	LANSYM	323	TIYSSSGSTS	395	GAM	
14040	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSTGRVLF	240	LSYTYM	324	SIDPSSGSTS	396	FGM	
14041	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFPTGHVLF	241	ISYSYI	325	TIYPSSGSTG	397	FGM	
14042	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYAPRHVLI	242	ISYSYI	325	SIYSSSSSTS	383	GAM	
14043	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFTSGLVLF	243	LSYLYI	326	SIYPSSSSTS	398	GGM	
14044	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGHVLF	244	ISYAYI	327	SIYSSPSSTS	399	GAM	
14045	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYPGAPVLI	245	IAYSYM	328	SIYPSSSSTS	398	GAM	
14046	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSSNVLI	236	FIWESLLVS	329	TIYPSSGSTA	393	FAM	
14047	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSANALF	246	ISHSYM	330	SIDSSSGSTS	400	GAL	
14048	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGDVLI	231	LRYSYI	331	TIYSASGSTT	401	GAL	

Table 2B	**FZD5 binding antibodies CDRs**													
Antibody ID	Antigen Name	Selection ID	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
14049	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSNHVLI	247	ISYAYM	314	SISPSDSSTS	402	GAL	
14050	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSAAHILF	248	ISYSYM	310	SIDPSSGLTS	403	GAL	
14051	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFASGHVLI	249	IRYAYM	332	TIDSFSGSTS	404	YAM	
14052	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSSGDSLI	250	ITHLYM	333	SIYPSSGSTS	405	AAL	
14053	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYASGNVLI	251	LSIFYM	334	TIYPSSSSTS	406	GAF	
14054	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSPGHLLI	252	LSYSYI	335	AIYPSPSSTS	407	GAM	
14055	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYPSGHVLF	253	ISYSFM	336	SIYSTSGSTS	408	GGL	
14056	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFAAGHVLI	254	IAYVGI	337	AITPSSSNTS	409	FGF	
14057	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFRSAHVLI	255	LSYSYM	338	SIDPSSSSTA	410	FGF	
14058	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFASGHILI	256	ISYSFM	336	SIYSRSGSTA	411	GAM	
14059	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSGGHALI	257	IAYFYI	339	TIDPSSGSTS	412	GGL	
14060	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFASAHVLF	258	LSSSYM	340	SIGPSSGSTS	413	FGF	
14061	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSPGHVLI	259	LSYSYM	338	SIYPSSSSTS	398	GGI	
14062	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYASGLVLI	260	IYYSYM	341	SIDPSSSSTS	414	GGM	
14063	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYTSGHVLF	261	ITYSYM	321	SIYPSPSSTS	415	GGM	
14064	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSFPHALI	262	LHYGGI	342	SISSSFSSTS	416	FGF	
14066	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYASGTDLI	263	ISYSYM	310	TIYSSSSSTA	417	GGM	
14067	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGRLLI	264	IGYAYM	343	SIYSSPGSTA	418	GAL	
14068	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSSPHVLF	265	LSYSSI	344	SICPFCSSTS	419	FGF	
14069	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFASASSLF	266	LSYDGI	345	TIYSSSGSTS	395	FGL	
14070	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYPSSHVLF	267	LSYAYM	346	SIHPFDGSTS	420	GAL	
14071	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFPAHHVLF	268	ISYSGI	347	SISSSSGSTA	421	FGM	
14072	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFPSGNVLF	269	ISSSYM	348	TIDPYAGSTS	422	FAM	
14073	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSNNVLI	270	LSYSYM	338	SIYPSSGSTA	423	GGM	
14074	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSSRHVLF	271	LSYSGM	349	TIYPSSSSTS	406	FGM	
14075	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYFSDHDLI	272	GFTISYFFM	350	SIYPSDSSTS	424	GAM	

Table 2B	**FZD5 binding antibodies CDRs**													
Antibody ID	Antigen Name	Selection ID	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
14076	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGGVLI	273	ISYSFI	351	SIYPSSGHTS	425	GAL	
14077	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFPSGHVLF	274	ISYSYM	310	SIDPSSGSTS	396	FGM	
14078	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSTHVLF	275	LSYTYM	324	SIYSSPGSTS	426	GGM	
14079	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYSSGSALI	276	ISHAYM	352	SIYSSPGSTA	418	FAL	
14080	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSPGSVLI	277	LLFFYM	353	SIDPSSGFTS	427	GAM	
14081	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYPSAHILF	278	IAYSYM	328	SIYPASSSTS	390	GGM	
14082	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYGSGGILI	279	LSYFYM	354	SIFSSSSSTS	428	GAM	
14083	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFTSGRDLF	280	GFTLISSSI	355	SIYPAPSSTP	429	GGM	
14084	FZD5	2919AM	SVSSA	1	SASSLYS	2	WYLSRNILI	281	LSYSYI	335	SIYSSSSSTS	383	GAM	
14085	FZD5	2919AM	SVSSA	1	SASSLYS	2	WFSGRDALF	282	ITNSYM	356	SIYSSPSSTS	399	GGL	
14369	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFFYPI	283	ISFSSI	357	SIYPSYGSSF	430	YYAF	483
14370	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	TIYPYYSSTL	431	YYAF	483
14371	FZD5	2928AM	SVSSA	1	SASSLYS	2	AHYFPI	285	ISYSSM	358	SIYSSYSSTY	432	YYAM	484
14372	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPSYSVTY	433	YYGM	485
14373	FZD5	2928AM	SVSSA	1	SASSLYS	2	SHYYPI	286	LSFSSM	359	SIYPYYGSTF	434	YYAM	484
14374	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYSSYSSTY	432	YYGF	486
14375	FZD5	2928AM	SVSSA	1	SASSLYS	2	GFYYPI	287	ISFGSI	360	SIYPSYSSTF	435	YYAM	484
14376	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ITYSSI	361	SIYPAYSSTY	436	YYAF	483
14377	FZD5	2928AM	SVSSA	1	SASSLYS	2	SFYFPI	289	ISYSAI	362	SIYSSYSSTF	437	YYAM	484
14378	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYSSYGSTY	438	YYAM	484
14379	FZD5	2928AM	SVSSA	1	SASSLYS	2	ADYFPI	290	ISYSSM	358	SIYPSYSSTY	439	YYGM	485
14380	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSI	363	SIYSYYGSTY	440	YYAM	484
14381	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISFSSI	357	TIYSLFGATF	441	YYGF	486
14382	FZD5	2928AM	SVSSA	1	SASSLYS	2	SFYFPI	289	ISYSSM	358	SIYPSYSSTY	439	YYAF	483
14383	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFHYPI	291	ISFSSI	357	SIYPSYSSTY	439	YYAM	484
14384	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISFSSI	357	SIYPAYGATF	442	YYGM	485

Table 2B	**FZD5 binding antibodies CDRs**													
Antibody ID	Antigen Name	Selection ID	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
14385	FZD5	2928AM	SVSSA	1	SASSLYS	2	AYYYPI	292	ISYSSI	363	SIYSSYSSTF	437	YYAF	483
14386	FZD5	2928AM	SVSSA	1	SASSLYS	2	VFYYPI	293	ISYSSM	358	SIYSSYSSTY	432	YYAF	483
14387	FZD5	2928AM	SVSSA	1	SASSLYS	2	SFYFPI	289	ISYSSM	358	SIYPYYSSTY	443	YYAM	484
14388	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LSYSSM	364	SIYPAYSSTY	436	YYGM	485
14389	FZD5	2928AM	SVSSA	1	SASSLYS	2	ANYFPI	294	ISFGSI	360	SIYSSYSSTY	432	YYAM	484
14390	FZD5	2928AM	SVSSA	1	SASSLYS	2	GFYFPI	295	ISYSSI	363	SIYPSFGSTY	444	YYAM	484
14391	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPSFSPTY	445	YYGM	485
14392	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	IAYSSM	365	SIYSSYGSTF	446	YYAF	483
14393	FZD5	2928AM	SVSSA	1	SASSLYS	2	AYYFPI	296	ISYSSI	363	SIYPAYSPTY	447	YYAF	483
14394	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFIFPI	297	ISYSAM	366	SIYPSYSSTY	439	YYAL	487
14395	FZD5	2928AM	SVSSA	1	SASSLYS	2	AYYYPI	292	ISYGVI	367	SIYSAYSSTF	448	YYAF	483
14396	FZD5	2928AM	SVSSA	1	SASSLYS	2	SFYFPI	289	ISYSSI	363	TIYPYYDPTY	449	YYAF	483
14397	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LSYSSM	364	SIYSSYGSTY	438	YYAM	484
14398	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSI	363	SIYPSYGSTY	450	YYGM	485
14399	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPHYGATF	451	YYGM	485
14400	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSI	363	SIYPSYGSTF	452	YYAM	484
14401	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFFFPI	298	ISYSSI	363	SIYSSYSATY	453	YYAM	484
14402	FZD5	2928AM	SVSSA	1	SASSLYS	2	SFYYPI	299	ISYSSM	358	SIYPSYSSTY	439	YYAF	483
14403	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	IPYGSM	368	SIYPSYGSTF	452	YYAM	484
14404	FZD5	2928AM	SVSSA	1	SASSLYS	2	ALYYPI	300	ISYSSM	358	SIYPSYSSTF	435	YYAM	484
14405	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSAM	366	SIYPYYGPTY	454	YYAF	483
14406	FZD5	2928AM	SVSSA	1	SASSLYS	2	VFYYPI	293	ISYSSI	363	SIYPFYGSTF	455	FYAF	488
14407	FZD5	2928AM	SVSSA	1	SASSLYS	2	RFYFPI	301	ISYSSI	363	AIYPSYSSTN	456	YYAM	484
14408	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSI	363	SIYPYYSSTH	457	YYAM	484
14409	FZD5	2928AM	SVSSA	1	SASSLYS	2	LYYFPI	302	IAYSAM	369	SIYPSYSTTY	458	YYAM	484
14410	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LSFSSI	370	SIYPSYSSTF	435	YYAF	483

Table 2B	**FZD5 binding antibodies CDRs**													
Antibody ID	Antigen Name	Selection ID	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
14411	FZD5	2928AM	SVSSA	1	SASSLYS	2	AYYFPI	296	ISYSSM	358	SIYSSYGSTY	438	YYGM	485
14412	FZD5	2928AM	SVSSA	1	SASSLYS	2	SSYFPI	303	ISYSSM	358	SIYSNYSSSY	459	YYAM	484
14413	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LTYSSI	371	TIYPSYGSTY	460	YYAM	484
14414	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPSFGSTF	461	YYAI	489
14415	FZD5	2928AM	SVSSA	1	SASSLYS	2	AHYFPI	285	LSYGSI	372	SIYPSYGSTY	450	YYGM	485
14416	FZD5	2928AM	SVSSA	1	SASSLYS	2	ASYFPI	304	ISYSSM	358	TIYPSYSSTY	462	YYAM	484
14417	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	IAYSSM	365	TIYSSYGATS	463	YYAF	483
14418	FZD5	2928AM	SVSSA	1	SASSLYS	2	AHYYPI	305	ISYSSI	363	SIYPSYSSTI	464	YYAM	484
14419	FZD5	2928AM	SVSSA	1	SASSLYS	2	AGFFPI	306	ISYSSI	363	TIYPYYGATY	465	YYGF	486
14420	FZD5	2928AM	SVSSA	1	SASSLYS	2	SSYYPI	307	ISYSSI	363	SIYSGYSATY	466	YYAM	484
14421	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ITYSSM	373	SIYPSYGSTY	450	YYGF	486
14422	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSI	363	TIYPSYSSTY	462	YYAM	484
14423	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LGYGSM	374	SIYPSYGSTY	450	YYAM	484
14424	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPSYSATF	467	YFAL	490
14425	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	IGYSSI	375	TIYPSYSSTF	468	YYAF	483
14426	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ITYGSI	376	AIYSSYGSTY	469	YYAF	483
14427	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSM	358	SIFPYYGSTY	470	YYGF	486
14428	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPFYSTTF	471	YYAM	484
14429	FZD5	2928AM	SVSSA	1	SASSLYS	2	SSYYPI	307	ISYGSM	377	SIYPSYSATF	467	YYGM	485
14430	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSM	358	SIYPSYGSTS	472	YYGM	485
14431	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	IYYSSM	378	SIYPTYGSTV	473	YYGM	485
14432	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSI	363	TIYPNYSSTY	474	YYAM	484
14433	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	IFYSSM	379	SIYPSYSATY	475	YYAM	484
14434	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSM	358	SIYPGYSSTY	476	YYAM	484
14435	FZD5	2928AM	SVSSA	1	SASSLYS	2	AHYFPI	285	IAYSSM	365	TIYPSYSSTY	462	YYAM	484
14436	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYSSI	363	SIYPSYSSTS	477	YYGM	485

Table 2B	**FZD5 binding antibodies CDRs**													
Antibody ID	Antigen Name	Selection ID	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
14437	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYSGYGSTY	478	YYGM	485
14438	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISYSSM	358	SIYPSYGSTY	450	YYGM	485
14439	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LSFSSM	359	SIYSGYSATY	466	YYAL	487
14440	FZD5	2928AM	SVSSA	1	SASSLYS	2	AYYFPI	296	ISYSSM	358	SIYPSYGSTN	479	YYAF	483
14441	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	LSYSSI	344	SIYPTYGSAY	480	YYGM	485
14442	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ITYSSM	373	TIYSSYGSTY	481	YYAM	484
14443	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYFPI	284	ISFSSM	380	AIYPYYGSTY	482	YYGF	486
14444	FZD5	2928AM	SVSSA	1	SASSLYS	2	AHYFPI	285	ISYSSM	358	SIYSSYGSTY	438	YYGM	485
14445	FZD5	2928AM	SVSSA	1	SASSLYS	2	ASYFPI	304	LSYSSM	364	SIYPSYSSTF	435	YYAM	484
14446	FZD5	2928AM	SVSSA	1	SASSLYS	2	AFYYPI	288	ISYGSM	377	SIYPSYGSTY	450	YYGM	485

EXAMPLE 2: Identification and characterization of LRP binding synthetic antibodies

A. Phage Clonal ELISA of Synthetic Antibodies targeting LRP5 and LRP6.

Single point ELISAs were performed on 96-well Maxisorp plates coated with the ECDs of mouse LRP5-his protein or human Fc and blocked with BSA (0.5%). The plates were incubated with monoclonal Fab-phage, or VH-phage and titers $>10^9$ phage/ml followed by incubation with horseradish peroxidase (HRP)-conjugated anti-M13 antibody. The wells were washed 8 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 5-10 min. the reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader. The results are presented in Figure 4. The results demonstrate that the synthetic antibodies bound to LRP5. LRP5 binding antibodies, 2459, 2460 and 8716, are described in US provisional application no. 62/886,913, incorporated herein by reference.

Single point ELISAs were performed on 96-well Maxisorp plates coated with the ECDs of human LRP6-Fc protein chimeras. The plates were incubated with the monoclonal Fab-phage, or VH-phage and titers >109 phage/ml followed by incubation with horseradish peroxidase (HRP)-conjugated anti-M13 antibody. The wells were washed 8 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 5-10 min. the reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader. The results are presented in Figures 5A and 5B. The results demonstrate the synthetic antibodies bound to LRP6. LRP6 binding antibodies, 2539, 2540, and 2542 are described in US provisional application no. 62/886,918, incorporated herein by reference.

B. Identification of the CDRs of the synthetic antibodies targeting LRP5 and LRP6.

The CDRs of the LRP5-binding and LRP6-binding immunoglobulins set forth in Tables 3 and 4 were identified according to the INTERNATIONAL IMMUNOGENETICS INFORMATION SYSTEM (IMGT numbering system; Lefranc et al., 2003, Development and Comparative Immunology 27:55-77) and annotated as described in Persson et al. J Mol Biol. 2013 Feb 22;425(4):803-11, both incorporated herein by reference.

Table 3	LRP5 – antibody		LRP5-binding antibodies CDRs											
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
2459	F	mLRP5-his	SVSSA	1	SASSLYS	2	ASYAPI	492	LSYYYM	527	SIYSSYGYTY	552	WSHVSGHYSGM	584
2460	F	mLRP5-his	SVSSA	1	SASSLYS	2	SSYSLI	130	FSSSSI	528	SISSSYGYTY	553	GGSGVSHYGSVYYSWWAL	585
8716	F	mLRP5-his	SVSSA	1	SASSLYS	2	YWAYYSPI	493	FSSSSI	528	SISSSYGYTY	553	SWAM	586
9931	F	mLRP5-his	SVSSA	1	SASSLYS	2	SSSGHLI	494	LYYYSM	529	YISSYYSYTS	554	WSHVVGAHYGWAI	587
9932	F	mLRP5-his	SVSSA	1	SASSLYS	2	PYGYPI	495	IYYYSM	530	SISSYYGYTS	555	SWWYWSYHGYAAM	588
9933	F	mLRP5-his	SVSSA	1	SASSLYS	2	FHGLI	496	ISSSYM	348	SIYSYSSYTS	556	GYSYVWYGVYYHGYGAM	589
9934	F	mLRP5-his	SVSSA	1	SASSLYS	2	YWFLI	497	LYYYYI	531	SISPYYGYTS	557	SGYGWYAM	590
9935	F	mLRP5-his	SVSSA	1	SASSLYS	2	HSYGYPI	498	ISYSYM	310	SISSSYGYTY	553	SYYWGYWAAL	591
9936	F	mLRP5-his	SVSSA	1	SASSLYS	2	YYAWYLI	499	ISYYSM	532	SIYSSYGYTY	552	GGVYYYPSYAGWPYGM	592
9937	F	mLRP5-his	SVSSA	1	SASSLYS	2	AAYSPI	500	ISSSYM	348	SIYPSYGYTY	558	HYAWWVGAF	593
9938	F	mLRP5-his	SVSSA	1	SASSLYS	2	YYSWYPPF	501	ISYSYM	310	SIYSYYSYTS	559	GGGAHGWGYSL	594
9939	F	mLRP5-his	SVSSA	1	SASSLYS	2	SFYPI	502	LSSYSI	29	SIYPYYGYTS	560	SGPVYASYSWAWYYYGAL	595
9940	F	mLRP5-his	SVSSA	1	SASSLYS	2	YYWYPF	503	LSYYYI	533	SIYSYYSSTY	561	YSWGAYGYGAM	596
9941	F	mLRP5-his	SVSSA	1	SASSLYS	2	WGSPI	504	FSSSSI	528	SIYPSSGSTY	562	YYYHYSVPVYAAL	597
9942	F	mLRP5-his	SVSSA	1	SASSLYS	2	YSSWYLI	505	LYYYSM	529	SIYPSSGSTY	562	SPYYGFYYSGFYHWVFYGF	598
9943	F	mLRP5-his	SVSSA	1	SASSLYS	2	GAYLI	506	LYYSSM	534	YIYSYYGYTY	563	AAWGWHPAF	599
9944	F	mLRP5-his	SVSSA	1	SASSLYS	2	HFYYYPI	507	IYSSYI	535	YISSYYGSTY	57	GGGFYYAGGWPYASYAWAF	600
9945	F	mLRP5-his	SVSSA	1	SASSLYS	2	AFHSPI	508	LYYSSM	534	YIYPYYGYTS	564	AWYSYYVGL	601
9946	F	mLRP5-his	SVSSA	1	SASSLYS	2	AWYPI	509	ISYSSM	358	SIYPYYGSTY	565	GVYYGGGYWAGGYYPAAL	602
12600	H	mLRP5-his	SVSSA	1	SASDLYS	491	YAGAGLI	510	FTAYAM	536	SIYPSGGYTA	566	RSYYFAL	603
12601	H	mLRP5-his	SVSSA	1	SASDLYS	491	SYSYPI	511	LGGYGI	537	GIYPSGGYTA	567	SSTYSSYYYHFYAL	604
12602	H	mLRP5-his	SVSSA	1	SASDLYS	491	YYRSRLI	512	FASAWM	538	RISPSGGYTA	568	STRWHSAYAYYYSHAM	605
12603	H	mLRP5-his	SVSSA	1	SASDLYS	491	SYFYPI	513	IGGAAM	539	GISASGGATA	569	SRPSWYWSYHYFAL	606
12604	H	mLRP5-his	SVSSA	1	SASDLYS	491	GFFPI	514	FSSSSI	528	GISTSGGATA	570	SYYGYSRGF	607
12605	H	mLRP5-his	SVSSA	1	SASDLYS	491	SHSYPI	515	FASYGM	540	SIYPSGGYTA	566	SYSFHYAWPRYHYGAL	608

Table 3	LRP5 – antibody		LRP5-binding antibodies CDRs											
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
12606	H	mLRP5-his	SVSSA	1	SASDLYS	491	SHYYPI	286	IAGSSI	541	GISASGGYTA	571	YDSGYYAWYYHDRAM	609
12607	H	mLRP5-his	SVSSA	1	SASDLYS	491	RGSGPI	516	LTGDWM	542	GIYPSGGATA	572	FGSPHYGM	610
12608	H	mLRP5-his	SVSSA	1	SASDLYS	491	RYSGGLI	517	FTSYSM	543	GIYPSGGSTA	573	PRYYAYYSGGF	611
12609	H	mLRP5-his	SVSSA	1	SASDLYS	491	SARYYYLI	518	LNAAAM	544	GISASRGATA	574	SHSSGSRSRGL	612
12610	H	mLRP5-his	SVSSA	1	SASDLYS	491	SSYSLI	130	LAGAGM	545	RISTSGGYTA	575	YSFRYPSYAM	613
12611	H	mLRP5-his	SVSSA	1	SASDLYS	491	SYRGYYLI	519	IGGAAM	539	GIYASGGATA	576	GSRYSGF	614
13218	2539AM	mLRP5-his	SVSSA	1	SASSLYS	2	FSWGLI	520	ISYYPM	546	YISPYSGYTF	577	HYYFRWSRGM	615
13219	2539AM	mLRP5-his	SVSSA	1	SASSLYS	2	YSWLPI	521	IVFGSI	547	HIAPYYGFTY	578	VNFIRRFRGM	616
13378	2542AM	mLRP5-his	SVSSA	1	SASSLYS	2	FFRPI	522	ISSNYI	548	SINPSYSYTF	579	AVRRSQGI	617
13379	2539AM	mLRP5-his	SVSSA	1	SASSLYS	2	YSRRLF	523	LTYTSM	549	SISPFHGHTF	580	FPYFAWVGGM	618
13380	2539AM	mLRP5-his	SVSSA	1	SASSLYS	2	FIRVPI	524	ITYYSM	550	SITSYYGNTD	581	SHYFPWTVAL	619
13558	2540AM	mLRP5-his	SVSSA	1	SASSLYS	2	FYVPF	525	*N.D.*		SIYPYYGFTD	582	ASYHASFDGL	620
13559	2540AM	mLRP5-his	SVSSA	1	SASSLYS	2	GYSFGQ	526	IADSSI	551	SISPYFSYTR	583	TSIFKRFAGM	621

Table 4 LRP6 – antibody			LRP6 binding antibodies CDRs											
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
2539	F	LRP6-Fc	SVSSA	1	SASSLYS	2	YSWGPF	622	ISYSSI	363	YISSYYGYTY	51	AHYFPWAGAM	813
2542	F	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	ISSYYI	683	SIYSSYGYTS	741	TVRGSKKPYFSGWAM	814
2540	F	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFLI	624	ISYSSI	363	SISPYYGYTY	742	SSYFPWFSAM	815
12612	H	LRP6-Fc	SVSSA	1	SASDLYS	491	YRYYWRPI	625	FSGDAM	684	RISSSGGYTA	743	ASYYSNYYYGPAM	816
12613	H	LRP6-Fc	SVSSA	1	SASDLYS	491	GPWGLI	626	ISGAWM	685	RIYPSGGTTD	744	GWFSFRSYYRSYYYYSAL	817

Table 4 LRP6 – antibody			LRP6 binding antibodies CDRs											
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
12614	H	LRP6-Fc	SVSSA	1	SASDLYS	491	RYSSPI	627	FTTYSI	686	GISTSGGYTD	745	SGHPRYYSRRHSYGM	818
12615	H	LRP6-Fc	SVSSA	1	SASDLYS	491	YRYWYGPI	628	FAASGI	687	YISPSGGYTD	746	SYYSNYYYYYDAM	819
12979	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSWALF	629	IFFSSM	688	GISSYYGFTY	747	AHYFPWAGAL	820
12980	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	ISWGLI	630	IRYSSI	689	GIFSNYGPTT	748	AHYFRRARGL	821
12981	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YFSYPI	631	LSYSSI	344	FISSYYSFTH	749	SHYFPWAGAM	822
12982	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YRWALF	632	LAYSSI	690	SISSYYGFTY	750	AHYFPWAGGM	823
12983	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSRILF	633	LRYASM	691	YIASFYGDTY	751	SYYYPRSRGM	824
12984	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSLRPI	634	LSFSSI	370	HISPYYGYTH	752	SHYFPWAVAM	825
12985	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSRGLI	635	IFYSSI	692	YISSYYSYTY	58	SHYFPWAVAM	825
12986	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YFWGLI	636	LSYSSM	364	NITPYYGYTS	753	SHYFPWFAAM	826
12987	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSWGLI	637	INYSSI	693	GISSYYSYTY	754	ANYFPWAYAM	827
12988	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	DSWGLF	638	ISYSSM	358	LITSYYGYTT	755	AHYFPWVVGM	828
12989	2539AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWGLI	639	LSYSSI	344	FISSYYGYTY	73	SHYFPWAGAL	829
13002	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYYLI	640	IAFSSI	694	SISSYYGYTS	555	SSYFPWFSAL	830
13003	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYILI	641	LFYSSM	695	FISPYYSFTN	756	SSYFPWLSDM	831
13004	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	HSFPI	642	ISYSSM	358	NITSYYGYTT	757	SSYFPWVSGM	832
13005	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YHHLI	643	ISFASM	696	SISPYYSYTS	758	SSYFPWFSAM	815
13006	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYSPI	644	IFYSSI	692	SISPYYGYTD	759	SSYLPWFSAL	833
13007	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYYPI	645	ISFYSI	697	SISSYYSYTD	760	SSYFPWFTAL	834
13008	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YHFLI	646	ISYSSI	363	AIYSYYSYTI	761	SSYFPWVGGF	835
13009	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	LSYSSI	344	SISPYYSYTS	758	SSRFPWFYGL	836
13010	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YDFLI	648	ISYSSM	358	SISSYYGYTS	555	SSYFPWFSAL	830
13394	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYILI	641	LFYASM	698	SISSYYGYTS	555	SSYFPWFSAM	815
13395	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYYLI	640	ISYSSI	363	SISPYYGFTL	762	SSYFPWFSAM	815
13396	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	IAYASI	699	SISSYYSYTY	763	SSYFPWFSAM	815
13397	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	ITYSSI	361	SISSYYGYTA	764	SSYFPWSSAM	837
13398	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	NSFLI	649	ISRSSI	700	GISSYYGYTR	765	SHYFPWLSAL	838

Table 4 LRP6 – antibody			LRP6 binding antibodies CDRs											
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
13399	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYNPI	650	ISYASI	701	SISPYYGYTR	766	ASYYPWFSAM	839
13400	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YGFLI	651	LDYSSI	702	SISPYYSYTT	767	SSYIPWRYAI	840
13401	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFLI	624	ISYSSI	363	SISPYYSYTN	74	SSYFPWISAM	841
13402	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	IYYYSM	530	GISSYYSYTS	768	SSYFPWISAL	842
13403	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	ISYSSM	358	SISPYYSFTS	769	SSRFPWISGM	843
13404	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YNFLI	652	ISYSSI	363	SISSYYGFTS	68	SSYFPWFSAL	830
13405	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	ISYSSI	363	SISSYYGFTS	68	SPYFPWSSAL	844
13406	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	LSYSAI	703	YISPYYGYTY	65	ASYLPWFSAM	845
13407	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSFLI	653	LSGFGI	704	FISSYYGYTA	770	SSYLPWITAM	846
13408	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YVFLI	654	LSFASM	705	SISSYYGYTP	771	SAYFPWFAAL	847
13409	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	LAYNSI	706	SIFSYYSYTN	772	SSYFPWFSAM	815
13410	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	FYGPI	655	ISFSSI	357	SISSYYGYTL	773	SSYFPWFFAM	848
13411	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YFFLI	656	LYYSNI	707	YISSYYGYTS	774	SSYFPWFSAL	830
13412	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYGPI	657	IHYYSI	708	SISPYYSFTD	775	SSYFPWFSAM	815
13413	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YDFLI	648	ISFASI	709	SIYSYYSFTN	776	SSHFPWVSAL	849
13414	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYSPI	644	IYYSSM	378	SISPYYGYTS	557	SSYFPWVSAM	850
13415	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFLI	624	LSYFSM	710	SIYSYYGFTN	777	SSHFPWFSAM	851
13422	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	FYGPI	655	LFYSSM	695	TISPYYGYTS	778	SSYFPWFSAL	830
13428	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YTLPI	658	ISFSSM	380	HISSYYGFTS	779	SSYFPWFSAL	830
13430	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YRFPI	659	ISYFSI	711	SISPYYSYTN	74	SSYFPWFSAI	852
13431	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YHLLI	660	LYYNSI	712	AIHPYYGYTS	780	SSRFPWFPAM	853
13432	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSFPI	661	LSYASI	713	SISSYYGYTG	781	SSYFPWFSAM	815
13435	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YFLPI	662	LSYSSM	364	SISPYYGFTY	782	SSYFPWFSAL	830
13436	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYFPI	647	ISYASM	714	SISSYYGYTD	783	SSYVPWFYAL	854
13437	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YDNLI	663	ITYSSI	361	SISSYYGFTS	68	SSYFPWFSAM	815

Table 4 LRP6 – antibody			LRP6 binding antibodies CDRs											
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
13438	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YLFPI	664	ISYYSI	715	SIYSYYGYTT	784	ASYFPWFPAM	855
13439	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YFFPI	665	LSHSSI	716	SISSHYGYTH	785	SSYFPWFFAL	856
13440	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYIPI	666	IAYNSM	717	SISSYYSYTD	760	SSYFPWFSAL	830
13441	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	FNFLI	667	LSYSSI	344	YISSYYGYTA	786	SSYYPWFSAL	857
13442	2540AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YNYLI	668	LAYSSI	690	SISSYYGYTY	787	SSYLPWVSAL	858
12990	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	ISLFFM	718	SIYSSYSYTS	788	SFNGAKKPYFSGWAM	859
12991	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	IPSYFM	719	SIYSSYSYTA	789	NVVVSRKPYFFRSAM	860
12992	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	ISSSYM	348	SIYSSYSYTG	790	TVPGSKRPYFASLAI	861
12993	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	ISSYFI	720	SIYPSYSYTS	791	NVRGFRKPYFSRWAM	862
12994	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	LSSYYM	721	SIYSRFSYTA	792	NVPGIKRPYFTAWAM	863
12995	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SYWPI	669	LHSYYI	722	NIYSSYGYTS	793	TIRGSKRPYFAASGL	864
12996	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	LSSYYM	721	SIYSSYSYTS	788	TARENKKPYFSGWAM	865
12997	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYRPI	670	IGSYYM	723	AIYSPYGYTS	794	TLPLSKKPYFSLWAF	866
12998	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	LGSYYI	724	TIYSYYSYTS	795	TFHGSKKPYFSGRAM	867
12999	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	LTSYYI	725	SIYPSYSYTS	791	SIRGSKKPYFSRLAL	868
13000	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	ISTYYM	726	SIYPSYSYTS	791	SVRGSKKPYFSHWAM	869
13001	2542AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YYWPI	623	ISSNYI	548	SIYSSFGYTS	796	NVRTSKKPYFPLWAM	870
13011	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	ASNNLI	671	IPLYTI	727	SISPSYSYTY	797	GVSGGSNYISIFRNSSGM	871
13012	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSYSLI	130	IFSTSI	728	SITSAYSYTY	798	GGLSVSHYNYVHSFKWGL	872
13013	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SAITPI	672	ISYSTM	729	SIVSSYSRTY	799	SCSSFCNYVSNYNARRAL	873
13014	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	FSYSPF	673	LSSSGM	730	AIYPFDGYTY	800	GNARVSNYISSYYAWRAM	874
13015	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSYNLI	674	FSSSSI	528	GIFSYFSYTY	801	GGYGFSYYNSVTFYRWAF	875

Table 4 LRP6 – antibody			LRP6 binding antibodies CDRs										
Antibody ID	Library	Antigen	L1	SEQ ID NO:	L2	SEQ ID NO:	L3	SEQ ID NO:	H1	SEQ ID NO:	H2	SEQ ID NO:	H3	SEQ ID NO:
13016	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SYNFPF	675	IRGPSI	731	SISPFCGFTY	802	VGSGVCNSLHNYFYKRGM	876
13017	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSTVPF	676	FSSTYM	732	SITPSYGYTN	803	SSSDISIDNSIRYTWGAM	877
13018	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSYSLI	130	INSSFM	733	SISPSYGYTY	804	GHSGVTNFISFYYRRRAM	878
13019	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SNYSLF	677	IFGYSM	734	SIFPCCSNTY	805	GVSGLDNNRTASYSRMGM	879
13020	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	STYSLI	678	FSSSTI	735	SIAPSFGHTY	806	GAASVNHIGSLYVSWRGL	880
13021	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SAFSLI	679	LSSSTM	736	SISPYYSYTR	807	HGSGLSHNATTSYYRSAI	881
13022	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSYSLI	130	ISYTSI	737	SIFSTYSYTY	808	SSSAVSRNSIVYYSRTAM	882
13023	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSYTPI	680	FSSSVM	738	SIAPSYSFTY	809	GVCRVSNYSSYFYSRGAM	883
13024	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YSNSLI	681	ISYSTM	729	SITPYYSTTS	810	AISHVAHYDNVIYSKWGI	884
13025	2460AM	LRP6-Fc	SVSSA	1	SASSLYS	2	SSYSLI	130	IASYSM	739	FISPYHSYTD	811	GHSVLSNYVSIHYYWAGF	885
13026	8716AM	LRP6-Fc	SVSSA	1	SASSLYS	2	YWAYFSPI	682	FSYSSM	740	SISSRYGYTY	812	SWAM	586

EXAMPLE 3: Tetravalent binding antibody molecule formats

A. We generated various formats of tetravalent binding antibody molecules comprising pan-FZD and LRP5/6 antibody fragments, e.g., scFv, diabodies and Fab, on either end of an Fc domain, see Table 5 and Figure 6, and assayed their Wnt agonist activity. DNA fragments encoding antibody variable domains were either amplified by PCR from phagemid DNA template or were constructed by chemical synthesis (Twist Biosciences). The DNA fragments were cloned into mammalian expression vectors (pSCSTa). Bispecific diabodies and IgGs contained an optimized version of a "knobs-in-holes" heterodimeric Fc (Ridgway et al. Protein Eng. 9, 617–621 (1996)). Diabody domains were arranged in a VH-VL orientation with the variable domains separated by a short GGGGS linker (SEQ ID NO: 886), which favors intermolecular association between VH and VL domains and thus favors diabody formation. To produce diabody fusion constructs, the diabody chains were fused to human IgG1 Fc. Diabody-fc-diabody proteins were constructed as VH-x-VL-y-[human IgG1 Fc]-z-VH-x-VL where linkers are x= GGGGS (SEQ ID NO: 886), y= LEDKTHTKVEPKSS (SEQ ID NO: 887), and z= SGSETPGTSESATPESGGG (SEQ ID NO: 888). In this format, the human IgG1 Fc or knob-in-hole IgG1 Fc fragments spanned from position 234-478 (Kabat numbering). For scFv-Fc fusions, the variable domains were arranged in a VL-VH orientation and were connected by a long GTTAASGSSGGSSSGA linker (SEQ ID NO: 889), which favors intramolecular association between VH and VL domains and thus favors scFv formation. Variants with a Fab domain fused to the C-terminus of the Fc were generated via chemical synthesis (Twist Biosciences). For all constructs, the entire coding region was cloned into a mammalian expression vector in frame with the secretion signal peptide.

These various of tetravalent binding antibody molecules comprising pan-specific FZD and LRP5/6 antibody fragments were tested in a TOPFLASH assay to monitor beta catenin-mediated gene reporter activity. Proteins were compared against the native ligand Wnt3a. Assays were performed by plating TOPFLASH cells to ~70% confluency in a 96-well tissue culture treated plate. Agonists were diluted in DMEM to provide a final assay concentration of 0.046 nM – 100 nM and cells were treated overnight at 37°C under 5% CO_2. Luciferase expression was quantified using the Dual-Luciferase Reporter Assay System (Promega) in 96-well black plates in accordance with the manufacturer's instructions. Briefly, HEK293T cells were transduced with lentivirus coding for the pBARls reporter (Biechele and Moon in *Wnt Signaling: Pathway Methods and Mammalian Models*, E. Vincan, Ed. (Humana Press, Totowa,

NJ, 2008), pp. 99–110) and with Renilla Luciferase as a control to generate a Wnt-βcatenin signaling reporter cell line. 1-2 x 10^3 cells in 120 µl were seeded in each well of 96-well plates for 24 hours prior to transfection or stimulation. The following day, FZD Agonists or Ab protein was added, and following 15-20 hours of stimulation, cells were lysed and luminescence was measured in accordance with the dual luciferase protocol (Promega) using an Envision plate reader (PerkinElmer). For the FZD4 Agonist assay, FZD4 cDNA was transfected for 6 hours prior to adding the FZD Agonist. For the Wnt inhibition assays, Wnt1 was introduced by cDNA transfection or WNT3A protein was applied for 6 hours prior to the addition of Ab protein. All assays were repeated at least three times. The results are presented in Table 5. As shown in Table 5, each of the tetravalent formats activate FZD signaling to differing degrees when clustering FZD4 and LRP5. These formats were also evaluated for stability, homogeneity and yield production from Expi293 (Figures 3 and 9). From these analyses, the Diabody-Fc-Fab format provides the best balance of activity, expression, stability. Finally, we applied the same modality arrangement for FZD5 and LRP6 and we observed potent agonist activity. The results in Table 5 show that the various tetravalent modalities elicit WNT agonism and that engagement of 2 LRP5/6 epitopes produces WNT signaling activity (maxima) higher than with 1 LRP5/6 epitope.

Table 5

Molecule	Modality	Paratopes	Binding specificity (Paratope Stoichiometry)	Topflash EC50 (nM) Avg	Stdev	% Wnt Maxima Avg	Stdev
Wnt3a	Recombinantly produced ligand	NA	FZD/LRP	6	3	100%	ND
CM0011	FZD Diabody-Fc-LRP Diabody	5019 (FZD Diabody); 2539, 2542 (LRP diabody)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.3	0.1	63%	10%
ANT-4	FZD Diabody-Fc-LRP Fab	5016(FZD Diabody); 2540,2542 (LRP Fab)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.5	0.1	63%	6%
ANT-5	FZD Diabody-Fc-LRP Fab	5016(FZD Diabody); 2540,2542 (LRP Fab)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.5	0.1	59%	8%
CT0001	FZD IgG-LRP Diabody	5016(FZD IgG); 2539,2542 (LRP Diabody)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.3	0.1	57%	17%
CT0002	LRP Diabody-Fc-FZD scFv (VL-VH)	2539, 2542 (LRP Diabody); 5016 (FZD scFv)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.5	0.1	55%	22%
CM0126	FZD Diabody-Fc-LRP Diabody	5016(FZD Diabody); 2539, 2542 (LRP Diabody)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.3	0.2	52%	1%
ANT-1	LRP Diabody-Fc-FZD Fab	2540, 2542 (LRP Diabody); 5016 (FZD Fab)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.7	0.5	49%	22%
CT0003	FZD Diabody-Fc-LRP scFv	5016 (FZD Diabody); 2539, 2542 (LRP scFv)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.4	0.1	42%	16%
ANT-2	LRP Diabody-Fc-FZD Fab	2540, 2542(LRP Diabody); 5016(FZD Fab)	FZD1/2/4/5/7/8, LRP6[1], LRP6[3] (2:1:1)	0.3	0.1	38%	25%
CM0042	FZD Diabody-Fc-LRP Diabody	5019(FZD Diabody); 2539 (LRP Diabody)	FZD1/2/4/5/7/8, LRP6[3] (2:2)	0.9	0.8	33%	22%
CM0302	FZD IgG-LRP Diabody	5056(FZD IgG)-2539(LRP Diabody)	FZD1/2/4/5/7/8/10, LRP6[3] (2:2)	0.3	0.2	18%	8%
CM0303	FZD IgG-LRP scFv	5056(FZD IgG); 2539(LRP scFv)	FZD1/2/4/5/7/8/10, LRP6[3] (2:2)	3.7	2.1	17%	13%
CM0299	FZD IgG-LRP Diabody	5016(FZD IgG)-, 2539(LRP Diabody)	FZD1/2/4/5/7/8, LRP6[3] (2:2)	0.1	0.1	14%	5%

Table 5 Cont'

Molecule	**Modality**	**Paratopes**	**Binding specificity (Paratope Stoichiometry)**	**Topflash EC_{50} (nM) Avg Stdev**		**% Wnt Maxima Avg**	**Stdev**
Wnt3a	**Recombinantly produced ligand**	**NA**	**FZD/LRP**	**6**	**3**	**100%**	**ND**
CM0300	FZD IgG-LRP scFv	5016(FZD IgG)-, 2539(LRP scFv)	FZD1/2/4/5/7/8, LRP6[3] (2:2)	0.3	0.2	5%	2%
CM0301	FZD IgG-LRP scFv	5016(FZD IgG)-, 2542(LRP scFv)	FZD1/2/4/5/7/8, LRP6[1] (2:2)	0.2	0.2	1%	1%
CM0156	Diabody-Fc-Diabody	4275	no FZD/LRP binding	NA	NA	NA	NA
4275	IgG	4275	no FZD/LRP binding	NA	NA	NA	NA

B. Diabody-Fc-Fab format FZD4 Agonists.

FZD Agonists having a bispecific LRP5-binding diabody and a FZD4 binding domain comprising FZD4-binding Fabs (FZD4 Agonists), a FZD5 binding domain comprising FZD5-binding Fabs (FZD5 Agonists), or a FZD binding domain that binds multiple FZD (pan-FZD Agonist) were generated using a knob-in-holes system. Briefly, the constructs were generated by chemical synthesis (Twist Biosciences) or by standard molecular biology techniques in a mammalian expression vector (pSCSTa). Diabody constructs were arranged in a VH-VL manner with a short (GGGGS (SEQ ID NO: 886)) linker linking the VH and VL to favor intermolecular pairing. For bispecific diabody arrangements, the variable domains for paratopes A and B, respectively, were arranged as VH(A) – VL(B) on the Hole Fc chain and VH(B)-VL(A) on the Knob Fc chain to facilitate proper paratope formation. Diabodies were fused to the N-terminus of an optimized knob-in-holes heterodimeric Fc (Ridgway et al. Protein Eng. 9, 617–621 (1996) via a GGGGSGGGGSEPKSS linker (SEQ ID NO: 890). The Fc region also contains the effector-null mutations D278A and N314G (Kabat numbering), corresponding to D655A/N297G (EU numbering). Fab domains were fused to the C-terminus of the heterodimeric Fc via a GGGSGGGSGGGSGGGSGSTG linker (SEQ ID NO: 891). Directly to this linker was fused the N-terminus of the Fab VH domain followed by CH1, terminating at T238 (Kabat numbering). This Fab pairs with a standard kappa light chain which was cloned as described above. For all constructs, the entire coding region was cloned into a mammalian expression vector in frame with the secretion signal peptide.

In addition, Diabody-fc-Fab formats were constructed as VH-x-VL-y-[human IgG1 Fc]-z-VH where linkers are x= GGGGS (SEQ ID NO: 886), y= GGGGSGGGGSEPKSSDKTHT (SEQ ID NO: 892), and z= GGGSGGGSGGGSGGGSGSTG (SEQ ID NO: 891). Diabody domains were arranged in a VH-VL orientation with the variable domains separated by a short GGGGS linker (SEQ ID NO: 886), which favors intermolecular association between VH and VL domains and thus favors diabody formation. Further, the Fc region may exhibit attenuated effector functions due amino acid mutations to N297G and D265A (DANG) variants or L234A, L235A, P331S (LALAPS) variants, and with the Fc region further comprising knob-in-hole heterodimerization variants Merrimack, Merchant or Merchant S:S.

Figure 7 is an illustration of the Diabody-Fc-Fab format FZD4 Agonists having a LRP5 binding domain comprised of a diabody that is bivalent and bispecific for LRP5 and a FZD4

binding domain comprised of two FZD4 binding Fab fragments formed by a VL and CL1 of the light chain construct pairing with the VH and CH1 of each of the heavy chain hole and heavy chain knob constructs. Table 12 presents the amino acid sequences of heavy chains and light chains of FZD4 Agonists ANT's (Diabody-Fc-Fab format): the heavy chain knob construct (ANT16 knob), the heavy chain hole construct (ANT hole) and the light chain construct. The light chain and heavy chain variable CDRs are in bold underlined italics.

Figure 16A depicts Diabody-Fc-Fab format FZD4 Agonists having Fc regions with attenuated effector functions due to amino acid mutations, e.g., N297G (NG) and D265A, (DANG) variants, and/or LALAPS variants, and with the Fc region further comprising knob-in-hole heterodimerization variants Merrimack, Merchant or Merchant S:S

B. IgG-Diabody format FZD4 Agonists.

FZD Agonists having two FZD-binding Fabs forming an N-terminal binding domain and a bispecific LRP5/6 binding diabody forming the C-terminal binding domain and an Fc domain were generated using a knob-in-holes system. IgG-Diabody proteins were constructed as VH-[human IgG1 Fc]-y- VH-x-VL where linkers are x= GGGGS (SEQ ID NO: 886) and y= GGGSGGGSGGGSGGGSGSTG (SEQ ID NO: 891).

Figure 15 presents an illustration of the IgG-Diabody format FZD4 Agonists having an FZD binding domain comprising two Fab fragments attached to the N- terminus of the Fc domain with each Fab binding an FZD. The LRP5/6 co-receptor binding domain is attached to the C-terminus of the Fc domain and is composed of a diabody that binds two different sites on the co-receptor, e.g., a Wnt1 site (E1-E2) and a Wnt3 site (E3-E4) on LRP5/6. The Fabs may be specific for a particular FZD, e.g. FZD4, or may be pan-specific, binding to more than one FZD, e.g., to FZD4 and one or more other FZD.

Figure 16B depicts IgG-Diabody FZD4 Agonists having Fc regions with attenuated effector functions due to amino acid mutations, e.g., N297G (NG) and D265A, (DANG) variants, and/or LALAPS variants, and with the Fc region further comprising knob-in-hole heterodimerization variants Merrimack, Merchant or Merchant S:S. Table 13 presents the amino acid sequences of heavy chains and light chains of FZD4 Agonist, ANT39 (Diabody-Fc-Fab format) and ANT39wi (IgG-Diabody format): the heavy chain knob construct (ANT39 and ANT39i knob), the heavy chain hole construct (ANT39 and ANT39i hole) and the light chain construct. Also included in Table 13 are amino acid sequences of heavy chains

and light chains of FZD4 Agonist, ANT39 and ANT39i variants DANG, LALAPS, LALAPS Merchant and LALAPS Merchant S-S. The light chain and heavy chain variable CDRs are in bold underlined italics.

Table 6A	LRP5 Diabody Site 1						LRP5 Diabody Site 2				
Molecule	[1]	[2]	SEQ ID NO	[3]	SEQ ID NO	[4]	SEQ ID NO	[5]	SEQ ID NO	[6]	SEQ ID NO
		CDR-H1		CDR-H2		CDR-H3		CDR-L2		CDR-L3	
ANT16-Hole	D	FSSSSI	528	SISSSYGYTY	553	SWAM	586	SASDLYS	491	YAGAGLI	510
ANT16-Knob	D	FTAYAM	536	SIYPSGGYTA	566	RSYYFAL	603	SASSLYS	2	YWAYYSPI	493
ANT18-Hole	N	LSYYYM	527	SIYSSYGYTY	552	WSHVSGHYSGM	584	SASSLYS	2	SSYSLI	130
ANT18-Knob	N	FSSSSI	528	SISSSYGYTY	553	GGSGVSHYGSVYYSWWAL	585	SASSLYS	2	ASYAPI	492
ANT20-Hole	N	LSYYYM	527	SIYSSYGYTY	552	WSHVSGHYSGM	584	SASDLYS	491	YAGAGLI	510
ANT20-Knob	D	FTAYAM	536	SIYPSGGYTA	566	RSYYFAL	603	SASSLYS	2	ASYAPI	492
ANT21-Hole	N	FSSSSI	528	SISSSYGYTY	553	SWAM	586	SASSLYS	2	SSYSLI	130
ANT21-Knob	N	FSSSSI	528	SISSSYGYTY	553	GGSGVSHYGSVYYSWWAL	585	SASSLYS	2	YWAYYSPI	493
ANT36-Hole	N	LSYYYM	527	SIYSSYGYTY	552	WSHVSGHYSGM	584	SASSLYS	2	SSYSLI	130
ANT36-Knob	N	FSSSSI	528	SISSSYGYTY	553	GGSGVSHYGSVYYSWWAL	585	SASSLYS	2	ASYAPI	492
ANT39-Hole	D	FSSSSI	528	SISSSYGYTY	553	SWAM	586	SASDLYS	491	YAGAGLI	510
ANT39-Knob	D	FTAYAM	536	SIYPSGGYTA	566	RSYYFAL	603	SASSLYS	2	YWAYYSPI	493
ANT42-Hole	D	FSSSSI	528	SISSSYGYTY	553	SWAM	586	SASDLYS	491	YAGAGLI	510
ANT42-Knob	D	FTAYAM	536	SIYPSGGYTA	566	RSYYFAL	603	SASSLYS	2	YWAYYSPI	493

In all the molecules the LRP5 Diabody site 2 CDR-L1 is SVSSA (SEQ ID NO: 1)

Table 6B		FZD4 FAb							
Molecule	[7]	[8]	SEQ ID NO:	[9]	SEQ ID NO:	[10]	SEQ ID NO:	[11]	SEQ ID NO:
		CDR-H1		CDR-H2		CDR-H3		CDR-L3	
ANT16-Hole	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT16-Knob	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT18-Hole	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT18-Knob	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT20-Hole	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT20-Knob	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT21-Hole	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT21-Knob	T	LSSYSM	24	YISSYYGYTY	51	PAPGHWGF	79	WYYAPI	3
ANT36-Hole	T	LSSYSM	24	YISSYDSITD	61	PAVGHMAF	90	WYNAPI	12
ANT36-Knob	T	LSSYSM	24	YISSYDSITD	61	PAVGHMAF	90	WYNAPI	12
ANT39-Hole	T	LSSYSM	24	YISSYDSITD	61	PAVGHMAF	90	WYNAPI	12
ANT39-Knob	T	LSSYSM	24	YISSYDSITD	61	PAVGHMAF	90	WYNAPI	12
ANT42-Hole	T	SDFYFI	164	TIYPFIGNTY	194	AFPGSYHPF	220	STGSLI	135
ANT42-Knob	T	SDFYFI	164	TIYPFIGNTY	194	AFPGSYHPF	220	STGSLI	135

In all the molecules the FZD FAB CDR-L1 and CDR-L2 are respectively SVSSA (SEQ ID NO: 1) and SASSLYS (SEQ ID NO: 2)

Table 6C	LRP6 Diabody Site 1						LRP6 Diabody Site 2				
Molecule	[1]	[2]	SEQ ID NO	[3]	SEQ ID NO	[4]	SEQ ID NO	[5]	SEQ ID NO	[6]	SEQ ID NO
		CDR-H1		CDR-H2		CDR-H3		CDR-L2		CDR-L3	
ANT59-Hole	D	ISSYFI	720	SIYPSYSYTS	791	NVRGFRKPYFSRWAM	862	SASSLYS	2	YFFPI	665
ANT59-Knob	D	LSHSSI	716	SISSHYGYTH	785	SSYFPWFFAL	856	SASSLYS	2	YYWPI	623
ANT9-Hole	D	ISSYFI	720	SIYPSYSYTS	791	NVRGFRKPYFSRWAM	862	SASSLYS	2	YFFPI	665
ANT9-Knob	D	LSHSSI	716	SISSHYGYTH	785	SSYFPWFFAL	856	SASSLYS	2	YYWPI	623

In all the molecules the CDR-L1 of all LRP abs are SVSSA (SEQ ID NO: 1)

Table 6D	FZD Paratope									
Molecule	FZD Specificity	7	H1 (8)	SEQ ID NO	H2 (9)	SEQ ID NO	H3 (10)	SEQ ID NO	L3 (11)	SEQ ID NO
			CDR-H1		CDR-H2		CDR-H3		CDR-L3	
ANT59-Hole	5	N	IAYSSM	365	TIYPSYSSTY	462	YYAM	484	AHYFPI	285
ANT59-Knob	5	N	IAYSSM	365	TIYPSYSSTY	462	YYAM	484	AHYFPI	285
ANT9-Hole	1,2,4,5,7,8	N	IHSSSI	893	ATYSSFGSIT	894	YHHPFGYAL	895	GVYLF	896
ANT9-Knob	1,2,4,5,7,8	N	IHSSSI	893	ATYSSFGSIT	894	YHHPFGYAL	895	GVYLF	896

In all molecules the CDR-L1 for FZD FAB are SVSSA (SEQ ID NO: 1) and CDR-L2 are SASSLYS (SEQ ID NO: 2)

C. FZD Agonists are highly specific for FZD4, bind with high specificity and are stable in solution.

Using biolayer interferometry (BLI) we have found that FZD4 Agonists described herein are highly specific for FZD4 over other FZD receptors. Recombinant FZD ECD proteins were immobilized on BLI sensors. The FZD4 Agonists in the Diabody-Fc-Fab format, having a LRP5 binding domain comprised of a diabody that is bivalent and bispecific for LRP5 and a FZD4 binding domain comprised of two FZD4 binding Fab fragments, were tested at a concentration of 100 nM in a buffer of PBS+0.05% Tween-20 and 1% BSA for binding to the ECD proteins. The results are presented in Figure 8A. Controls in the assay included CM0199, a diabody-Fc-diabody format FZD agonist that recognizes FZD4 and LRP5 and Immunoglobulin 4275, which is an IgG that does not bind FZD or LRP.

The FZD4 Agonists also did not recognize common non-specific antigens. The FZD4 Agonists were tested at 100 nM for binding to a panel of antigens essentially as described in Monquet et al. “Polyreactivity increases the apparent affinity of anti-HIV antibodies by heteroligation” Nature 2010 Sep 30;467(7315):591-5(PMC3699875), and Jain et al., “Biophysical properties of the clinical-stage antibody landscape” Proc Natl Acad Sci 2017 Jan 31;114(5):944-949. (PMC5293111). Controls in the assay included CM0199, a diabody-Fc-diabody format FZD agonist that recognizes FZD4 and LRP5 and immunoglobulin 6606, which is an IgG that is particularly prone to non-specific binding in this assay. The results are presented in Figures 8B.

The FZD4 Agonists comprising binding domains for FZD4 and LRP5 bind both FZD4 and LRP5 with high affinity. The apparent affinity of the FZD4 Agonists for recombinant ECD of FZD4 were determined by biolayer interferometry essentially as described in Elife. 2019 Aug 27; 8: e46134., Briefly, BLI assays were performed using an Octet HTX instrument (ForteBio). For measuring binding to antigen, FZD-Fc proteins were captured on AHQ BLI sensors (18–5001, ForteBio) to achieve a BLI response of 0.6–1 nm and remaining Fc-binding sites were saturated with human Fc (009-000-008, Jackson ImmunoResearch). FZD-coated or control (Fc-coated) sensors were transferred into 100-0.1 nM tetravalent FZD agonist in assay buffer (PBS, 1% BSA, 0.05% Tween20) and association was monitored for 300 s. Sensors were then transferred into assay buffer and dissociation was monitored for an

additional 300 s. Shake speed was 1000 rpm and temperature was 25°C. The results are presented in Table 7.

Table 7		
Molecule	FZD4 KD (nM)	LRP5 EC50 (nM)
CM0199	0.7	7.5
ANT16	0.6	1.4
ANT18	2.6	ND
ANT20	0.7	ND
ANT21	2.2	ND
ANT36	<0.1*	ND
ANT39	0.3	ND

The FZD4 Agonists were also analyzed by SEC as compared to trastuzumab IgG. The results are presented in Figure 9A and demonstrate that the diabody-Fc-Fab format Agonists are stable and homogenous in solution.

The FZD4 Agonists are also stable in solution. Purified FZD4 Agonists, ANT16, ANT18, ANT20, ANT21 and ANT 36 were resuspended to 1 mg/ml (except for ANT18, which was resuspended at 0.34 mg/ml) in 10 mM Histidine, 140 mM NaCl, 0.9% sucrose, pH 6 and stored either at 4°C or 40°C for a period of 6 days. Samples were removed at various time points, centrifuged to remove precipitated protein and residual protein concentration was measured. The results are presented in Tables 8 and 9.

Table 8				
	Soluble Protein Remaining (%)			
Time at 40 degrees (days)	**0**	**1**	**2**	**6**
CM0199	100%	60%	64%	40%
ANT-16	100%	102%	104%	104%
ANT-18	100%	92%	83%	105%
ANT-20	100%	97%	67%	104%
ANT-21	100%	102%	75%	102%
ANT-36	100%	100%	149%	106%

Table 9		
	Active Protein Remaining (%)	
Time at 40 degrees (days)	0	6
CM0199	100%	42%
ANT-16	100%	34%
ANT-18	100%	42%
ANT-20	100%	30%
ANT-21	100%	25%

On Day 6, the amount of FZD4-specific binding sites remaining in the samples were quantified using BLI. Analysis by differential scanning fluorimetry showed that the FZD4 Agonists having a Diabody-Fc-Fab formats with an LRP-binding diabody on the N-terminal of the Fc domain and two FZD4-binding Fabs on the C-terminal of the Fc domain, have thermal denaturation profiles similar to that of Trastuzumab. IgGs generally display two peaks in a thermal stability assay, the first corresponding to CH2, the later to the Fab domain and CH3, see Figure 9B.

The FZD4 Agonists were also assayed for induction of the beta-catenin target gene *AXIN2* in a mouse endothelial cell line (bEND3.1) and were shown to induce transcription in a concentration dependent manner. These results are presented in Figure 10.

TABLE 10			
Antibody No.		FZD recognized	Co-Receptor recognized
5019		FZD1, FZD2, FZD4, FZD5, FZD7, FZD8	
5027		FZD4	
5044		FZD4	
5016		FZD1, FZD2, FZD4, FZD5, FZD7, FZD8	
5056		FZD1, FZD 2, FZD 4, FZD5, FZD7, FZD8, FZD10	
2459			LRP5-W3
2460			LRP5-W1
8716			LRP5-W3

TABLE 10

Antibody No.		FZD recognized	Co-Receptor recognized
12600			LRP5-W1
12608			LPR5-W1
2539			LRP6-W3
2540			LRP6-W3
2542			LRP6-W1
CM0199		FZD4	LRP5
6066		N/A Positive control for non-specificity assay	
4275		no FZD/LRP binding	

EXAMPLE 4. The FZD4 agonist was assayed for its ability to oppose the effect on cell junction disassembly and increased permeability mediated by VEGF, a cytokine released during tissue hypoxia. VEGF treatment of bEND3.1 cells leads to junction disassembly as seen by loss of plasma membrane staining of CLDN3, CLDN5 and ZO-1. Co-treatment of cells with VEGF and the FZD4 agonist leads to a near-complete rescue of this effect (Fig. 11). This decrease cell-cell junction stability mediated by VEGF treatment translates into increase endothelial cell permeability as monitor in a transendothelial permeability assay measuring the passage of 40-kDa FITC-dextran across a confluent endothelial monolayer of bEnd.3 grown on transwell filters. Co-treatment of cells with VEGF and the FZD4 agonist completely rescues that VEGF-mediated increase in cell permeability. These results indicate that the FZD4 agonist promotes endothelial cell barrier functions in a mechanism independent of VEGF.

A) Immunofluoresence of ZO-1 (green)/CLDN3(red) and ZO-1 (green)/CLDN5(red) localization on bEnd.3 cell junctions. bEnd.3 cells were treated or not with 30nM of F4L5.13 (aka CM0199) and Norrin in the presence or absence of VEGF (100ng/ml) for 1h. DAPI (blue) stain the nucleus. B) Transendothelial permeability was determined by measuring the passage of FITC-dextran through the bEnd.3 monolayer. Passage of FITC-dextran was measured after bEnd.3 treatment with VEGF (100ng/ml) and F4L5.13 (30nM) alone or

simultaneously or upon pre-treatment with VEGF for 1h followed by F4L5.13 treatment for 1h. Error bar indicate SEM, n=5. The results are presented in Figure 11.

EXAMPLE 5. New FZD5 antibodies bind FZD5 at a site overlapping with 2919 identified from affinity maturation libraries.

Single point ELISAs were performed on 96-well Maxisorp plates coated with the ECDs of human FZD5 protein in the presence or absence of a saturating concentration of 2919 IgG. The plates were incubated with the monoclonal Fab-phage followed by incubation with horseradish peroxidase (HRP)-conjugated anti-M13 antibody. Wells were subsequently washed 8 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 5-10 min. the reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader. The results are presented in Figure 12.

EXAMPLE 6. New FZD5 antibodies from 2928 affinity maturation library selectively bind FZD5.

Single point ELISAs were performed on 96-well Maxisorp plates coated with the ECDs of human FZD2, FZD5, or FZD8 protein. The plates were incubated with the monoclonal Fab-phage followed by incubation with horseradish peroxidase (HRP)-conjugated anti-M13 antibody. Wells were subsequently washed 8 times followed by incubations with 3,3,'5,5'-tetramethylbenidine/H_2O_2 peroxidase (TMB) substrate for 5-10 min. the reaction was stopped by adding 1M H_3PO_4 and the absorbance was measured spectrophotometrically at 450 nm in a microtiter plate reader. The results are presented in Figure 13.

EXAMPLE 7. Pan-FZD/LRP6 ANT9 and FZD5-specific/LRP6 ANT9 activate Wnt signaling in cells.

TOPFLASH HEK293 cells were treated overnight with varying concentrations of FZD agonist or a non-targeting control molecule (CM0156) and TCF/LEF-driven luciferase expression was measured using a standard luciferase assay. Both molecules are able to activate FZD-mediated luciferase expression in a concentration-responsive manner. ANT9,

which is able to bind to 7 of the 10 FZD receptor subtypes produces a higher maximal activation signal than the FZD5-specific ANT59.

In vivo Experiments

DSS induced colitis model

In figure 24, C57/BL6 mice were given 2% DSS in the drinking water for 7 days and 0.5% DSS for an additional 3 days to induce colitis. Control-FLAg, Pan-FLAg and ANT59 were administered via intraperitoneal injection on days 4 and 7 at a dosage of 10 mg/kg. Mice were weighed daily. On day 10 mice were euthanized and tissues were harvested for measurement of colon length and histology.

Histology

For histological analysis, harvested tissues were fixed in 4% paraformaldehyde and embedded in paraffin. Sections of 5 μm were stained with haematoxylin and eosin (H&E). Images were captured using a Nikon Eclipse microscope (figure 23).

Organoid Culture and Viability Measurement

Small intestine crypts were harvested from 8-week-old, female, C57BL/6 mice and cultured as previously described (O'Rourke et al., 2016). Organoid cultures were passaged and embedded in 25 μl Growth Factor Reduced Matrigel (Corning, 356231) and plated in triplicates in a 48-well plate. Organoid cultures were treated with DMSO, 1 μM LGK974, 1 μM LGK974 +50% WNT3A conditioned media, 1 μM LGK974 +30 nM Pan-FLAg, 1 μM LGK974 +30 nM FZD2-FLAg, 1 μM LGK974 +30 nM FZD4-FLAg, 1 μM LGK974 +30 nM FZD5-FLAg, 1 μM LGK974 +30 nM FZD7-FLAg. Treatments were prepared in 250 μl of complete media, added to each well on day of passaging and changed every 2–3 days. At the endpoint (7 days), 150 μl Cell Titer-Glo3D (Promega) was added to 150 μl media in each well. Organoids were lysed on a rocking platform for 30 min at room temperature. The luminescence reading was measured in duplicates for 20 μl lysate from each well on the Envision multilabel plate reader. The average luminescence reading for each condition was normalized to the control condition to calculate relative viability (figure 22).

EXAMPLE 8. Transient expression of 8 ANT39 variants. A series of eight ANT39 variants (Figures 16A and 16B) were transiently expressed in CHO cells using standard manufacture

lipid based protocols (ThermoFisher). Briefly cells were grown to a density of approximately 2.0 x106 cells/ml in growth media and relevant DNAs were transfected with appropriate transfection reagent. For each variant two alternate input plasmid ratios were tested, either 1:1:2 or 2:1:3 (knob heavy chain : hole heavy chain : light chain). Conditioned media was harvested 7 days later, purified by Protein A Sepharose and the titre measured.

Table 11

Molecule	**DNA Ratio (Knob:Hole:LC)**	**Titer (mg/L)**
ANT39	1:1:2	390
	2:1:3	290
ANT39i	1:1:2	260
	2:1:3	250
ANT39 LALAPS	1:1:2	330
	2:1:3	250
ANT39i LALAPS	1:1:2	300
	2:1:3	270
ANT39 LALAPS Merchant	1:1:2	340
	2:1:3	280
ANT39i LALAPS Merchant	1:1:2	240
	2:1:3	280
ANT39 LALAPS Merchant S:S	1:1:2	320
	2:1:3	190
ANT39i LALAPS Merchant S:S	1:1:2	300
	2:1:3	250
ANT42*	1:1:2	107
ANT42 LALA*	1:1:2	287
ANT42 LALAPS*	1:1:2	95
ANT42i LALAPS*	1:1:2	49

*Variants were transiently expressed in HEK293 cells

Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, numerous equivalents to the specific procedures described herein. Such

equivalents are considered to be within the scope of the inventions. Various substitutions, alterations and modifications may be made to the invention without departing from the spirit and scope of the invention. Other aspects, advantages, and modifications are within the scope of the invention.

The contents of all references, issued patents, and published patent applications cited through this application are hereby incorporated by reference. The appropriate component, process and methods of those patents, applications and other documents may be selected for the invention and embodiments thereof.

Throughout the specification and the claims which follow, unless the context requires otherwise, the word ‘comprise’, and variations such as ‘comprises’ and ‘comprising’, will be understood to imply the inclusion of a stated integer, step, group of integers or group of steps but not to the exclusion of any other integer, step, group of integers or group of steps.

To clarify the use of and to hereby provide notice to the public, the phrases "at least one of <A>, <B>, … and <N>" or "at least one of <A>, <B>, … or <N>" or "at least one of <A>, <B>, … <N>, or combinations thereof" or "<A>, <B>, … and/or <N>" are defined by the Applicant in the broadest sense, superseding any other implied definitions hereinbefore or hereinafter unless expressly asserted by the Applicant to the contrary, to mean one or more elements selected from the group comprising A, B, … and N. In other words, the phrases mean any combination of one or more of the elements A, B, … or N including any one element alone or the one element in combination with one or more of the other elements which may also include, in combination, additional elements not listed. Unless otherwise indicated or the context suggests otherwise, as used herein, "a" or "an" means "at least one" or "one or more."

Table 12
Diabody-Fc-Fab amino acid sequences of the "heavy chain" hole construct, "heavy chain" knob construct and the "light chain" construct of the FZD4 Agonists, ANT16, ANT18, ANT20, ANT21, ANT39, and ANT42.

The CDRs of the chains are underlined, italicized. The CDRs may be replaced with the CDRs of another antibody to alter the binding specificity, e.g., the specificity could be altered to bind another site on the FZD or LPR5/6, or to another FZD or LPR.

FZD4 Agonist ANT16	
Knob Hc construct	EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQ MNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGK APKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKTSDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVES GGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAED TAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 897)
Hole Hc construct	EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMN SLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKL LIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQ PGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYC AR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 898)
Light Chain	DIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYY CQQ***WYYAPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 899)

FZD4 Agonist ANT18	
Knob Hc construct	MNLLLILTFVAAAVAEVQLVESGGGMVQPGGSLRLSCAASGF***NFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***GGSGVSHYGSVYYSWWAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSAS VGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***ASYAPI***TFG QGTKVEIKGGGGSGGGGSEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKN QVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYY GYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHT (SEQ ID NO: 900)
Hole Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NLSYYYM***HWVRQAPGKGLEWVA***SIYSSYGYTY***YADSVKG RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***WSHVSGHYSGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVT ITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SSYSLI***TFGQGTKVEI KGGGGSGGGGSEPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCA VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGG GSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***YADS VKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH T (SEQ ID NO: 901)
Light Chain	MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGT DFTLTISSLQPEDFATYYCQQ***WYYAPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 902)

FZD4 Agonist ANT20	
Knob Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***ASYAPI***TFGQGTKVEIKGGGGSGG GGSEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY GSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGG GSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNT AYLQMNSLRAEDTAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 903)
Hole Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NLSYYYM***HWVRQAPGKGLEWVA***SIYSSYGYTY***YADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCAR***WSHVSGHYSGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCR ASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASDLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGG GGSGGGGSEPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGG GSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADT SKNTAYLQMNSLRAEDTAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 904)
Light Chain	MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDF TLTISSLQPEDFATYYCQQ***WYYAPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 902)

FZD4 Agonist ANT21	
Knob Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***GGSGVSHYGSVYYSWWAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSAS VGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***T FGQGTKVEIKGGGGSGGGGSEPKTSDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ*PREPMVFDLPPSREEMTKNQVSL WCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG KGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***Y ADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHT (SEQ ID NO: 905)
Hole Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SSYSLI***TFGQGTKVEIKGGGGSG GGGSEPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGG GSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISA DTSKNTAYLQMNSLRAEDTAVYYCAR***PAPGHWGF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 906)
Light Chain	MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGT DFTLTISSLQPEDFATYYCQQ***WYYAPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 902)

FZD4 Agonist ANT39	
Knob Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVK GRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITC RAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVE IKGGGGSGGGGSEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVH NAKTKPREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSL WCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP GKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD*** YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHT (SEQ ID NO: 907)
Hole Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QS VSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGG GSGGGGSEPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGF YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGG GSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 908)
Light Chain	MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSG TDFTLTISSLQPEDFATYYCQQ***WYNAPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD NALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 909)

FZD4 Agonist ANT42	
Knob Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVK GRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCR AS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK GGGGSGGGGSEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNA KTKPREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCM VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGG GSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADS VKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH T (SEQ ID NO: 910)
Hole Hc construct	MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASDLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGG SGGGGSEPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGG SGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFT ISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 911)
Light Chain	MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRASQ***SVSSAVA***WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGT DFTLTISSLQPEDFATYYCQQ***STGSLI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 912)

FZD5-LRP6 ANT 59	
Knob Hc construct	EVQLVESGGGLVQPGGSLRLSCAASGF***DLSHSSI***HWVRQAPGKGLEWVA***SISSHYGYTH***YADSVKGRFTISADTSKNTAYLQM NSLRAEDTAVYYCAR***SSYFPWFFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKP GKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGGGGSGGGGSEPKTSDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVES GGGLVQPGGSLRLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAED TAVYYCAR***YYAM***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 913)
Hole Hc construct	EVQLVESGGGLVQPGGSLRLSCAASGF***DISSYFI***HWVRQAPGKGLEWVA***SIYPSYSYTS***YADSVKGRFTISADTSKNTAYLQMN SLRAEDTAVYYCAR***NVRGFRKPYFSRWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAW YQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YFFPI***TFGQGTKVEIKGGGGSGGGGSEPKSS DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEV QLVESGGGLVQPGGSLRLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNS LRAEDTAVYYCAR***YYAM***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 914)
Light Chain	DIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYY CQQ***AHYFPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 915)

pFZD-LRP6 ANT9	
Knob Hc construct	EVQLVESGGGLVQPGGSLRLSCAASGF***DLSHSSI***HWVRQAPGKGLEWVA***SISSHYGYTH***YADSVKGRFTISADTSKNTAYLQM NSLRAEDTAVYYCAR***SSYFPWFFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKP GKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGGGGSGGGGSEPKTSDKTHT CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVES GGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADTSKNTAYLQMNSLRAEDT AVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 916)
Hole Hc construct	EVQLVESGGGLVQPGGSLRLSCAASGF***DISSYFI***HWVRQAPGKGLEWVA***SIYPSYSYTS***YADSVKGRFTISADTSKNTAYLQMN SLRAEDTAVYYCAR***NVRGFRKPYFSRWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAW YQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YFFPI***TFGQGTKVEIKGGGGSGGGGSEPKSS DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEV QLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADTSKNTAYLQMNSL RAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 917)
Light Chain	DIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYY CQQ***GVYLF***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 918)

diabody-Fc-diabody FZD4 CM0199	
Knob Hc construct	EFEVQLVESGGGLVQPGGSLRLSCAASGF***NSSFYFM***HWVRQAPGKGLEWVA***TVYPYLDYTY***YADSVKGRFTISADTSKNTAYL QMNSLRAEDTAVYYCAR***AFPGSYHPM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQ KPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SSYSLI***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESG GGLVQPGGSLRLSCAASGF***NFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTA VYYCAR***GGSGVSHYGSVYYSWWAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKP GKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***ASYAPI***TFGQGTKVEIK (SEQ ID NO: 919)
Hole Hc construct	EFEVQLVESGGGLVQPGGSLRLSCAASGF***NSSFYFM***HWVRQAPGKGLEWV***ATVYPYLDYTY***YADSVKGRFTISADTSKNTAYL QMNSLRAEDTAVYYCAR***AFPGSYHPM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQ KPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SSYSLI***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGG GLVQPGGSLRLSCAASGF***NLSYYYM***HWVRQAPGKGLEWVA***SIYSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTA VYYCAR***WSHVSGHYSGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLL IY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SSYSLI***TFGQGTKVEIK (SEQ ID NO: 920)

Table 13

Diabody-Fc-Fab and IgG-Diabody amino acid sequences of the "heavy chain" hole construct, "heavy chain" knob construct and the "light chain" construct of the FZD4 Agonists, ANT39 and ANT42, ANT39 and ANT42, and ANT39i and ANT42i having Fc domain amino acid mutations DANG, LALAPS, LALAPS and Merchant or LALAPS and Merchant S-S. Mature sequences do not include the 5' leader peptide. The V-region CDRs of the chains are underlined, italicized and bolded, Fc null mutations are italicized, CH3 heterodimerisation mutations are underlined and italicized, CH3 cys disulphide bridges are bolded, and linkers are underlined.

ANT39i HC hole DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPG
KGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPS
SLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFG
QGTKVEIK* (SEQ ID NO: 921)

ANT39i HC hole LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPG
KGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPS
SLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFG
QGTKVEIK* (SEQ ID NO: 922)

ANT39i HC hole LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAP
GKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQS
PSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***T
FGQGTKVEIK* (SEQ ID NO: 923)

ANT39i HC hole LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAP
GKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQS
PSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***T
FGQGTKVEIK* (SEQ ID NO: 924)

Mature ANT39i HC hole DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
V*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***

YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID NO: 925)

Mature ANT39i HC hole LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK<u>GGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID NO: 926)

Mature ANT39i HC hole LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK<u>GGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID NO: 927)

Mature ANT39i HC hole LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV

VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQV**C**
TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID
NO: 928)

ANT39i HC knob DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQ
APGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQ
MTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWA***
YYSPITFGQGTKVEIK* (SEQ ID NO: 929)

ANT39i HC Knob LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQ
APGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQ
MTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWA***
YYSPITFGQGTKVEIK* (SEQ ID NO: 930)

ANT39i HC Knob LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQA
PGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQM
TQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYY***
SPITFGQGTKVEIK* (SEQ ID NO: 931)

ANT39i HC Knob LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQA
PGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQM
TQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYY***
SPITFGQGTKVEIK* (SEQ ID NO: 932)

Mature ANT39i HC knob DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
V*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP*M*V*F*
*D*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTI

TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 933)

Mature ANT39i HC Knob LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREP*M*V*F*
*D*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 934)

Mature ANT39i HC Knob LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 935)

Mature ANT39i HC Knob LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV

VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 936)

ANT39 Hc Hole DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
L*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAAS
GF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQ
GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYI
CNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 908)

ANT39 Hc Hole LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
L*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAAS
GF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQ
GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYI
CNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 937)

ANT39 Hc Hole LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAA
SGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTY
ICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 938)

ANT39 Hc Hole LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAA
SGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTY
ICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 939)

Mature ANT39 Hc Hole DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPELLGGPSVFLF
PPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQ

APGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPS
VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK
KVEPKSCDKTHT* (SEQ ID NO: 940)

Mature ANT39 Hc Hole LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
A*S*IEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVRQ
APGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGPS
VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK
KVEPKSCDKTHT* (SEQ ID NO: 941)

Mature ANT39 Hc Hole LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
A*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVR
QAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGP
SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHT* (SEQ ID NO: 942)

Mature ANT39 Hc Hole LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPSVFLF

PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
A*S*IEKTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***HWVR
QAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSASTKGP
SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHT* (SEQ ID NO: 943)

ANT39 Hc knob DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSL
RLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMA***
FDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 944)

ANT39 Hc knob LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKT
HTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSL
RLSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMA***
FDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 945)

ANT39 Hc knob LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKT
HTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLR
LSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 946)

ANT39 Hc knob LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKT
HTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLR
LSCAASGF***TLSSYSM***HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT*(SEQ ID NO: 947)

Mature ANT39 Hc knob DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPELLGGPS
VFLFPPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPAPIEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***

HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKKVEPKSCDKTHT* (SEQ ID NO: 948)

Mature ANT39 Hc knob LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPA*S*IEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***
HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKKVEPKSCDKTHT* (SEQ ID NO: 949)

Mature ANT39 Hc knob LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPA*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***
HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKKVEPKSCDKTHT* (SEQ ID NO: 950)

Mature ANT39 Hc knob LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPS

VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPA*S*IEKTISKAKGQPREPQVYTLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TLSSYSM***
HWVRQAPGKGLEWVA***YISSYDSITD***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PAVGHMAF***DYWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN
TKVDKKVEPKSCDKTHT* (SEQ ID NO: 951)

ANT39 LC

MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCQQ***WYNAPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT
EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC* (SEQ ID NO: 909)

Mature ANT39 LC

DIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***W***
YNAPITFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL
SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 952)

ANT42i HC hole DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPG
KGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPS
SLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFG
QGTKVEIK* (SEQ ID NO: 953)

ANT42i HC hole LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPG
KGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPS
SLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFG
QGTKVEIK* (SEQ ID NO: 954)

ANT42i HC hole LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAP
GKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQS
PSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***T
FGQGTKVEIK* (SEQ ID NO: 955)

ANT42i HC hole LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAP

GKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQS
PSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***T
FGQGTKVEIK* (SEQ ID NO: 956)

Mature ANT42i HC hole DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
V*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK<u>GGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID
NO: 957)

Mature ANT42i HC hole LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK<u>GGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID
NO: 958)

Mature ANT42i HC hole LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV

VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID NO: 959)

Mature ANT42i HC hole LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQV**C**
TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYT***
YYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRA
S***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIK* (SEQ ID NO: 960)

ANT42i HC knob DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQ
APGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQ
MTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWA***
YYSPITFGQGTKVEIK* (SEQ ID NO: 961)

ANT42i HC Knob LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQ
APGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQ
MTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWA***
YYSPITFGQGTKVEIK* (SEQ ID NO: 962)

ANT42i HC Knob LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQA
PGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQM
TQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYY***
SPITFGQGTKVEIK* (SEQ ID NO: 963)

ANT42i HC Knob LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IE
KTISKAKGQPREPQVYTLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQA

PGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSS<u>GGGGS</u>DIQM
TQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYY***
SPITFGQGTKVEIK* (SEQ ID NO: 964)

Mature ANT42i HC knob DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
V*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP*M*V*F*
*D*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK<u>GGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 965)

Mature ANT42i HC Knob LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREP*M*V*F*
*D*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK<u>GGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 966)

Mature ANT42i HC Knob LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV

VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 967)

Mature ANT42i HC Knob LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVY
TLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGG***
YTAYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTI
TCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK*
(SEQ ID NO: 968)

ANT42 Hc Hole DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
L*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAAS
GF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQ
GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYI
CNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 911)

ANT42 Hc Hole LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF
L*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAAS
GF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQ
GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYI
CNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 969)

ANT42 Hc Hole LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAA
SGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTY
ICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 970)

ANT42 Hc Hole LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKP
GKAPKLLIY***SASDLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPP
CPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FL*V*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAA

SGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWG
QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTY
ICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 971)

Mature ANT42 Hc Hole DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPELLGGPSVFLF
PPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQ
APGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGP
SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHT* (SEQ ID NO: 972)

Mature ANT42 Hc Hole LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
A*S*IEKTISKAKGQPREPQVYTLPP*I*RE*L*MT*S*NQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVRQ
APGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKGP
SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHT* (SEQ ID NO: 973)

Mature ANT42 Hc Hole LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPSVFLF

PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
A*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVR
QAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKG
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHT* (SEQ ID NO: 974)

Mature ANT42 Hc Hole LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***DFSSSSI***HWVRQAPGKGLEWVA***SISSSYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***SWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASDLY***
SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YAGAGLI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
A*S*IEKTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL*S*C*A*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL*V*SKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***HWVR
QAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSSASTKG
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHT* (SEQ ID NO: 975)

ANT42 Hc knob DANG

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSL
RLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHP***
FDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 976)

ANT42 Hc knob LALAPS

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK<u>GGGGSGGGGSEPKSSDKT</u>
<u>HT</u>CPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK<u>GGGSGGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSL
RLSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHP***
FDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 977)

ANT42 Hc knob LALAPS Merchant

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK<u>GGGGSGGGGSEPKSSDKT</u>
<u>HT</u>CPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK<u>GGGSGGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLR
LSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 978)

ANT42 Hc knob LALAPS Merchant S-S

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSS<u>GGGGS</u>DIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWY
QQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIK<u>GGGGSGGGGSEPKSSDKT</u>
<u>HT</u>CPPCPAPE*AA*GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPA*S*IEKTISKAKGQPREPQVYTLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK<u>GGGSGGGSGGGSGGGSGGGSGSTG</u>EVQLVESGGGLVQPGGSLR

LSCAASGF***TSDFYFI***HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT* (SEQ ID NO: 979)

Mature ANT42 Hc knob DANG

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPELLGGPS
VFLFPPKPKDTLMISRTPEVTCVVV*A*VSHEDPEVKFNWYVDGVEVHNAKTKPREEQY*G*STYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPAPIEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***
HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSS
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHT* (SEQ ID NO: 980)

Mature ANT42 Hc knob LALAPS

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPA*S*IEKTISKAKGQPREP*M*V*FD*LPPSREEMTKNQVSL*W*C*M*VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***
HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSS
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHT* (SEQ ID NO: 981)

Mature ANT42 Hc knob LALAPS Merchant

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPS

VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPA*S*IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***
HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSS
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHT* (SEQ ID NO: 982)

Mature ANT42 Hc knob LALAPS Merchant S-S

EVQLVESGGGLVQPGGSLRLSCAASGF***DFTAYAM***HWVRQAPGKGLEWVA***SIYPSGGYTA***YADSVKGRFTISADTSKNTAYLQMNSLR
AEDTAVYYCAR***RSYYFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SAS***
SLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YWAYYSPI***TFGQGTKVEIKGGGGSGGGGSEPKSSDKTHTCPPCPAPE*AA*GGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPA*S*IEKTISKAKGQPREPQVYTLPP**C**REEMTKNQVSL*W*CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSLRLSCAASGF***TSDFYFI***
HWVRQAPGKGLEWVA***TIYPFIGNTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AFPGSYHPF***DYWGQGTLVTVSS
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHT* (SEQ ID NO: 983)

ANT42 LC

MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCQQ***STGSLI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC* (SEQ ID NO: 912)

Mature ANT42 LC

DIQMTQSPSSLSASVGDRVTITCRAS***QSVSSA***VAWYQQKPGKAPKLLIY***SASSLY***SGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***S***
TGSLITFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL
SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 984)

ANT80-1 Hole

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSYSYI***HWVRQAPGKGLEWVA***SIYSYTGATD***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YWSTNRILSYGGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***
VAWYQQKPGKAPKLLIYSASSLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YFDPIT***FGQGTKVEIKGGGGSGGGGSEPKSSD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSL
RLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYAM***DYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT
YICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 986)

ANT80-2 Knob

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DLSHSSI***HWVRQAPGKGLEWVA***SISSHYGYTH***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***SSYFPWFFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***DVSTA***VA
WYQQKPGKAPKLLIY***SASFLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***HYTTPP***TFGQGTKVEIKGGGGSGGGGSEPKTSDK
THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGS
LRLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYAM***DY
WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
QTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 987)

ANT98-1 Hole

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSYSYI***HWVRQAPGKGLEWVA***SIYSYTGATD***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YWSTNRILSYGGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***
VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YFDPI***TFGQGTKVEIKGGGGSGGGGSEPKSSD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSL

RLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***DYAM***DYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT
YICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 988)

ANT98-2 Knob

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DLSHSSI***HWVRQAPGKGLEWVA***SISSHYGYTH***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***SSYFPWFFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***DVSTA***VA
WYQQKPGKAPKLLIY***SASFLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***HYTTPP***TFGQGTKVEIKGGGGSGGGGSEPKTSDK
THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGS
LRLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***DYAM***DY
WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
QTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 989)

ANT99-1 Hole

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***TLSYSYI***HWVRQAPGKGLEWVA***SIYSYTGATD***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YWSTNRILSYGGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***
VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YFDPI***TFGQGTKVEIKGGGGSGGGGSEPKSSD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGSL
RLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYDM***DYW

GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT
YICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 990)

ANT99-2 Knob

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***DLSHSSI***HWVRQAPGKGLEWVA***SISSHYGYTH***YADSVKGRFTISAD
TSKNTAYLQMNSLRAEDTAVYYCAR***SSYFPWFFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***DVSTA***VA
WYQQKPGKAPKLLIY***SASFLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***HYTTPP***TFGQGTKVEIKGGGGSGGGGSEPKTSDK
THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGSTGEVQLVESGGGLVQPGGS
LRLSCAASGF***NIAYSSM***HWVRQAPGKGLEWVA***TIYPSYSSTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYDM***DY
WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
QTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 991)

ANT80 ANT98 ANT99 LC

MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCQQ***AHYFPI***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 992)

CM0042 (Dia-Fc-Dia)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDS
DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSC
AASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***D
YWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTL
TISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 993)

CM0011 Hole (Dia-Fc-Dia)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH
NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD
GSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSCA
ASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGW***
AMDYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGT
DFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 994)

CM0011 Knob (Dia-Fc-Dia)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLS
CAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***
DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDF
TLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 995)

CM0126 Hole (Dia-Fc-Dia)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH
NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD
GSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSCA
ASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGW***

AMDYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGT DFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 996)

CM0126 Knob (Dia-Fc-Dia)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISA DTSKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLS CAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM*** DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDF TLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 997)

CM0107 Hole (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD GSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTITCR ASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIKGTTAASG SSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAY LQMNSLRAEDTAVYYCAR***AHYFPWAGA***MDYWGQGTLVTVSS (SEQ ID NO: 998)

CM0107 Knob (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD

WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTIT
CRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIKGTTAA
SGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNT
AYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSS (SEQ ID NO: 999)

CM0108 Hole (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH
NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD
GSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTITCR
ASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGTTAASGSS
GGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQ
MNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1000)

CM0108 Knob (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTIT
CRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGTTAAS
GSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTA
YLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1001)

CM0108 Hole (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH
NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD
GSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTITCR
ASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGTTAASGSS
GGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQ
MNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1000)

CM0108 Knob (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTIT
CRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGTTAAS
GSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTA
YLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1001)

CM0109 Hole (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKSSDKTH
NCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD
GSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTITCR
ASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGTTAASGSS

GGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQ
MNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1000)

CM0109 Knob (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTIT
CRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIKGTTAA
SGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNT
AYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSS (SEQ ID NO: 999)

CT003 Hole (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***V
AWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKLEDKTHTKVEPKTSDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
GGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQ
MNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1000)

CM0109 Knob (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKTHTKVEPKTSDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTIT
CRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIKGTTAA
SGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNT
AYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSS (SEQ ID NO: 999)

CT003 Hole (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S***
VSSAVAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIKLEDKTHTKVEP
KSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPG
GSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHHPF***
GYALDYWGQGTLVTVSSGTTAASGSSGGSSSGADIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***
GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIK (SEQ ID NO: 1002)

CT003 Knob (Dia-Fc-scFv)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***V
AWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKLEDKTHTKVEPKTSDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ

DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRL
SCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYA***LD
YWGQGTLVTVSSGTTAASGSSGGSSSGADIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRF
SGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIK (SEQ ID NO: 1003)

CM0112 Hole (scFv-Fc-Dia)

MNLLLILTFVAAAVAEFDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLT
ISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAP
GKGLEWVA***SIYSAFASTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSLEDKTHTK
VEPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLV
QPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***TV***
RGSKKPYFSGWAMDYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***G
VPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1004)

CM0112 Knob (scFv-Fc-Dia)

MNLLLILTFVAAAVAEFDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLT
ISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAP
GKGLEWVA***SIYSAFASTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSLEDKTHTK
VEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGL
VQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***A***
HYFPWAGAMDYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSR
FSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1005)

CM0110 Hole (scFv-Fc-scFv)

MNLLLILTFVAAAVAEFDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLT
ISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAP
GKGLEWVA***SIYSAFASTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSLEDKTHTK
VEPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSA
SVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKV
EIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTIS
ADTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSS (SEQ ID NO: 1006)

CM0110 Knob (scFv-Fc-scFv)

MNLLLILTFVAAAVAEFDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLT
ISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAP
GKGLEWVA***SIYSAFASTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSLEDKTHTK
VEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLS
ASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGT
KVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRF
TISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSS (SEQ ID NO: 1007)

CT001 CM0299 CM0300 CM0301 ANT1 LC

MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 1008)

CT001 Hole (bsIgG-dia)

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLE
WVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDI
QMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YS***
WGPFTFGQGTKVEIK (SEQ ID NO: 1009)

CT001 Knob (bsIgG-dia)

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKG
LEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQM
TQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***
TFGQGTKVEIK (SEQ ID NO: 1010)

CM0299 Hc (IgG-Dia)

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGL
EWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMT

QSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1011)

CM0300 Hc (IgG-scFv)

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPK
LLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQ
PGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHY***
FPWAGAMDYWGQGTLVTVSS (SEQ ID NO: 1012)

CM0301 Hc (IgG-scFv)

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPK
LLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQP
GGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***TVRG***
SKKPYFSGWAMDYWGQGTLVTVSS (SEQ ID NO: 1013)

ANT1 Hole (Dia-Fc-Fab)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S***
VSSAVAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYFLI***TFGQGTKVEIKLEDKTHTKVEPKS
SDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT

VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPP
VLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSL
RLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYA***
LDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 1014)

ANT1 Knob (Dia-Fc-Fab)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***SISPYYGYTY***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***SSYFPWFSAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***V
AWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIKLEDKTHTKVEPKTSDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRL
SCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCA***RYHHPFGYAL***D
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHT (SEQ ID NO: 1015)

Fab-Dia Hc (Fab-Dia)

MNLLLILTFVAAAVAEVQLVESGGGLVQPGGSLRLSCAASGF***NIHSSSI***HWVRQAPGKGLEWVA***ATYSSFGSIT***YADSVKGRFTISADT
SKNTAYLQMNSLRAEDTAVYYCAR***YHHPFGYAL***DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTGGSGGEVQLVESGGGLVQPGG
SLRLSCAASGF***TISYSSI***HWVRQAPGKGLEWVA***SISPYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SSYFPWF***
SAMDYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSG
TDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1016)

Fab-Dia LC (Fab-Dia)

MNLLLILTFVAAAVADIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGGGSEVQLVESGGGLVQPGGSLRLSCAASGF***TISSYYI***H
WVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTL

VTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPE
DFATYYCQQ***YYFLI***TFGQGTKVEIK (SEQ ID NO: 1017)

CH3 (Dia-CH3-Dia)

MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA
WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKDKTHTKVEPKTSDKTHTC
PPCPGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGKGTTAASGSSGGSSSGAGRTEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLE
WVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMTQ
SPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***T
FGQGTKVEIK (SEQ ID NO: 1018)

CM0156

EVQLVESGGGLVQPGGSLRLSCAASGF***NISYSYM***HWVRQAPGKGLEWVA***SISPYYSYTS***YADSVKGRFTISADTSKNTAYLQMNSLRA
EDTAVYYCAR***PSAWSHYYPSSSSSAF***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAP
KLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SSYSLI***TFGQGTKVEIKLEDKTHTKVEPKSSDKTHTCPPCPAPELLG
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV
DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSYM***
HWVRQAPGKGLEWVA***SISPYYSYTS***YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***PSAWSHYYPSSSSSAF***DYWGQGT
LVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQP
EDFATYYCQQ***SSYSLI***TFGQGTKVEIK (SEQ ID NO: 1019)

Table 14

Comparison of expression titers and monodispersity of FZD agonists following Protein A purification. See corresponding figure 21.

Molecule	Format	N-term Paratope	C-term Paratope	Expression titer mg/l	% Monomer	Monomer Yield (mg/l)
CM0042	Dia – Fc – Dia	5019	2539	8±4	43	3
CM0011	Dia – Fc – Dia	5019	2539/2542	12±3	81±5	10
CM0126	Dia – Fc – Dia	5016	2539/2542	8±0.7	ND	ND
CM0107	Dia – Fc - scFv	5019	2539	90	87	80
CM0108	Dia – Fc - scFv	5019	2542	47	89	40
CM0109	Dia – Fc - scFv	5019	2539/2542	79	86	70
CT003	Dia – Fc - scFv	2539/2542	5016	47	67	30
CM0112	scFv – Fc – Dia	5019	2539/2542	15	79	10
CM0110	scFv - Fc - scFv	5019	2539/2542	82	81	70
CT001	bsIgG-dia	5016	2539/2542	47±21	44±11	30
CM0299	IgG-dia	5016	2539	20±8	ND	ND
CM0300	IgG – scFv	5016	2539	134±38	66±7	100
CM0301	IgG – scFv	5016	2542	134±27	71±8	90
ANT1	Dia-Fc-Fab	5016	2539/2542	294±75	53±9	150
CH3	Dia-CH3-Dia	5019	2539	<1	ND	ND
Fab-Dia	FAb-Dia	5016	2540/2542	1	ND	ND

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Table 15

Functional comparison of FZD agonists. Concentration-response curves of each FZD agonist were generated using the TOPFLASH assay. Figure 20 shows representative traces of the A) Diabody-Fc-Diabody and B) Diabody-Fc-Fab format overlaid with Wnt3a for comparison. Calculated EC50 and maximum efficacy relative to recombinant Wnt3a control were derived and are presented as the average ± SD.

Name	Format	N-term Paratope	C-term Paratope	EC_{50} (nM)	Maximal Signal (% Wnt3a maxima)
Wnt3a	Recombinant Protein	NA	NA	6±3	100
CM0042	Dia – Fc – Dia	5019	2539	0.9±0.8	33±22
CM0011	Dia – Fc – Dia	5019	2539/2542	0.3±0.1	63±10
CM0126	Dia – Fc –Dia	5016	2539/2542	0.3±0.2	52±1
CM0107	Dia-Fc-scFv	5019	2539	ND	ND
CM0108	Dia-Fc-scFv	5019	2542	ND	ND
CM0109	Dia-Fc-scFv	5019	2539/2542	ND	ND
CT003	Dia-Fc-scFv	2539/2542	5016	0.4±0.1	42±16
CM0112	scFv-Fc-Dia	5019	2539/2542	ND	ND
CM0110	scFv-Fc-scFv	5019	2539/2542	ND	ND
CT001	bsIgG-dia	5016	2539/2542	0.3±0.1	57±17
CM0299	IgG-dia	5016	2539	0.1±0.1	14±5
CM0300	IgG-scFv	5016	2539	0.3±0.2	5±2
CM0301	IgG-scFv	5016	2542	0.2±0.2	1±1
ANT1	Dia-Fc-Fab	5016	2539/2542	0.7±0.5	50±18
CH3	Dia-CH3-Dia	5019	2539	ND	22±10
FAb-Dia	Fab-Dia	5016	2540/2542	0.4±0.2	42±16

Table 16

FZD2-LRP6 CM0072	
Knob construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIYYSSI***HWVRQAPGKGLEWVA***SIYPYYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYHYGL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SYWHSYLI***TFGQGTKVEIKLEDKT HTKVEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESAT PESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNT AYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1020)
Hole construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIYYSSI***HWVRQAPGKGLEWVA***SIYPYYGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYHYGL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SYWHSYLI***TFGQGTKVEIKLEDKT HTKVEPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPES GGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYL QMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA*** VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1021)

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FZD5-LRP6 CM0024	
Knob construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***SIYPSYSSTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVS SA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***AFYYPI***TFGQGTKVEIKLEDKTHTKV EPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGG GEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKNTAYLQM NSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQQKP GKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1022)
Hole construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***SIYPSYSSTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YYAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVS SA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***AFYYPI***TFGQGTKVEIKLEDKTHTKV EPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATPESGGG EVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTAYLQMN SLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VAWYQ QKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1023)

FZD7-LRP6 CM0172	
Knob construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISSSSM***HWVRQAPGKGLEWVA***SIYSYYGSTY***YADSVKG RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***WYGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***PGSWYFPPI***TFGQGTKVEIKLEDK THTKVEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESA TPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1024)
Hole construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISSSSM***HWVRQAPGKGLEWVA***SIYSYYGSTY***YADSVKG RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR***WYGM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***S VSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***PGSWYFPPI***TFGQGTKVEIKLEDK THTKVEPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESAT PESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTA YLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA*** VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1025)

PanFZD-LRP6 CM0011	
Knob construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRA SQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKT HTKVEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESA TPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1026)
Hole construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NIGSSSI***HWVRQAPGKGLEWVA***SIYSAFASTS***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***YHFPFGFAL***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRA SQ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***GVYLF***TFGQGTKVEIKLEDKT HTKVEPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATP ESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTA YLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA*** VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1027)

FZD4-LRP6 CM0016	
Knob construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYYYI***HWVRQAPGKGLEWVA***SIYPSSGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SSFYWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SYAAYLF***TFGQGTKVEIKLEDKT HTKVEPKSSDKTHNCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPIRELMTSNQVSLSCAVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESATP ESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISSYYI***HWVRQAPGKGLEWVA***SIYSSYGYTS***YADSVKGRFTISADTSKNTA YLQMNSLRAEDTAVYYCAR***TVRGSKKPYFSGWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA*** VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YSWGPF***TFGQGTKVEIK (SEQ ID NO: 1028)
Hole construct	MNLLLILTFVAAAVAEFEVQLVESGGGLVQPGGSLRLSCAASGF***NISYYYI***HWVRQAPGKGLEWVA***SIYPSSGYTY***YADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCAR***SSFYWAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ ***SVSSA***VAWYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***SYAAYLF***TFGQGTKVEIKLEDKT HTKVEPKTSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPMVFDLPPSREEMTKNQVSLWCMVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKSGSETPGTSESA TPESGGGEVQLVESGGGLVQPGGSLRLSCAASGF***NISYSSI***HWVRQAPGKGLEWVA***YISSYYGYTY***YADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCAR***AHYFPWAGAM***DYWGQGTLVTVSSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQ***SVSSA***VA WYQQKPGKAPKLLIY***SASSLYS***GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQ***YYWPI***TFGQGTKVEIK (SEQ ID NO: 1029)

WE CLAIM

1. A tetravalent binding antibody molecule comprising:

(a) an Fc domain or fragment thereof comprising a constant heavy chain domain 3 (CH3),

(b) a bivalent low-density lipoprotein receptor-related protein 5 (LRP5) binding domain and

(c) a bivalent Frizzled (FZD) binding domain,

wherein the LRP5 binding domain is attached to one terminus of the Fc domain and the FZD binding domain is attached to the other end of the Fc domain,

wherein the LRP5 binding domain comprises a diabody that binds LRP5 and the FZD binding domain comprises two scFv or two Fab that bind FZD4.

2. The tetravalent binding antibody molecule of claim 1, wherein

(a) the LRP5 binding domain diabody is attached to the N-terminal of the Fc domain, and

(b) the FZD4 binding domain is attached to the C-terminal of the Fc domain.

3. The tetravalent binding antibody molecule of claim 2, wherein

(a) the LRP5 binding domain diabody is attached to the N-terminal of the Fc domain via a VL or VH of the diabody, and

(b) the FZD binding domain comprises two FZD binding Fabs fused to the C-terminal of the Fc, wherein each Fab is attached to the Fc domain via a heavy or light chain variable domain (VH or VL) of the Fab linked to the CH3 domain of the Fc domain.

4. A tetravalent binding antibody molecule comprising an N-terminal LRP5-binding diabody and a C-terminal domain comprising two FZD4-binding scFv, the tetravalent binding antibody molecule comprising

a dimer of a first and second monomer, wherein each monomer comprises a single-chain polypeptide comprising, from N-terminus to C-terminus:

(a) a first peptide, said first peptide comprising a first heavy chain variable domain (VH) and a first light chain variable (VL) domain that bind LRP5,

(b) an Fc region, or fragment thereof comprising a constant heavy chain domain 3 (CH3), and

(c) a second peptide, said second peptide comprising a second VL and a second VH that bind a FZD4, and

a first and second light chain monomer, each light chain monomer comprising from N terminus to C terminus a VL that binds the FZD4, linked to a constant light chain domain 1 (CL1 domain),

wherein the first and second monomers dimerize via the Fc regions or fragments thereof, the first VH and VL of each monomer pairs with the first VH and VL of the other monomer forming a diabody that binds LRP5 and the second VL and VH of each monomer pair to form a scFvs that bind FZD4, and

wherein the LRP5-binding diabody forms the N-terminal LRP5-binding domain of the tetravalent binding antibody molecule and the two FZD4-binding scFvs form the C-terminal FZD-binding domain of the tetravalent binding antibody molecule.

5. The tetravalent binding antibody molecule of claim 1, wherein the FZD binding domain is attached to the N-terminal of the Fc domain and the LRP5 binding domain is attached to the C-terminal of the Fc domain.

6. The tetravalent binding antibody molecule of claim 5, wherein

(a) the FZD binding domain comprises two Fabs that bind the FZD4, wherein each Fab is attached to N-terminal of the Fc domain via a heavy or light chain variable domain (VH or VL) of the Fab linked to the CH2 domain of the Fc domain, and

(b) the LRP5 binding domain comprises a diabody or two scFv that bind LRP5, wherein the diabody or two scFv are attached to the C-terminal of the Fc domain via a VL or VH of the diabody or scFv linked to the CH3 of the Fc domain.

7. A tetravalent binding antibody molecule comprising an Fc domain or fragment thereof comprising a constant heavy chain domain 3 (CH3), an N-terminal FZD4 binding domain comprising two FZD4-binding Fabs and a C-terminal LRP5 binding domain comprising a LRP5 binding diabody, the tetravalent binding antibody molecule comprising

(a) a first and second heavy chain monomer, wherein each heavy chain monomer comprises a single-chain polypeptide comprising from N-terminus to C-terminus:

(i) a heavy chain variable domain (VH) that binds FZD4, linked to

(ii) a heavy chain constant region domain 1 (CH1 domain), linked to

(iii) the CH2 domain of the Fc region linked to

(iv) a peptide comprising a VH that binds a LRP5 co-receptor, linked to a light chain variable domain (VL) that binds a LRP5 co-receptor, and

(b) a first and second light chain monomer, each light chain monomer comprising from N terminus to C terminus a VL that binds the FZD4, linked to a constant light chain domain 1 (CL1 domain),

wherein the first and second heavy chain monomers dimerize via their Fc regions, or fragments thereof,

wherein a linker between the VH and VL that binds the LRP5 is of a length that promotes the pairing of the VH and VL of the first heavy chain monomer with the VL and VH of the second heavy chain monomer thereby forming a LRP5 co-receptor binding diabody and the FZD-binding Fabs are formed by the pairing of each heavy chain monomer with a light chain monomer such that the VH that binds FZD4 and CH1 of each of the heavy chain monomer, pairs with the VL that binds FZD4 and CL1 of the light chain monomers, and

wherein the Fabs form the FZD4-binding domain on the N-terminus of the Fc domain and the diabody forms the LRP5 co-receptor-binding domain on the C-terminus of the Fc domain.

8. The tetravalent binding antibody molecule of any one of claims 1 to 7, wherein the LRP5 binding diabody is a bispecific bivalent LRP5 binding domain that binds to two epitopes within the LRP5 co-receptor extracellular domain.

9. The tetravalent binding antibody molecule of claim 8 wherein the LPR5 binding domain interacts with the Wnt1 and Wnt3 epitopes of the LRP5 co-receptor.

10. The tetravalent binding antibody molecule of any one of claims 1 to 9, wherein the FZD binding domain is monospecific.

11. The tetravalent binding antibody molecule of any one of claims 1 to 10, wherein

the diabody of the LRP5 binding domain binds LRP5 and comprises heavy chain complementary determining regions CDR-H1, CDR-H2 and CDR-H3 and light chain complementary determining regions CDR-L1, CDR-L2 and CDR-L3, of an antibody set forth in the sequences in Table 3 or Table 6A.

12. The tetravalent binding antibody molecule of any one of claims 1 to 11 wherein the Fc domain or fragment thereof dimerize via a knob-in-hole configuration of the Fc regions or fragments thereof.

13. The tetravalent binding antibody molecule of claim 12, wherein the Fc region of the first heavy chain monomer comprises the mutations T366S, L368A and Y407V, and the Fc region of the second heavy chain monomer comprises the mutation T366W, according to EU numbering.

14. The tetravalent binding antibody molecule of claim 13, wherein the Fc region of the first heavy chain monomer further comprises the mutations S354I and E357L, and the Fc region of the second heavy chain monomer further comprises the mutations Q347M, Y349F, T350D and L368M, according to EU numbering.

15. The tetravalent binding antibody molecule of claim 13, wherein an additional disulfide bond is introduced between the Fc region of the first heavy chain monomer and the second heavy chain monomer, preferably wherein the first heavy chain monomer comprises the mutation Y349C and the second heavy chain monomer comprises the mutation S354C, according to EU numbering.

16. The tetravalent binding antibody molecule of any one of claims 1 to 15, wherein the Fc domain lacks one or more effector functions.

17. The tetravalent binding antibody molecule of claim 16, wherein the Fc regions contain mutations that alter their effector function due to amino acid mutations, N297G (NG) and/or D265A (DA) variants, according to EU numbering.

18. The tetravalent binding antibody molecule of claim 16, wherein the Fc regions contain mutations that alter their effector function due to amino acid mutations L234A, L235A and/or P331S, according to EU numbering.

19. The tetravalent binding antibody molecule of claim 18, wherein the Fc regions contain mutations that alter their effector function due to amino acid mutations L234A and L235A (LALA).

20. The tetravalent binding antibody molecule of claim 19, wherein the Fc regions contain mutations that alter their effector function due to amino acid mutations L234A, L235A and P331S (LALAPS).

21. The tetravalent binding antibody molecule of any one of claims 1 to 20, wherein the LRP5 binding domain and FZD binding domain are each attached to the Fc domain by a linker.

22. The tetravalent binding antibody molecule of claim 21, wherein the linker comprises 1 to 100, 1 to 50, 1-30, 1-25, 1- 10, 1-6 amino acids, 1-5 amino acids, or 2-4 amino acids.

23. The tetravalent binding antibody molecule of claim 21 or 22, wherein the diabodies forming the LRP5 co-receptor-binding domain were fused to the Fc domain via a GGGGSGGGGSEPKSSDKTHT (SEQ ID NO: 892) linker.

24. The tetravalent binding antibody molecule of any one of claims 21 to 23, wherein the FZD4-binding Fabs are fused to the Fc region via a GGGSGGGSGGGSGGGSGSTG (SEQ ID NO: 891) linker.

25. The tetravalent binding antibody molecule of any one of claims 1 to 24, wherein the VH that binds the LRP5 co-receptor is linked to the VL that binds a LRP5 co-receptor via a short GGGGS (SEQ ID NO: 886) linker.

26. The tetravalent binding antibody molecule of any one of claims 1 to 25, wherein the FZD binding domain comprises two Fabs that bind FZD4.

27. The tetravalent binding antibody molecule of claim 26, wherein the FZD-binding Fab comprise light chain complementary determining regions CDR-L1, CDR-L2 and CDR-L3 and heavy chain CDRs, CDR-H1, CDR-H2 and CDR-H3 of an antibody set forth in the sequences inTable 1, Table 2 or Table 6.

28. The tetravalent binding antibody molecule of any one of claims 1 to 4 and 8 to 27 comprising,

(a) a dimer of a first and second heavy chain monomer, each monomer comprising a single-chain polypeptide comprising, from N-terminus to C-terminus:

(1) a peptide comprising a heavy chain variable domain (VH) that binds LRP5 and a light chain variable domain (VL) that binds LRP5,

(2) an Fc region, or fragment thereof comprising the CH3,

(3) a VH that binds FZD4, and

(4) a constant heavy chain domain 1 (CH1),

wherein

(5) the VH that binds LRP5 comprises heavy chain CDRs (CDR-H1, CDR-H2 and CDR-H3), of an antibody set forth in the sequences in Table 3 or Table 6, and

(b) the VL that binds LRP5 comprises light chain CDRs (CDR-L1, CDR-L2 and CDR-L3), of an antibody set forth in the sequences in Table 3 or Table 6,

(c) the VH that binds FZD4, comprises the heavy chain CDRs (CDR-H1, CDR-H2 and CDR-H3), of an antibody set forth in the sequences in Table 1, Table 2 or Table 6, and

(d) a third and fourth light chain monomer each comprising a VL that binds FZD4, and a constant light chain domain 1 (CL1), the VL that binds FZD4, comprising the light chain CDRs (CDR-L1, CDR-L2 and CDR-L3), of an antibody set forth in the sequences in Table 1, Table 2 or Table 6,

wherein the first and second heavy chain monomer dimerize via their Fc regions and the VL and VH that bind LRP5 of the first monomer pair with the VH and VL that bind LRP5 or of the second monomer forming a bivalent diabody that binds LRP5, and

the CL1 and VLs that bind FZD4, of the third and fourth light chain monomers pair with the CH1 and VHs that bind FZD4, of the first and second heavy chain monomers forming two Fabs that bind FZD4, wherein the diabody forms the N-terminal bivalent LRP5 binding domain and the two Fabs form the C-terminal bivalent FZD4, binding domain.

29. The tetravalent binding antibody molecule of any one of claims 5 to 7 comprising,

(a) a dimer of a first and second heavy chain monomer, each monomer comprising a single-chain polypeptide comprising, from N-terminus to C-terminus:

(1) a VH that binds FZD4

(2) an Fc region, or fragment thereof comprising the CH3,

(3), a peptide comprising a VH that binds LRP5 and a VL that binds LRP5 and

(4) a constant heavy chain domain 1 (CH1),

wherein

(5) the VH that binds LRP5 comprises heavy chain CDRs (CDR-H1, CDR-H2 and CDR-H3), of an antibody set forth in the sequences in Table 3 or Table 6, and

(b) the VL that binds LRP5 comprises light chain CDRs (CDR-L1, CDR-L2 and CDR-L3), of an antibody set forth in the sequences in Table 3 or Table 6,

(c) the VH that binds FZD4, comprises the heavy chain CDRs (CDR-H1, CDR-H2 and CDR-H3), of an antibody set forth in the sequences in Table 1, Table 2 or Table 6,

and

(d) a third and fourth light chain monomer each comprising from N terminus to C terminus a VL that binds FZD4, and a constant light chain domain 1 (CL1), the VL that binds FZD4, comprising the light chain CDRs (CDR-L1, CDR-L2 and CDR-L3), of an antibody set forth in the sequences in Table 1, Table 2 or Table 6,

wherein the first and second heavy chain monomer dimerize via their Fc regions and the VL and VH that bind LRP5 of the first monomer pair with the VH and VL that bind LRP5 or of the second monomer forming a bivalent diabody that binds LRP5, and

the CL1 and VLs that bind FZD4, of the third and fourth light chain monomers pair with the CH1 and VHs that bind FZD4, of the first and second heavy chain monomers forming two Fabs that bind FZD4, wherein the diabody forms the C-terminal bivalent LRP5 binding domain and the two Fabs form the N-terminal bivalent FZD4, binding domain.

30. The tetravalent binding antibody molecule of claim 28 or 29, wherein the LRP5 binding diabody is bispecific, wherein

the CDRs of the VHs that bind LRP5 of the first heavy chain monomer and the CDRs of the VHs that bind LRP5 of the second heavy chain monomer are non-identical, and

the CDRs of the VLs that bind LRP5 of the first heavy chain monomer and the CDRs of the VLs that bind LRP5 second heavy chain monomer are non-identical.

31. The tetravalent binding antibody molecule of claim 30, wherein

in the first heavy chain monomer

(a) the CDR-H1 and CDR-H2 of the VH that binds LRP5 comprise respectively FSSSSI (SEQ ID NO: 528) and SISSSYGYTY (SEQ ID NO: 553), or the CDR-H1 and CDR-H2 of the VH that binds LRP5 comprise respectively LSYYYM (SEQ ID NO: 527) and SIYSSYGYTY (SEQ ID NO: 552) and

(b) the CDR-L2 and CDR-L3 of the VL that binds LRP5 comprise respectively SASDLYS (SEQ ID NO: 491) and YAGAGLI (SEQ ID NO: 510), or the CDR-L2 and CDR-L3 of the VL that binds LRP5 comprise respectively SASSLYS (SEQ ID NO: 2) and SSYSLI (SEQ ID NO: 130), and

in the second heavy chain monomer

(c) the CDR-H1 and CDR-H2 of the VH that binds LRP5 comprises respectively FTAYAM (SEQ ID NO: 536) and SIYPSGGYTA (SEQ ID NO: 566), or the CDR-H1 and CDR-H2 of the VH that binds LRP5 comprises respectively FSSSSI (SEQ ID NO: 528) and SISSSYGYTY (SEQ ID NO: 553) and

(d) the CDR-L2 and the CDR-L3 of the VL that binds LRP5 comprises respectively SASSLYS (SEQ ID NO: 2) and YWAYYSPI, or the CDR-L2 and the CDR-L3 of the VL that binds LRP5 comprises respectively SASSLYS (SEQ ID NO: 2) and ASYAPI.

32. The tetravalent binding antibody molecule of any one of claims 28 to 31, wherein in the first and second heavy chain monomer the CDR-H1 and CDR-H2 of the VH that binds FZD4 comprises respectively LSSYSM (SEQ ID NO: 24) and YISSYYGYTY (SEQ ID NO: 51), or the CDR-H1 and CDR-H2 of the VH that binds FZD4 comprises respectively LSSYSM (SEQ ID NO: 24) and YISSYDSITD (SEQ ID NO: 61).

33. The tetravalent binding antibody molecule of any one of claims 28 to 32, wherein in the third and fourth light chain monomers the CDR-L1 and CDR-L2 of the VL that bind FZD4 comprise respectively SVSSA (SEQ ID NO: 1) and SASSLYS (SEQ ID NO: 2), and the CDR-L3 of the VL that binds FZD4 comprises WYYAPI (SEQ ID NO: 3) or WYNAPI (SEQ ID NO: 12).

34. The tetravalent binding antibody molecule of any one of claims 28, 29, 30, 32 and 33, comprising a bivalent, bispecific LRP5 binding domain, wherein

(a) in the first heavy chain monomer,

the VH that binds LRP-5 comprises CDR-H1 of SEQ ID NO: 528, CDR-H2 of SEQ ID NO: 553 and CDR-H3 of SEQ ID NO: 586, and the VL that binds LRP-5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 491 and CDR-L3 of SEQ ID NO: 510 of ANT16-Hole of Table 6A, or

the VH that binds LRP-5 comprises CDR-H1 of SEQ ID NO: 527, CDR-H2 of SEQ ID NO: 552 and CDR-H3 of SEQ ID NO: 584 and the VL that binds LRP-5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 130 of ANT18-Hole of Table 6A, or

the VH that binds LRP-5 comprises CDR-H1 of SEQ ID NO: 527, CDR-H2 of SEQ ID NO: 552 and CDR-H3 of SEQ ID NO: 584 and the VL that binds LRP-5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 491 and CDR-L3 of SEQ ID NO: 510 of ANT20-Hole of Table 6A, or

the VH that binds LRP-5 comprises CDR-H1 of SEQ ID NO: 528, CDR-H2 of SEQ ID NO: 553 and CDR-H3 of SEQ ID NO: 586 and the VL that binds LRP-5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 130 of ANT21-Hole of Table 6A, or

the VH that binds LRP-5 comprises CDR-H1 of SEQ ID NO: 527, CDR-H2 of SEQ ID NO: 552 and CDR-H3 of SEQ ID NO: 584 and the VL that binds LRP-5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 130 of ANT36-Hole of Table 6A, or

the VH that binds LRP-5 comprises CDR-H1 of SEQ ID NO: 528, CDR-H2 of SEQ ID NO: 553 and CDR-H3 of SEQ ID NO: 586 and the VL that binds LRP-5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 491 and CDR-L3 of SEQ ID NO: 510 of ANT39-Hole of Table 6A,

and

the VH that binds FZD4 comprises the FZD4 VH CDRs CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT16 Hole of Table 6B, or

the VH that binds FZD4 comprises the FZD4 VH CDRs CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT18-Hole of Table 6B, or

the VH that binds FZD4 comprises the FZD4 VH CDRs CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT20-Hole of Table 6B, or

the VH that binds FZD4 comprises the FZD4 VH CDRs CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT21-Hole of Table 6B, or

the VH that binds FZD4 comprises the FZD4 VH CDRs CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 61 and a CDR-H3 of SEQ ID NO: 90 of ANT36-Hole of Table 6B, or

the VH that binds FZD4 comprises the FZD4 VH CDRs CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 61 and a CDR-H3 of SEQ ID NO: 90 of ANT39-Hole of Table 6B,

wherein the FZD CDR-L1 and CDR-L2 are respectively SVSSA (SEQ ID NO: 1) and SASSLYS (SEQ ID NO: 2), and

(b) in the second monomer

the VH that binds LRP5 comprises CDR-H1 of SEQ ID NO: 536, CDR-H2 of SEQ ID NO: 566 and CDR-H3 of SEQ ID NO: 603 and the VL that binds LRP5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 493 of ANT16-Knob of Table 6A, or

the VH that binds LRP5 comprises CDR-H1 of SEQ ID NO: 528, CDR-H2 of SEQ ID NO: 553 and CDR-H3 of SEQ ID NO: 585 and the VL that binds LRP5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 492 of ANT18-Knob of Table 6A, or

the VH that binds LRP5 comprises CDR-H1 of SEQ ID NO: 536, CDR-H2 of SEQ ID NO: 566 and CDR-H3 of SEQ ID NO: 603 and the VL that binds LRP5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 492 of ANT20-Knob of Table 6A, or

the VH that binds LRP5 comprises CDR-H1 of SEQ ID NO: 528, CDR-H2 of SEQ ID NO: 553 and CDR-H3 of SEQ ID NO: 585 and the VL that binds LRP5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 493 of ANT21-Knob of Table 6A, or

the VH that binds LRP5 comprises CDR-H1 of SEQ ID NO: 528, CDR-H2 of SEQ ID NO: 553 and CDR-H3 of SEQ ID NO: 585 and the VL that binds LRP5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 492 of ANT36-Knob of Table 6A, orthe VH that binds LRP5 comprises CDR-H1 of SEQ ID NO: 536, CDR-H2 of SEQ ID NO: 566 and CDR-H3 of SEQ ID NO: 603 and the VL that binds LRP5 comprises CDR-L1 of SEQ ID NO: 1, CDR-L2 of SEQ ID NO: 2 and CDR-L3 of SEQ ID NO: 493 of ANT39-Knob of Table 6A,

and the VH that binds FZD4 comprises,

FZD4 Fab CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT16 Knob of Table 6B, or

FZD4 Fab CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT18 Knob of Table 6B, or

FZD4 Fab CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT20 Knob of Table 6B, or

FZD4 Fab CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 51 and a CDR-H3 of SEQ ID NO: 79 of ANT21 Knob of Table 6B, or

FZD4 Fab CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 61 and a CDR-H3 of SEQ ID NO: 90 of ANT36 Knob of Table 6B, or

FZD4 Fab CDR-H1 of SEQ ID NO: 24, a CDR-H2 of SEQ ID NO: 61 and a CDR-H3 of SEQ ID NO: 90 of ANT39 Knob of Table 6B,

and

(c) in each of the third and fourth monomers

the VL comprises the FZD4 Fab CDR-L1, CDR-L2 and CDR-L3 of SEQ ID NO: 3 of ANT16- Knob of Table 6B, or

the VL comprises the FZD4 Fab CDR-L1, CDR-L2 and CDR-L3 of SEQ ID NO: 3 of ANT18- Knob of Table 6B, or

the VL comprises the FZD4 Fab CDR-L1, CDR-L2 and CDR-L3 of SEQ ID NO: 3 of ANT20- Knob of Table 6B, or

the VL comprises the FZD4 Fab CDR-L1, CDR-L2 and CDR-L3 of SEQ ID NO: 3 of ANT21- Knob of Table 6B, or

the VL comprises the FZD4 Fab CDR-L1, CDR-L2 and CDR-L3 of SEQ ID NO: 12 of ANT36- Knob of Table 6B, or

the VL comprises the FZD4 Fab CDR-L1, CDR-L2 and CDR-L3 of SEQ ID NO: 12 of ANT39- Knob of Table 6B,

wherein the FZD4 Fab CDR-L1 comprises SVSSA (SEQ ID NO: 1) and CDR-L2 comprises SASSLYS (SEQ ID NO: 2).

35. The tetravalent binding antibody molecule of any one of claims 1 to 34 wherein the tetravalent binding antibody molecule does not comprise a FZD binding domain comprising the

CDRs of the FZD-binding antibody 5044 in combination with the Wnt co-receptor binding domain comprising the CDRs of LRP6-binding antibody 2542 and/or antibody 2539.

36. The tetravalent binding antibody molecule of any one of claims 1 to 35, wherein the tetravalent binding antibody molecule comprises

(a) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 898, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 897 and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 899 wherein the amino acid sequence of the CDRs are the amino acid sequence of the CDRs of ANT16; or

(b) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 901, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 900 and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 902 wherein the amino acid sequence of the CDRs are the amino acid sequence of the CDRs of ANT 18; or

(c) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 904, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 903 and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 902 wherein the amino acid sequence of the CDRs are the amino acid sequence of the CDRs of ANT20; or

(d) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 906, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 905 and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 902 wherein the amino acid sequence of the CDRs are the amino acid sequence of the CDRs of ANT21; or

(e) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 908, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 907 and a light chain comprising the amino acid

sequence of the light chain construct of SEQ ID NO: 909 wherein the amino acid sequence of the CDRs are the amino acid sequence of the CDRs of ANT39; or

(f) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct selected from the group consisting of SEQ ID NO: 921; SEQ ID NO: 922; SEQ ID NO: 923; SEQ ID NO: 924; SEQ ID NO: 925; SEQ ID NO: 926; SEQ ID NO: 927; and SEQ ID NO: 928; a second heavy chain comprising the amino acid of a knob heavy chain construct selected from the group consisting of SEQ ID NO: 929; SEQ ID NO: 930; SEQ ID NO: 931; SEQ ID NO: 932; SEQ ID NO: 933; SEQ ID NO: 934; SEQ ID NO: 935; and SEQ ID NO: 936; and a light chain comprising the amino acid sequence of the light chain construct selected from the group consisting of SEQ ID NO: 909 and SEQ ID NO: 952.

37. The tetravalent binding antibody molecule of any one of claims 1 to 35, wherein the tetravalent binding antibody molecule comprises

(a) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 921 or SEQ ID NO: 925, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 929 or SEQ ID NO: 933, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

b) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 922 or SEQ ID NO: 926, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 930 or SEQ ID NO: 934, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

c) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 923 or SEQ ID NO: 927, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 931 or SEQ ID NO: 935, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

d) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 924 or SEQ ID NO: 928, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 932 or SEQ ID NO: 936, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

e) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 908 or SEQ ID NO: 940, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 944 or SEQ ID NO: 948, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

f) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 937 or SEQ ID NO: 941, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 945 or SEQ ID NO: 949, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

g) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 938 or SEQ ID NO: 942, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 946 or SEQ ID NO: 950, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952; or

h) a first heavy chain comprising the amino acid sequence of the hole heavy chain construct of SEQ ID NO: 939 or SEQ ID NO: 943, a second heavy chain comprising the amino acid a knob heavy chain construct of SEQ ID NO: 947 or SEQ ID NO: 951, and a light chain comprising the amino acid sequence of the light chain construct of SEQ ID NO: 909 or SEQ ID NO: 952.

38. A pharmaceutical composition comprising a tetravalent binding antibody molecule of any one claims 1 to 37 and a pharmaceutically acceptable carrier.

39. A method for promoting endothelial cell barrier functions in a tissue comprising administering an effective amount of a tetravalent binding antibody molecule of any one of claims 1 to 37 to a tissue.

40. The method of claim 39, wherein the tissue is brain, kidney or eye tissue.

41. The method of claim 40, wherein the tetravalent binding antibody molecule is administered to eye tissue by intravitreal injection.

42. A method for increasing retinal or brain endothelial cell barrier functions, decreasing endothelial cell permeability, enhancing or restoring blood retina and blood brain barrier maintenance in a subject in need thereof comprising contacting an endothelial cell comprising an FZD4 receptor and an LRP5 in a subject in need thereof with an effective amount of a tetravalent binding antibody molecule of any one of claim 1 to 37.

43. The method of claim 42, wherein the tetravalent binding antibody molecule is administered to the subject in need thereof by injection, topically, or orally.

44. The method of claim 42, wherein the tetravalent binding antibody molecule is administered subcutaneously, intravenously, intraperitoneally, intrathecally, intravitreously, or intraocularly.

45. The tetravalent binding antibody molecule of any one of claims 1 to 37 or the pharmaceutical composition of claim 38 for use as a medicament.

46. The tetravalent binding antibody molecule or pharmaceutical composition of claim 45 for use in the treatment or prevention of a disorder or condition characterized by defective retinal or brain angiogenesis and/or characterized by reduced endothelial cell barrier function and/or vascular leakage.

47. A method of treating or preventing a disorder or condition characterized by defective retinal or brain angiogenesis and/or reduced endothelial cell barrier function and/or vascular leakage comprising administering to a person in need thereof a therapeutically effective amount of the tetravalent binding antibody molecule of any one of claims 1 to 37 or the pharmaceutical composition of claim 38.

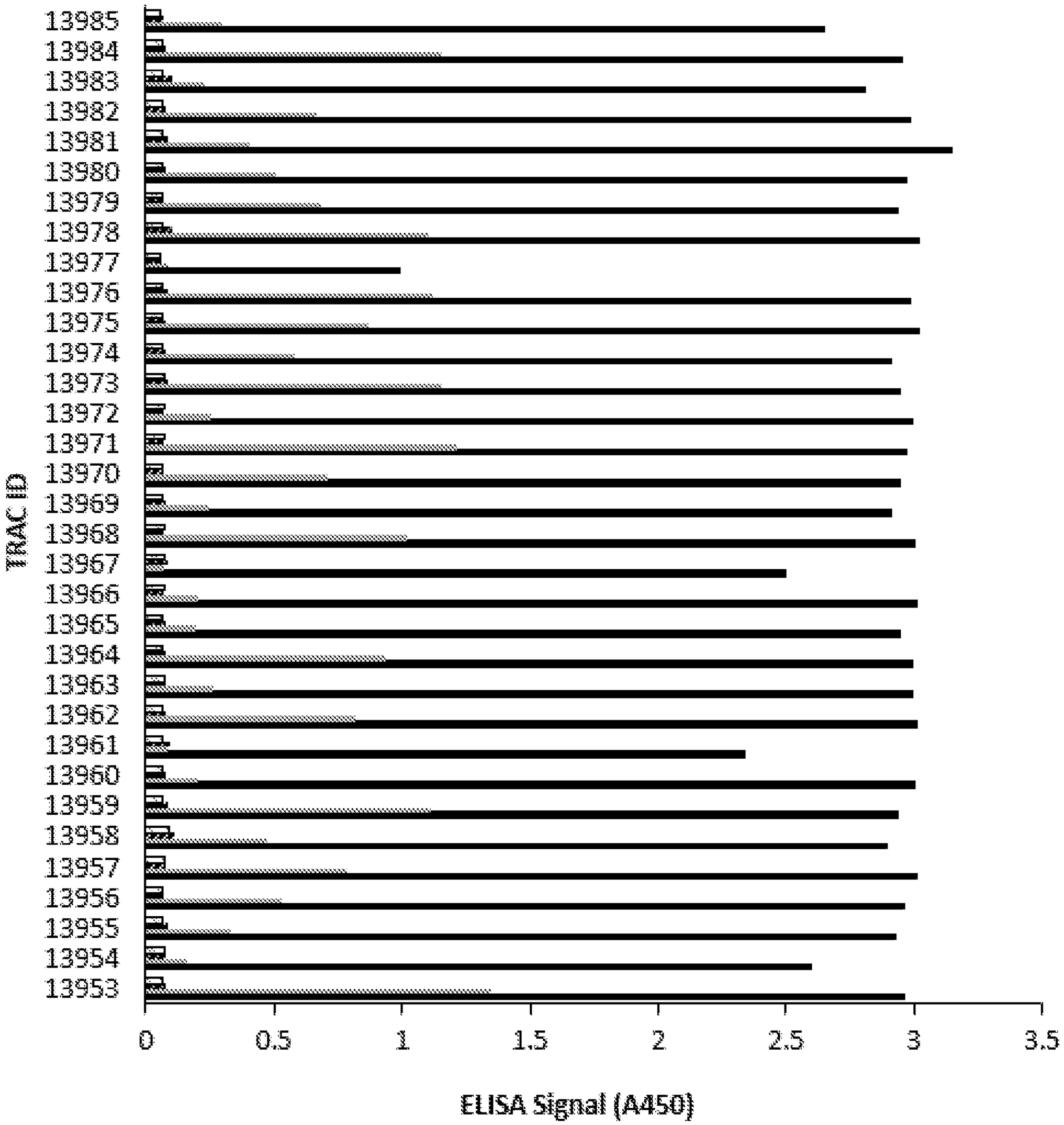
48. Use of the tetravalent binding antibody molecule of claims 1 to 37 or the pharmaceutical composition of claim 38 for the manufacture of a medicament for the treatment or prevention of a disorder or condition characterized by defective retinal or brain angiogenesis and/or reduced endothelial cell barrier function and/or vascular leakage.

49. The tetravalent binding antibody molecule or pharmaceutical composition for use, method or use of any one of claims 46 to 48 wherein the disorder is selected from diabetic retinopathy, retinopathy of prematurity, Coats' disease, FEVR, Norrie disease, macular degeneration, diabetic macular edema, pediatric vitreoretinopathies, Alzheimer's disease, epilepsy, multiple sclerosis, stroke and ischemia.

50. The tetravalent binding antibody molecule of any one of claims 1 to 37 or the pharmaceutical composition of claim 37, for use in the treatment or prevention of an ocular disorder e.g. a disorder of the retina or macula e.g. selected from diabetic retinopathy, retinopathy of prematurity, Coats' disease, FEVR, Norrie disease, macular degeneration, diabetic macular edema and pediatric vitreoretinopathies or in the treatment or prevention of a disorder selected from Alzheimer's disease, epilepsy, multiple sclerosis, stroke and ischemia.

51. A method of treating or preventing an ocular disorder e.g. a disorder of the retina or macula e.g. selected from diabetic retinopathy, retinopathy of prematurity, Coats' disease, FEVR, Norrie disease, macular degeneration, diabetic macular edema and pediatric vitreoretinopathies or in the treatment or prevention of a disorder selected from Alzheimer's disease, epilepsy, multiple sclerosis, stroke and ischemia comprising administering to a person in need thereof a therapeutically effective amount of the tetravalent binding antibody molecule of any one of claims 1 to 37 or the pharmaceutical composition of claim 38.

52. Use of the tetravalent binding antibody molecule of claims 1 to 36 or the pharmaceutical composition of claim 38 for the manufacture of a medicament for the treatment or prevention of an ocular disorder e.g. a disorder of the retina or macula e.g. selected from diabetic retinopathy, retinopathy of prematurity, Coats' disease, FEVR, Norrie disease, macular degeneration, diabetic macular edema and pediatric vitreoretinopathies or in the treatment or prevention of a disorder selected from Alzheimer's disease, epilepsy, multiple sclerosis, stroke and ischemia.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13953
0
0.5
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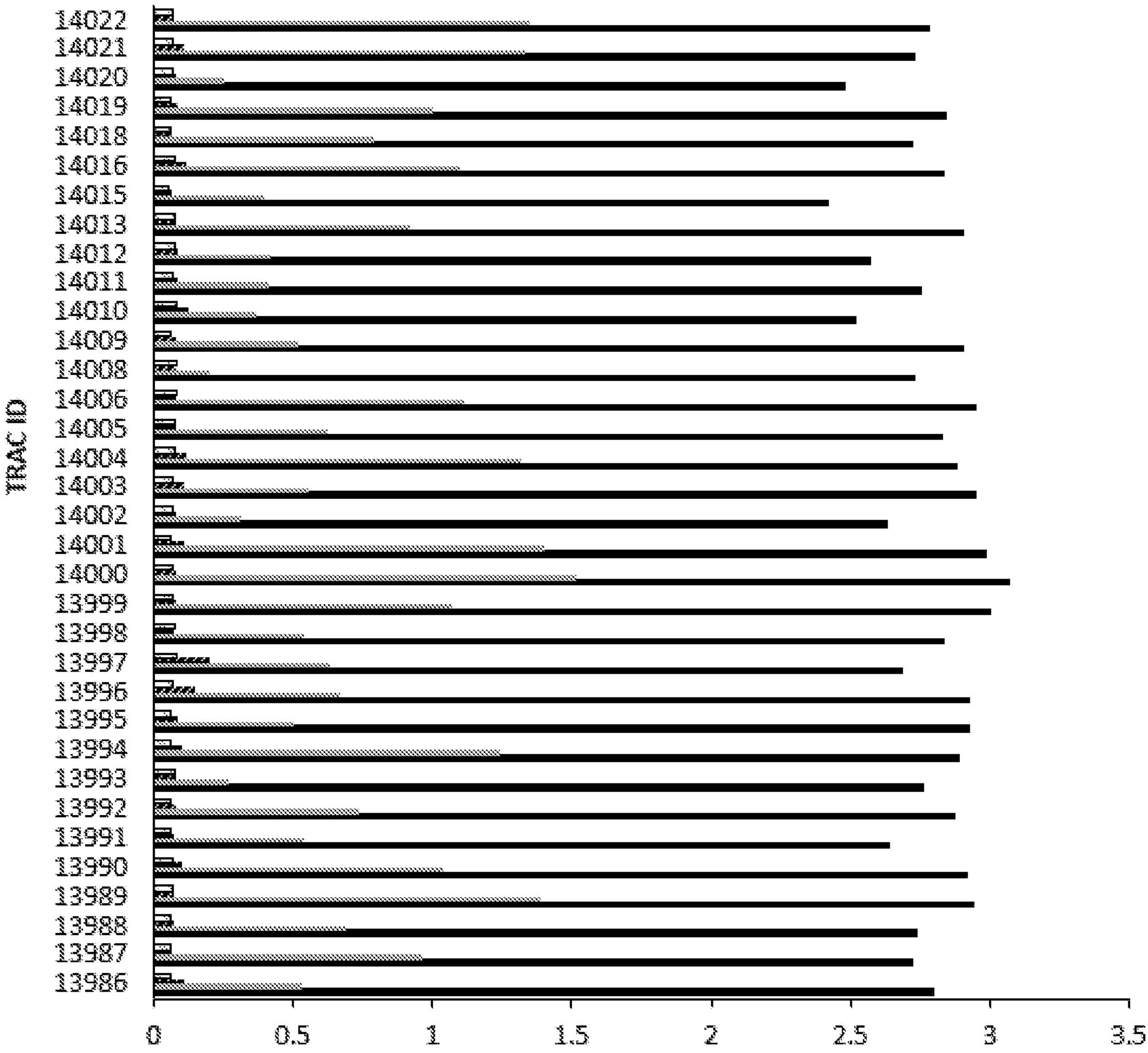
ELISA Signal (A450)
BSA
Fc
Fzd4+Blocking Ab.
Fzd4

FIG 1A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13996
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13993
13992
13991
13990
13989
13988
13987
13986
0
0.5
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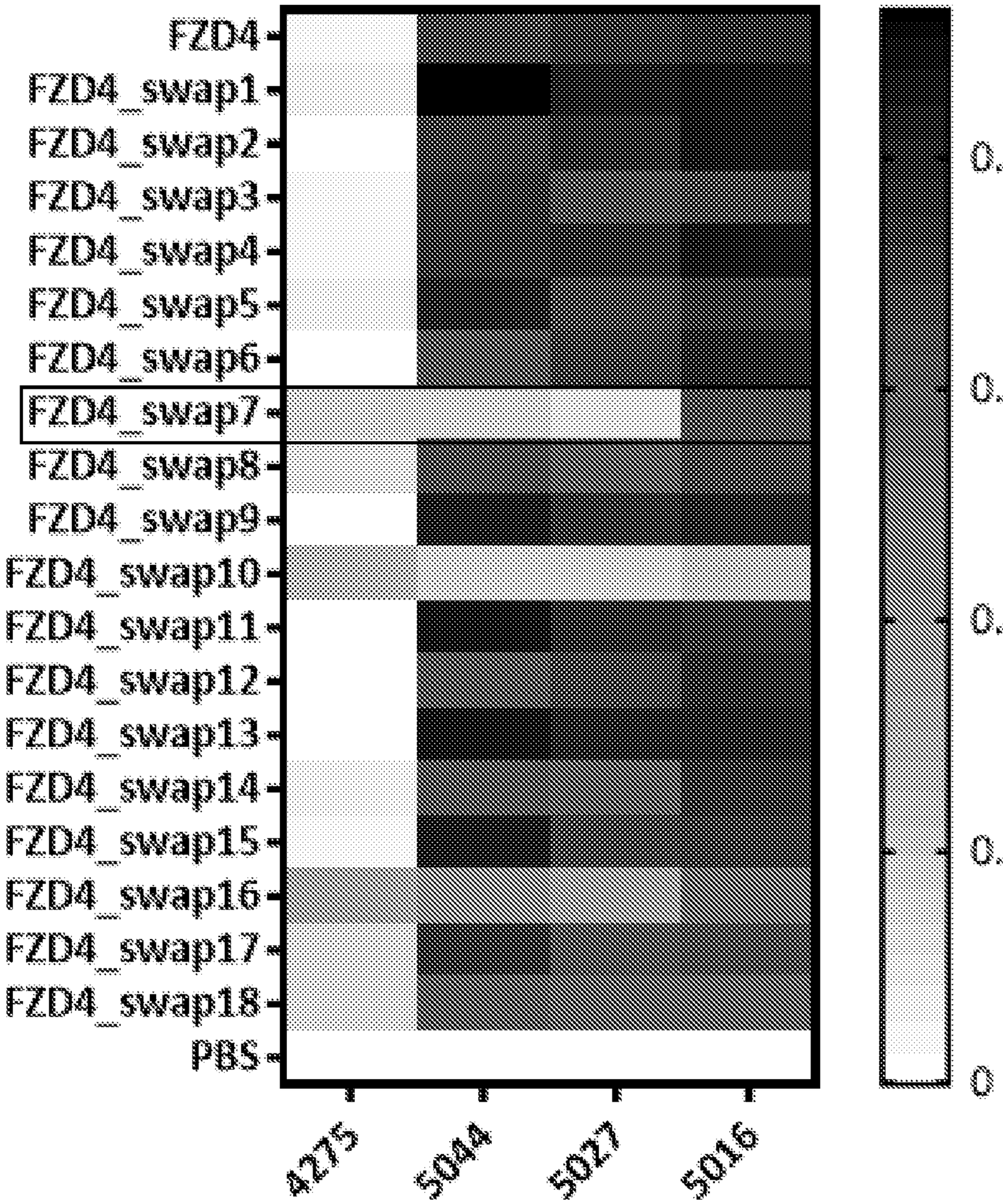
Fc
Fzd4+Blocking Ab.
Fzd4

FIG 1B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FZD4_swap2
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FZD4_swap4
FZD4_swap5
FZD4_swap6
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FZD4_swap17
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0.4
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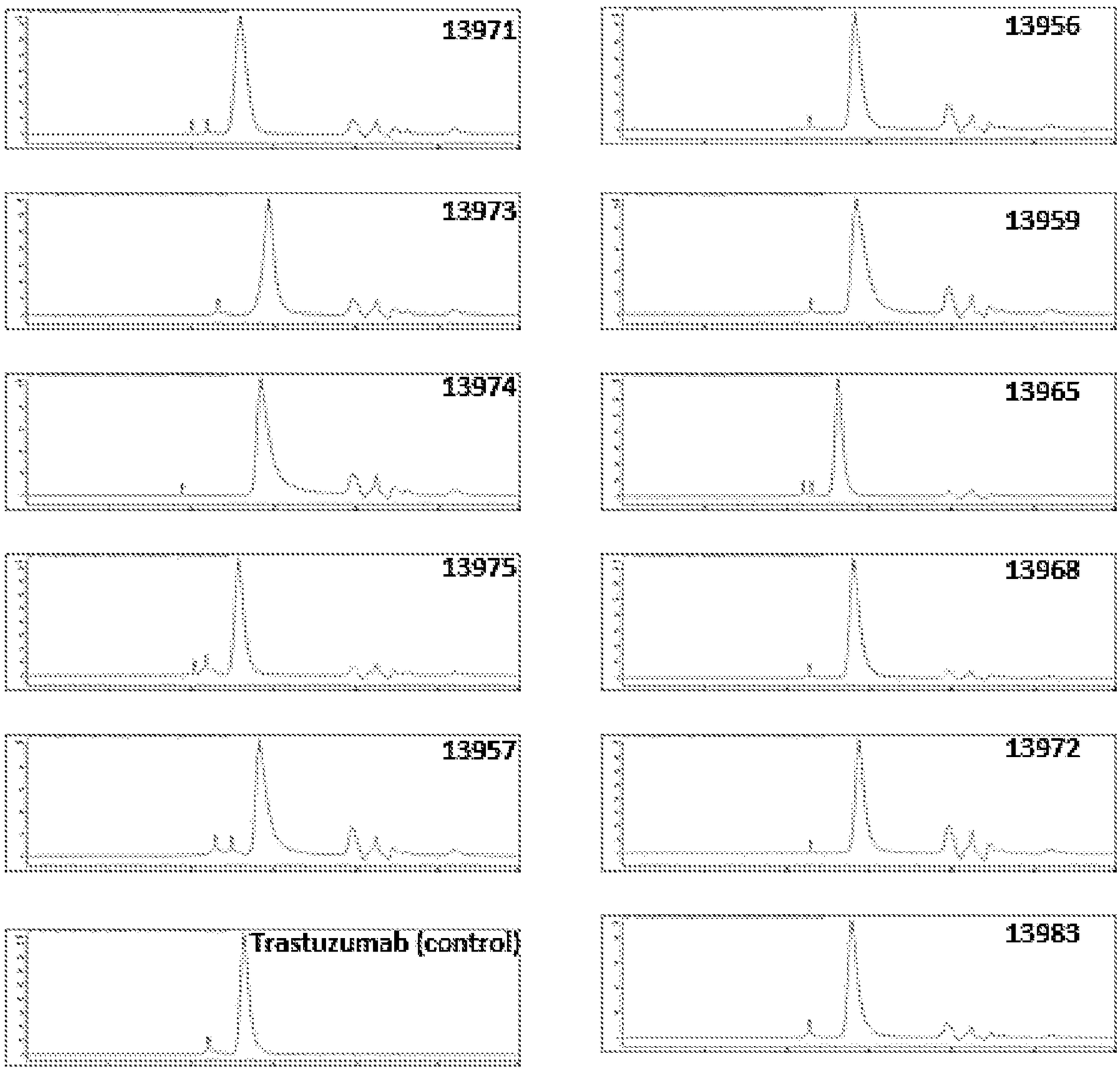
0
Baseline Corrected AI450

FIG 2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13972
Trastuzumab (control)
13983

FIG 3A


ELISA Signal (A450)
1.5
1.0
0.5
0
FZD4
FZD1
FZD10
BSA
Mock
1398179
1398175
1398178
1398173
1398174
1398176
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1398172
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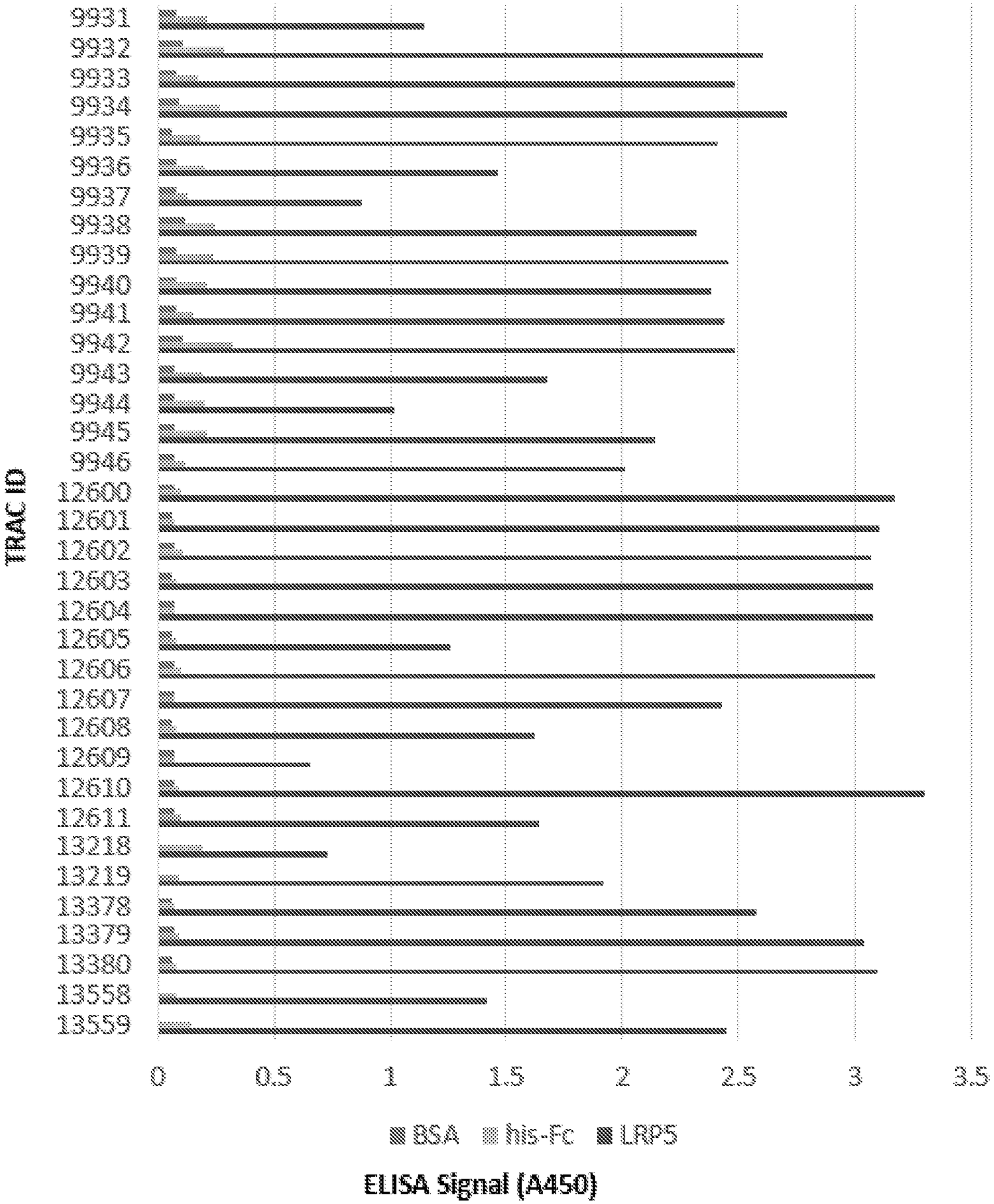
FIG 3B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12606
12607
12608
12609
12610
12611
13218
13219
13378
13379
13380
13558
13559
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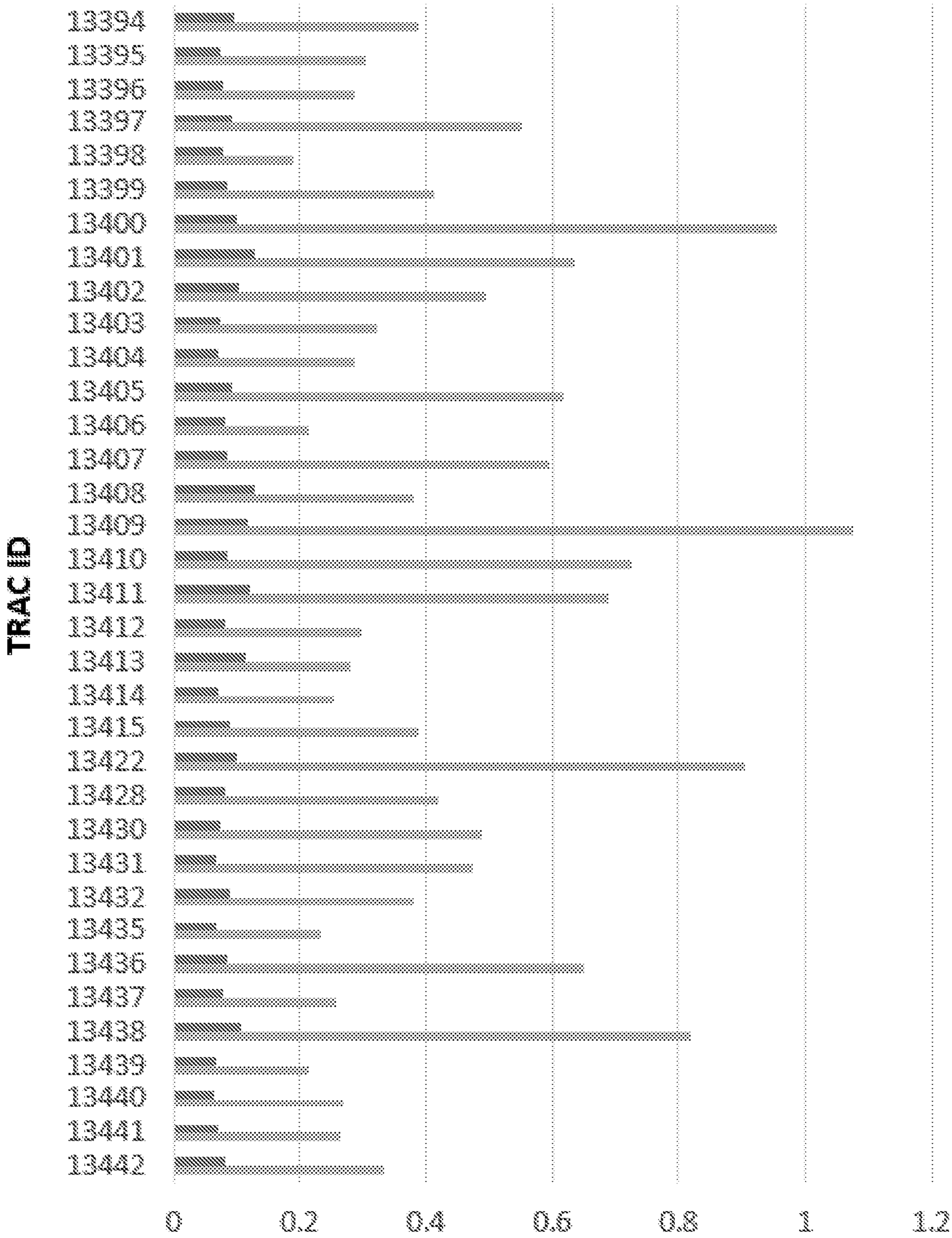
2
2.5
3
3.5
BSA
his-Fc
LRP5
ELISA Signal (A450)

FIG 4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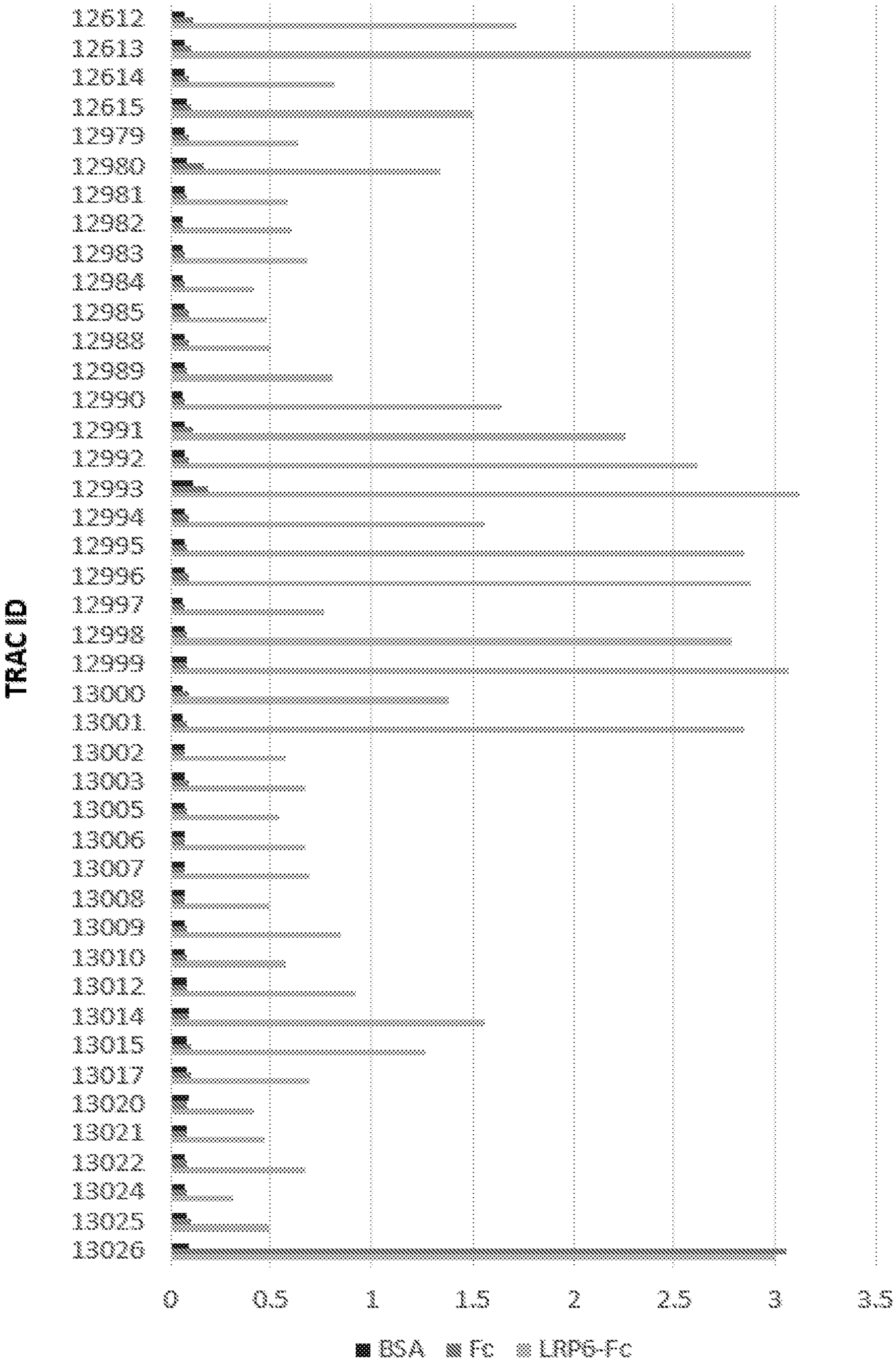
13414
13415
13422
13428
13430
13431
13432
13435
13436
13437
13438
13439
13440
13441
13442
0
0.2
0.4
0.6
0.8
1
1.2
Fc
LRP6-Fc
ELISA Signal (A450)

FIG 5A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13005
13006
13007
13008
13009
13010
13012
13014
13015
13017
13020
13021
13022
13024
13025
13026
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1
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2
2.5
3
3.5
BSA
Fc
LRP6-Fc
ELISA Signal (A450)

FIG 5B

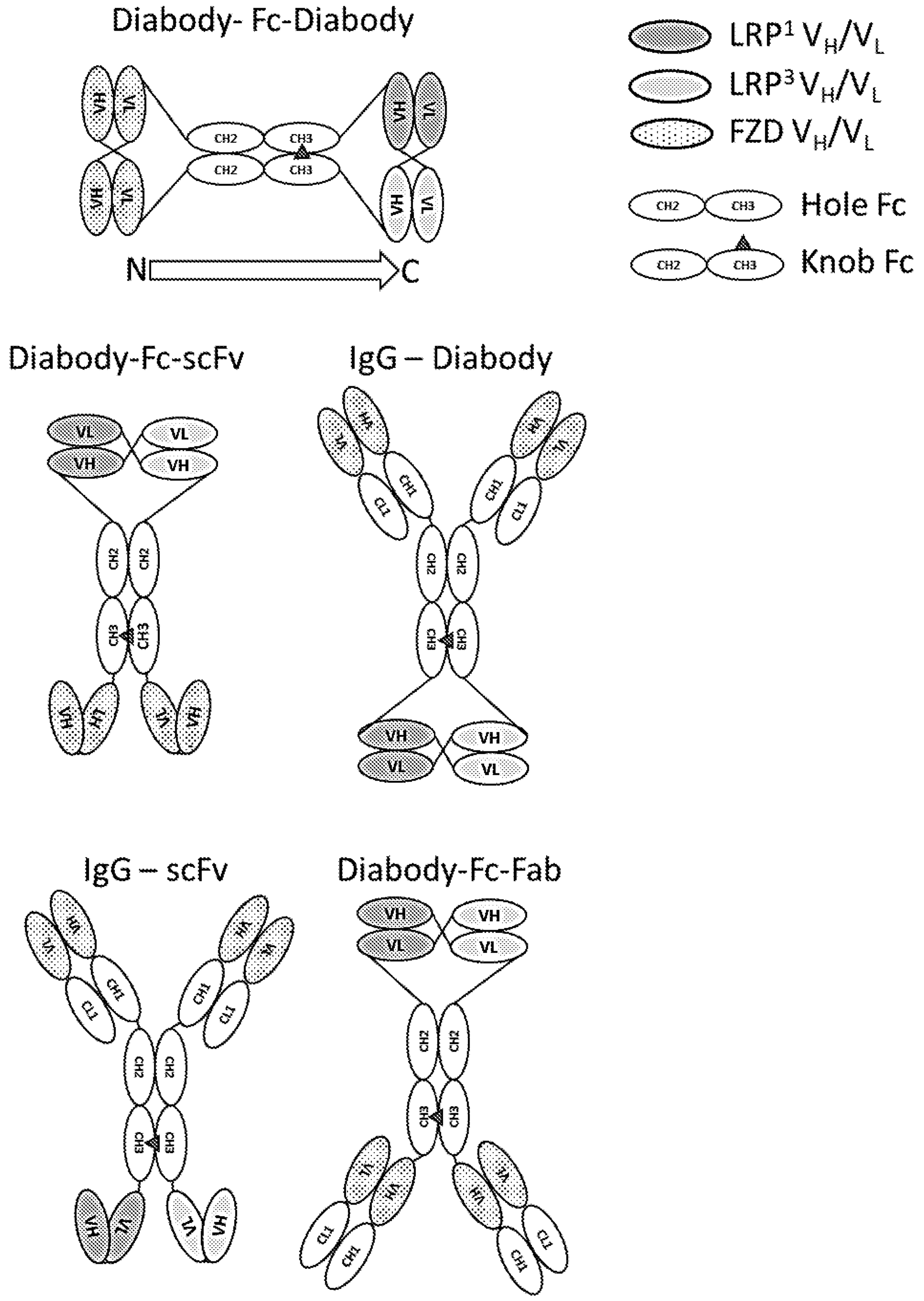

Diabody- Fc-Diabody
VH
VL
CH2
CH3
N
C
LRP1 VH/VL
LRP3 VH/VL
FZD VH/VL
Hole Fc
Knob Fc
Diabody-Fc-scFv
IgG – Diabody
IgG – scFv
Diabody-Fc-Fab
CH1
CL1

FIG 6

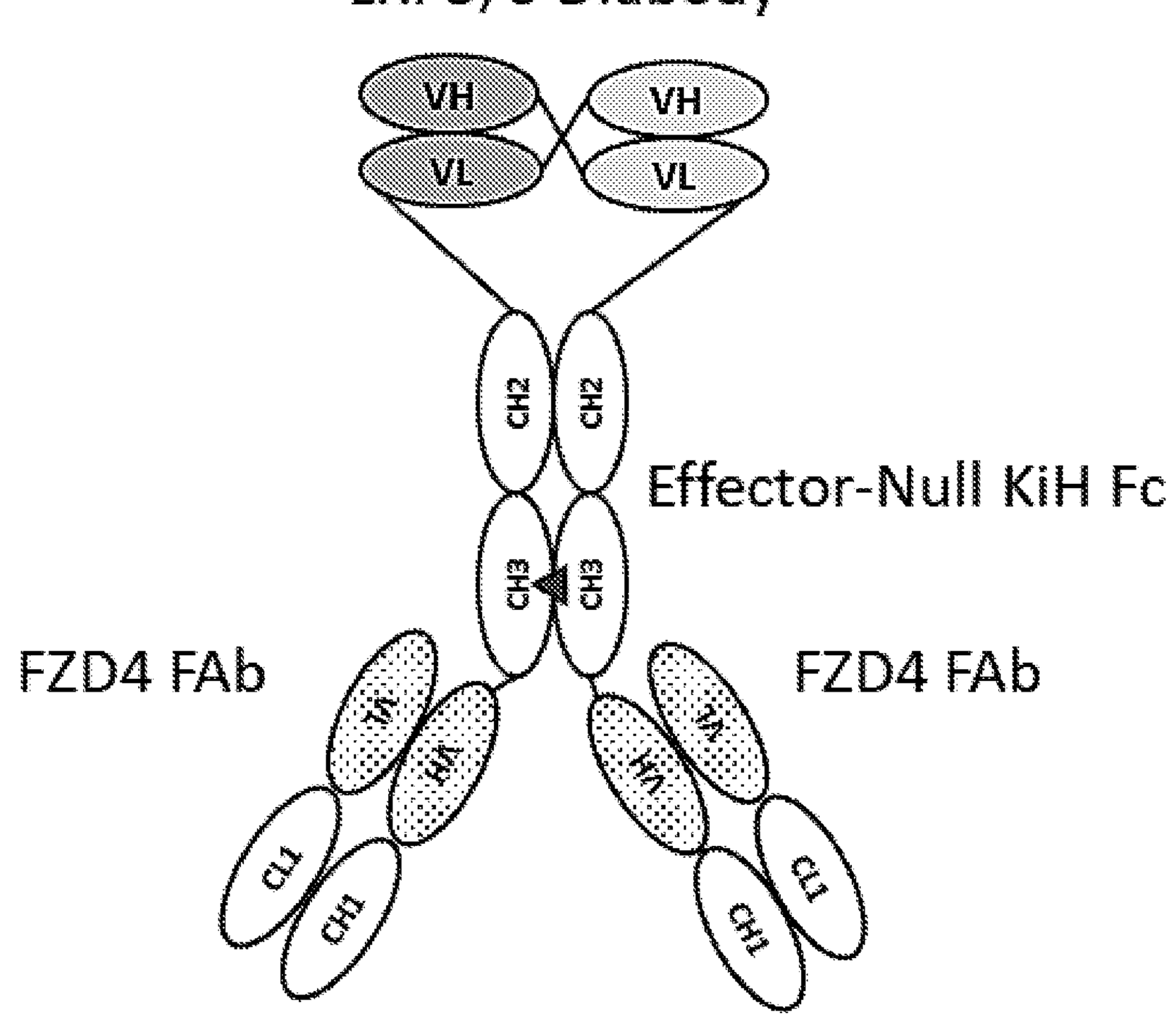

LRP5/6 Diabody
VH
VH
VL
VL
CH2
CH2
Effector-Null KiH Fc
CH3
CH3
FZD4 FAb
FZD4 FAb
VH
VH
CL
CH1
CL
CH1

FIG 7

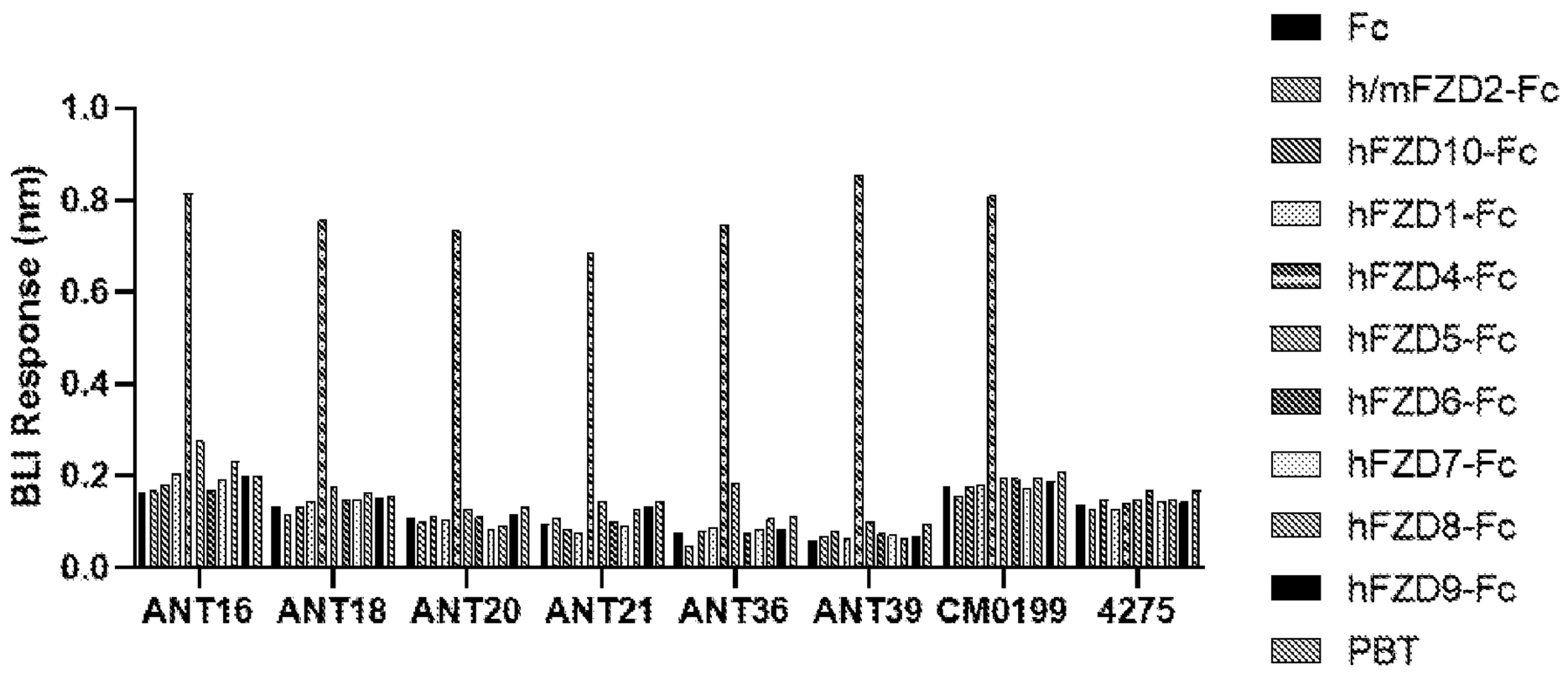

BLI Response (nm)
1.0
0.8
0.6
0.4
0.2
0.0
ANT16
ANT18
ANT20
ANT21
ANT36
ANT39
CM0199
4275
Fc
h/mFZD2-Fc
hFZD10-Fc
hFZD1-Fc
hFZD4-Fc
hFZD5-Fc
hFZD6-Fc
hFZD7-Fc
hFZD8-Fc
hFZD9-Fc
PBT

FIG 8A

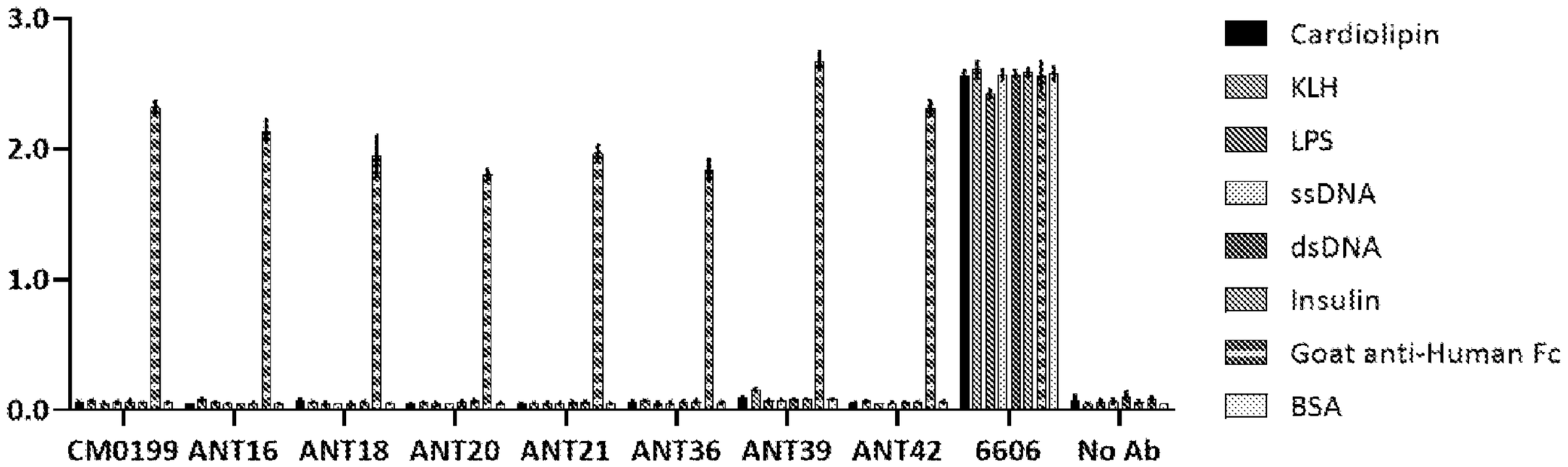
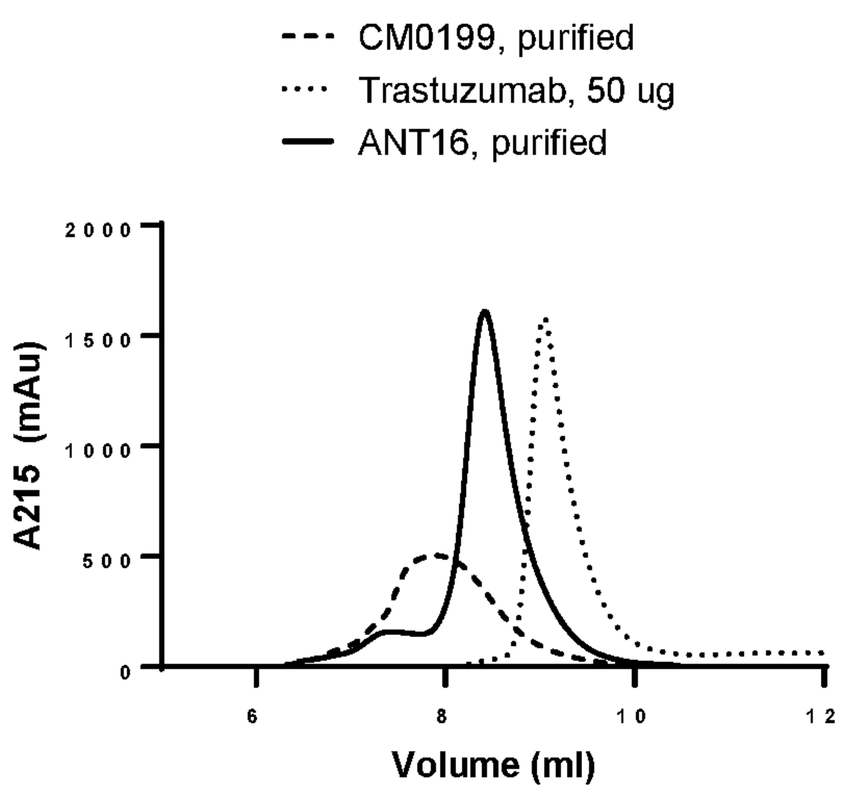
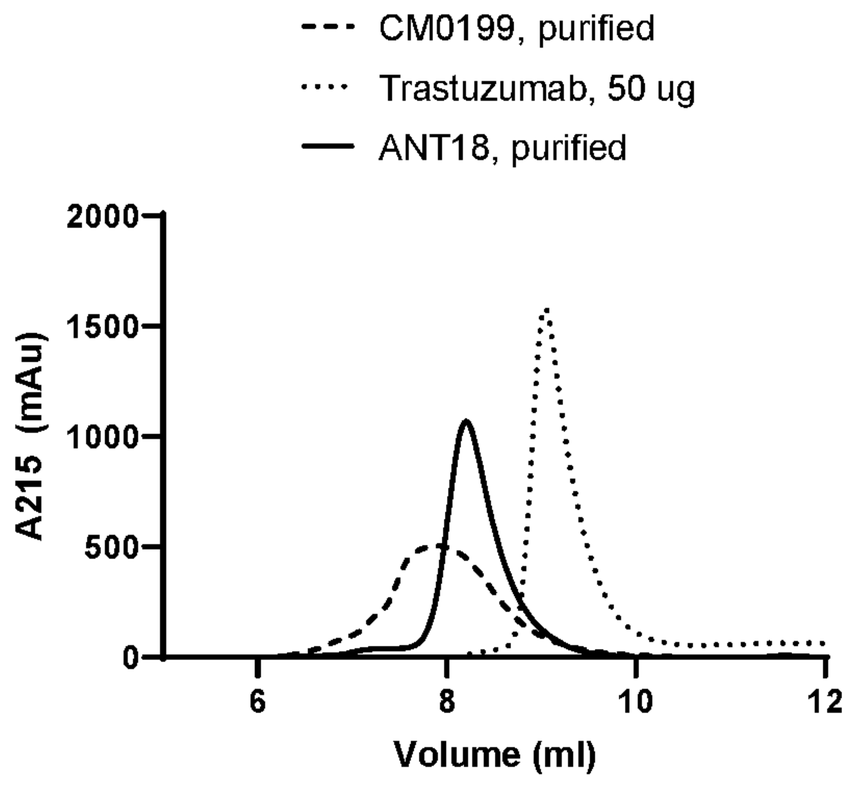
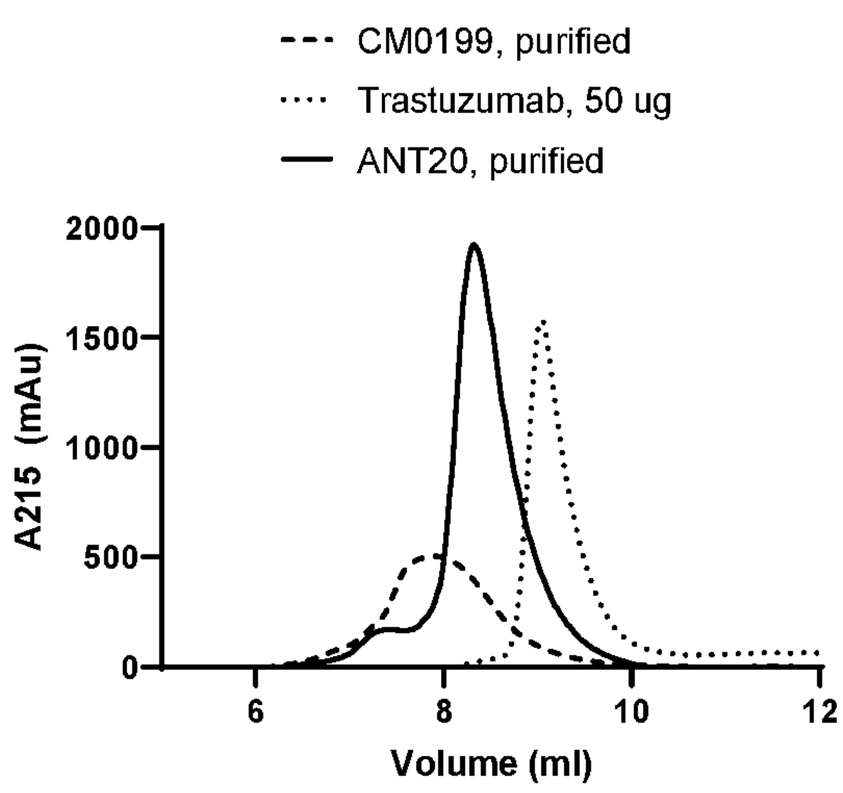
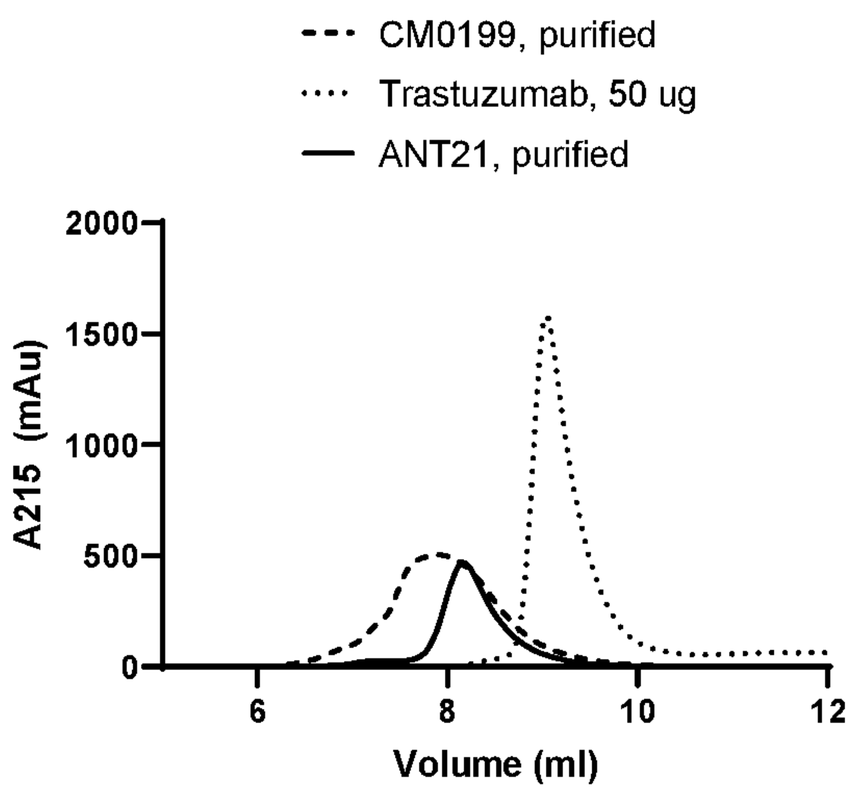

3.0
2.0
1.0
0.0
CM0199
ANT16
ANT18
ANT20
ANT21
ANT36
ANT39
ANT42
6606
No Ab
Cardiolipin
KLH
LPS
ssDNA
dsDNA
Insulin
Goat anti-Human Fc
BSA

FIG 8B


CM0199, purified
Trastuzumab, 50 ug
ANT16, purified
A215 (mAu)
Volume (ml)


CM0199, purified
Trastuzumab, 50 ug
ANT18, purified
A215 (mAu)
Volume (ml)


CM0199, purified
Trastuzumab, 50 ug
ANT20, purified
A215 (mAu)
Volume (ml)


CM0199, purified
Trastuzumab, 50 ug
ANT21, purified
A215 (mAu)
Volume (ml)

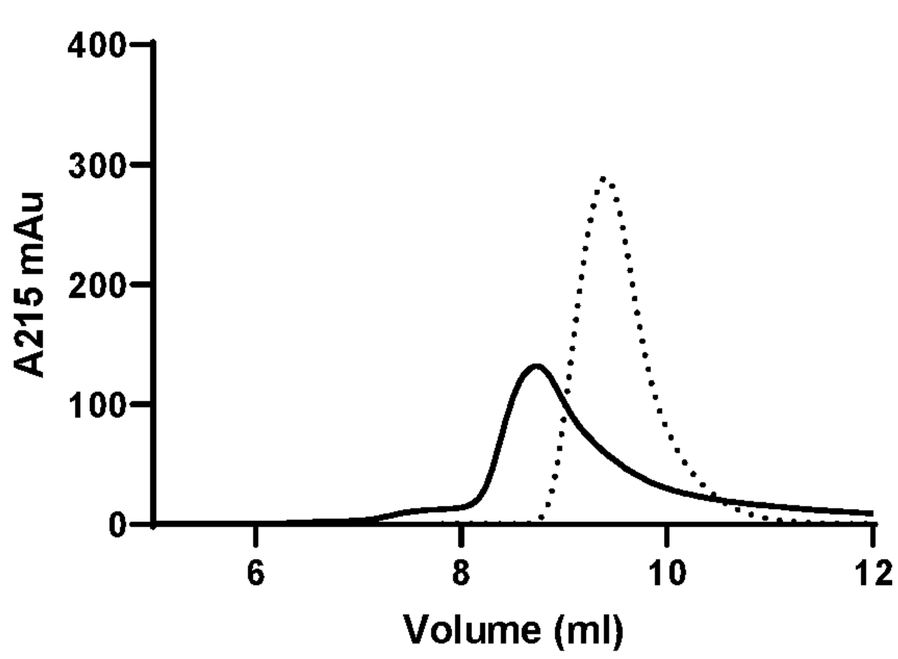
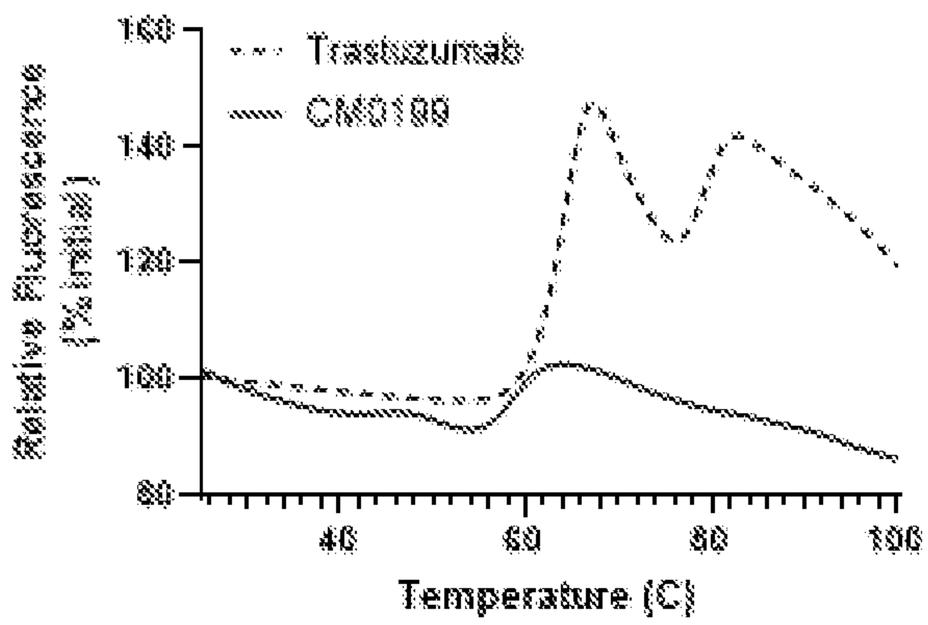
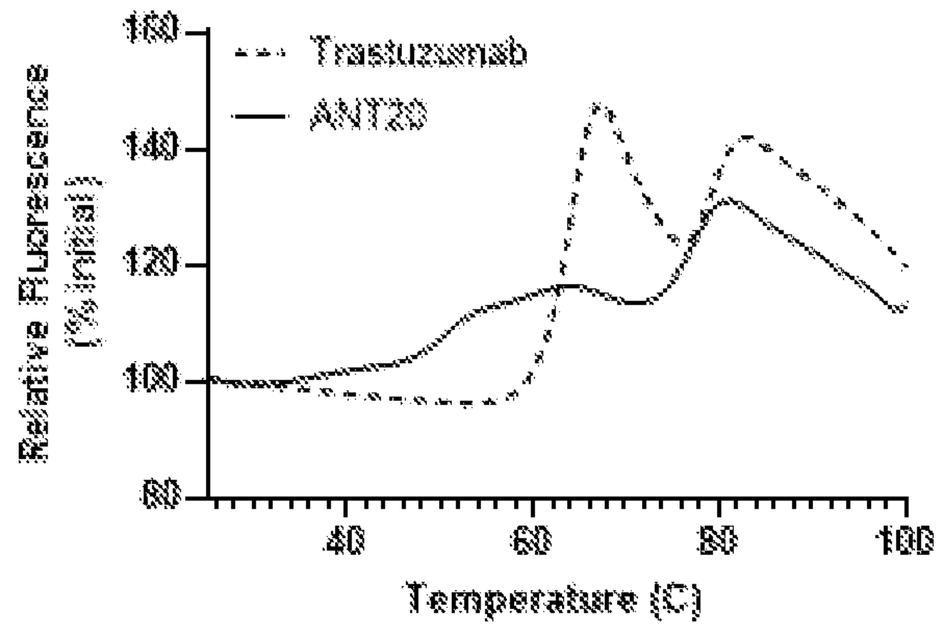
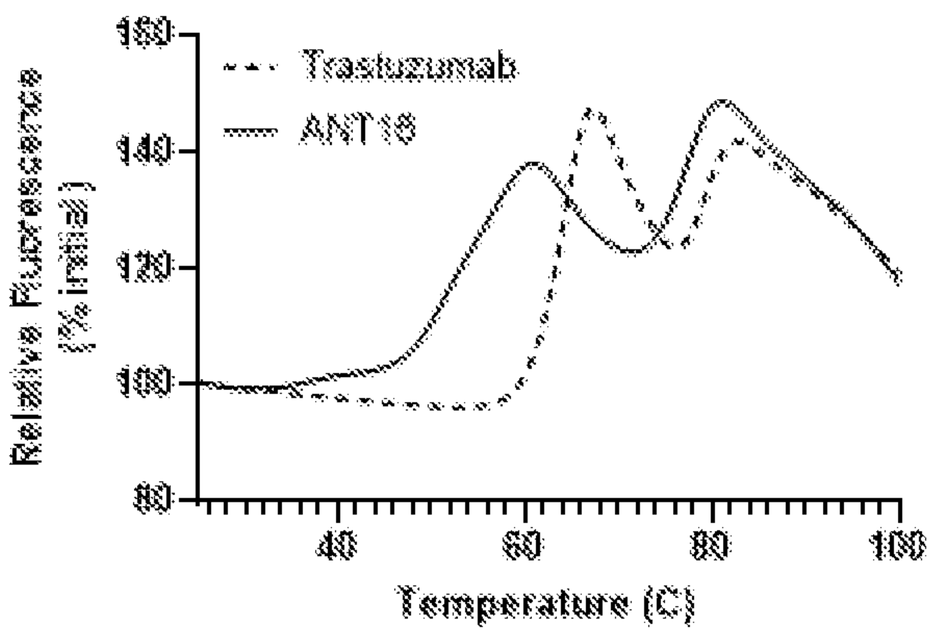
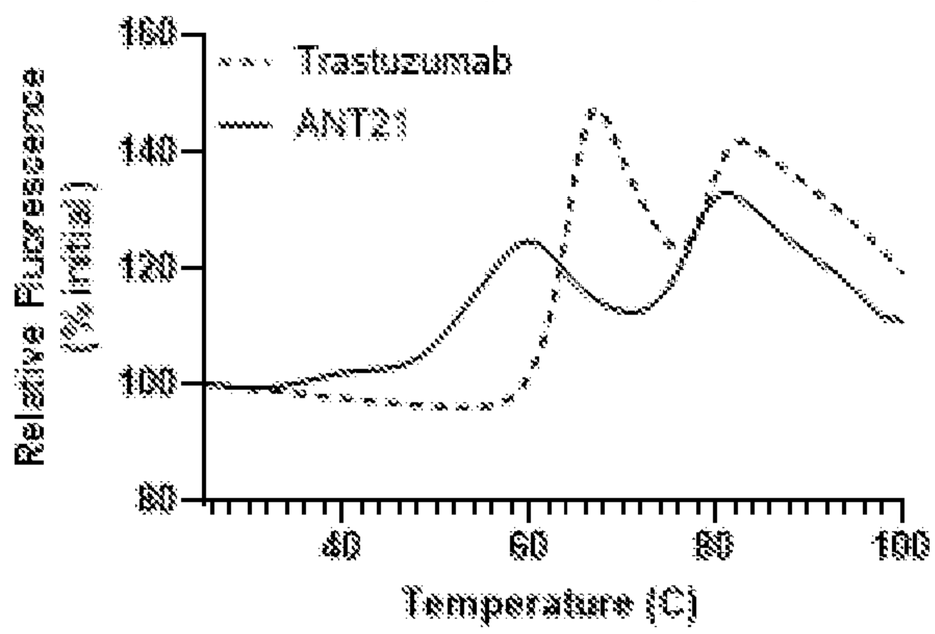

ANT39, purified
Trastuzumab
A215 mAu
Volume (ml)

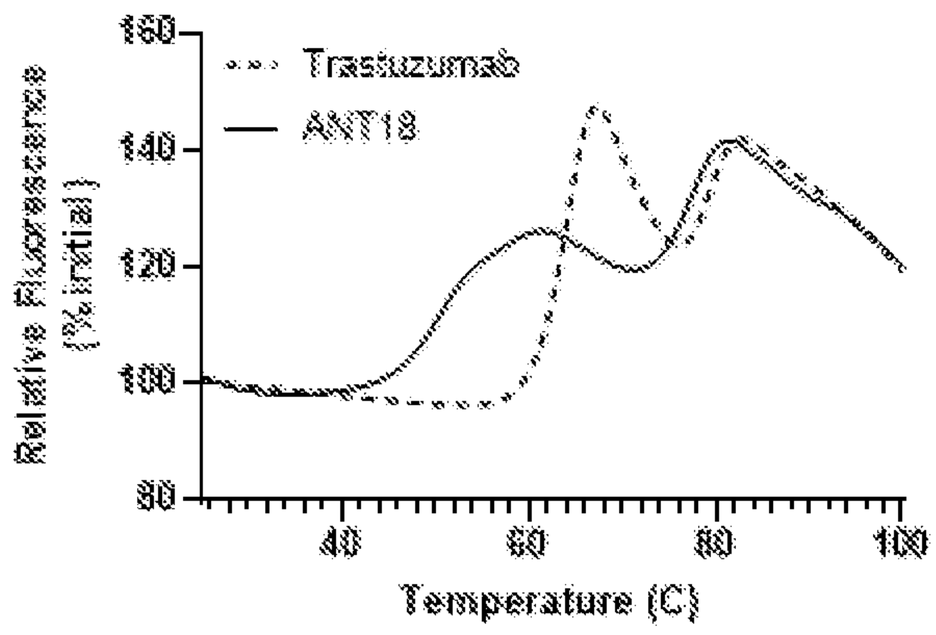
FIG 9A


Trastuzumab
CM0199
Relative Fluorescence (% initial)
160
140
120
100
80
40
60
80
100
Temperature (C)


Trastuzumab
ANT20
Relative Fluorescence (% initial)
160
140
120
100
80
40
60
80
100
Temperature (C)


Trastuzumab
ANT18
Relative Fluorescence (% initial)
160
140
120
100
80
40
60
80
100
Temperature (C)


Trastuzumab
ANT21
Relative Fluorescence (% initial)
160
140
120
100
80
40
60
80
100
Temperature (C)


Trastuzumab
ANT19
Relative Fluorescence (% initial)
160
140
120
100
80
40
60
80
100
Temperature (C)

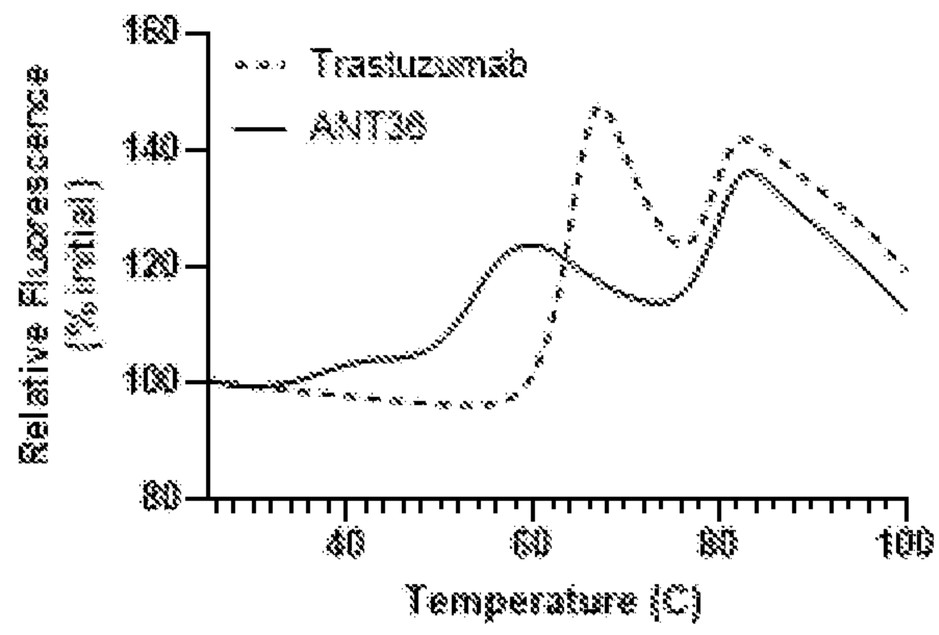

Trastuzumab
ANT39
Relative Fluorescence (% initial)
160
140
120
100
80
40
60
80
100
Temperature (C)

FIG 9B

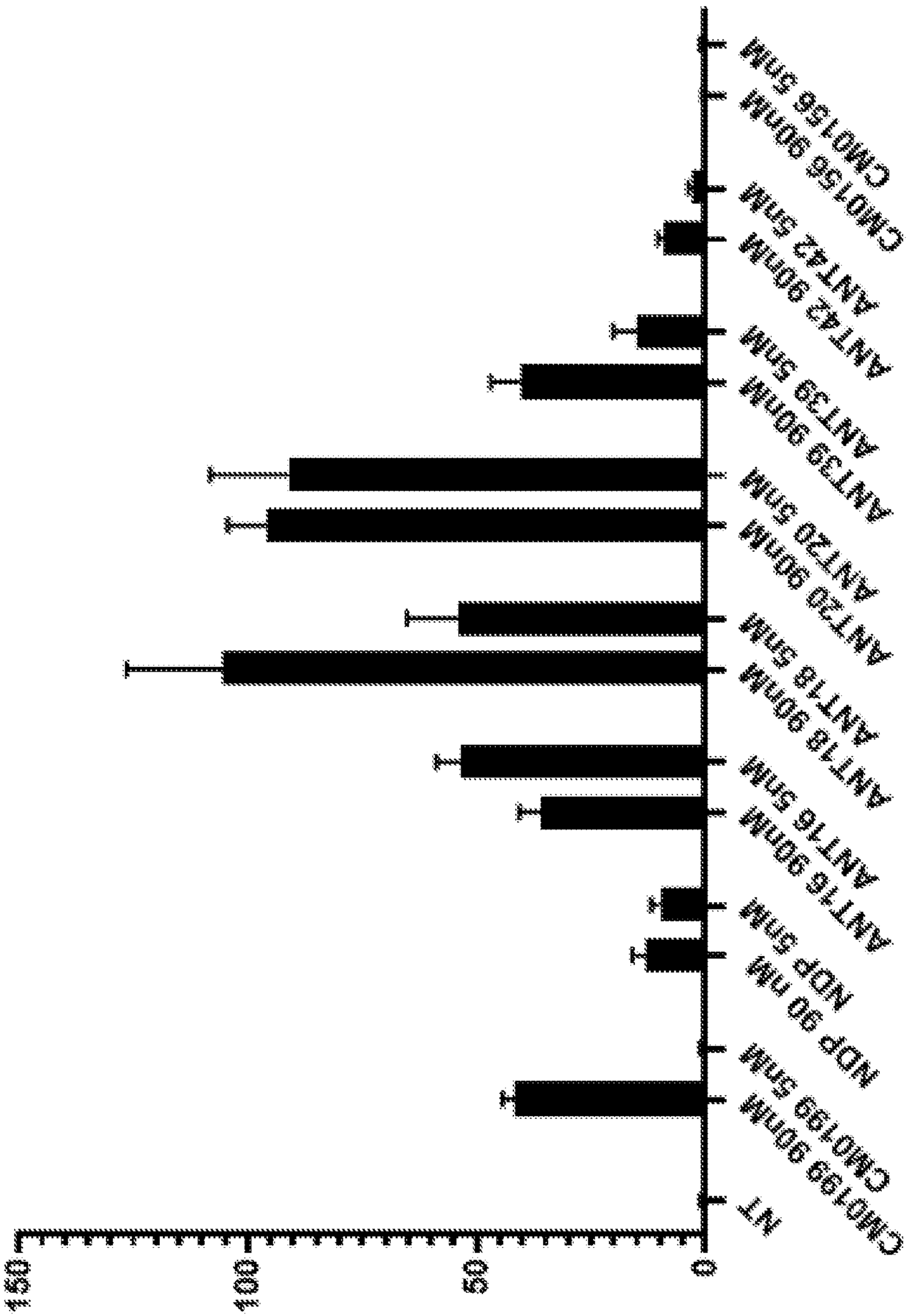
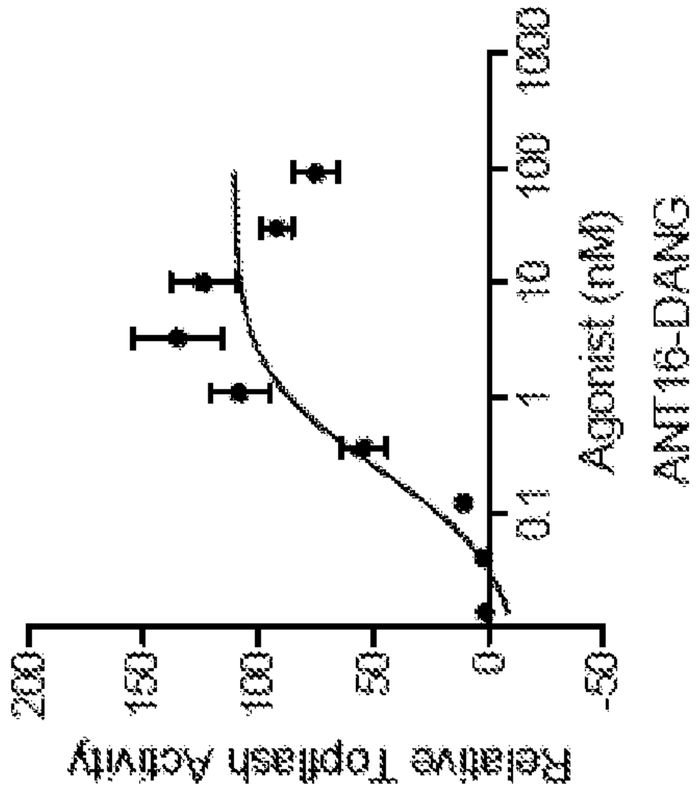
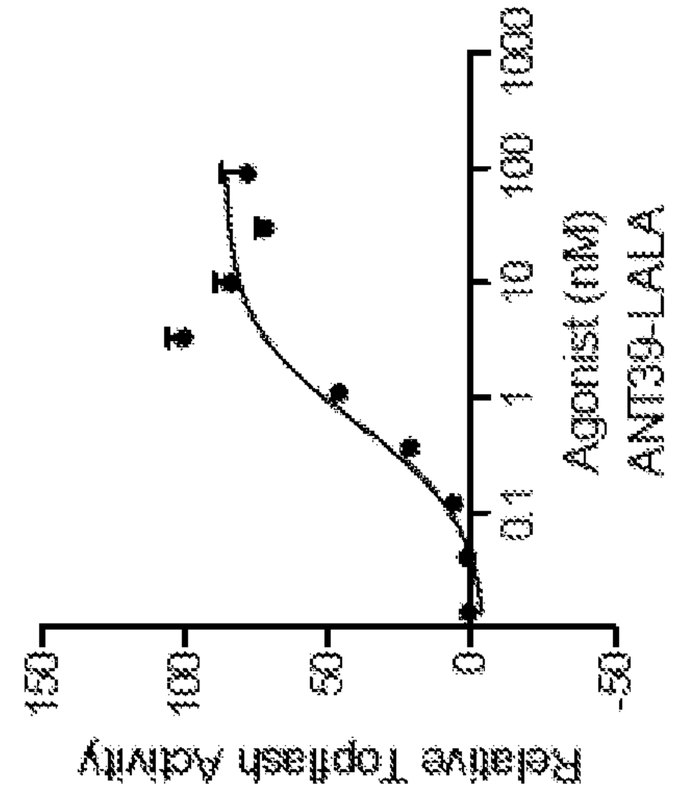
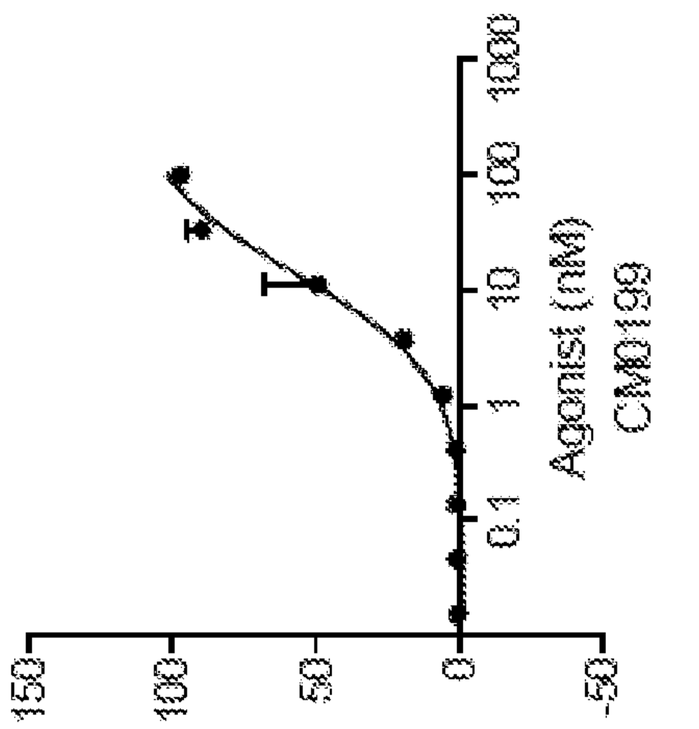

Axin2 mRNA levels
160
120
80
40
0
NT
CM01199 90nM
CM01199 5nM
NDP 90 nM
NDP 5nM
AMT16 90nM
AMT16 5nM
AMT18 90nM
AMT18 5nM
AMT20 90nM
AMT20 5nM
AMT39 90nM
AMT39 5nM
AMT42 90nM
AMT42 5nM
CM01156 90nM
CM01156 5nM

FIG 10


Relative Topflash Activity
200
150
100
50
0
-50
0.1
1
10
100
1000
Agonist (nM)
ANT16-DAMG


Relative Topflash Activity
150
100
50
0
-50
0.1
1
10
100
1000
Agonist (nM)
ANT39-LALA


Relative Topflash Activity
150
100
50
0
-50
0.1
1
10
100
1000
Agonist (nM)
CM0199

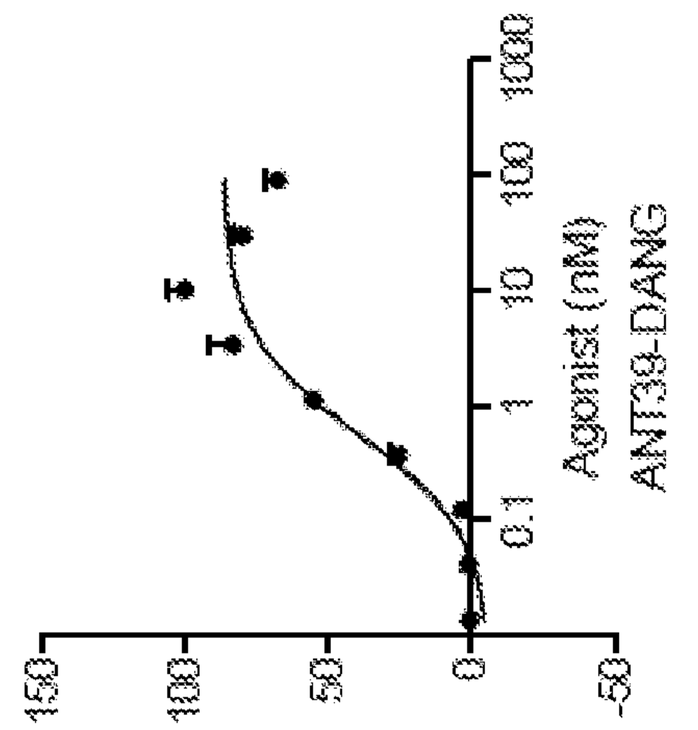
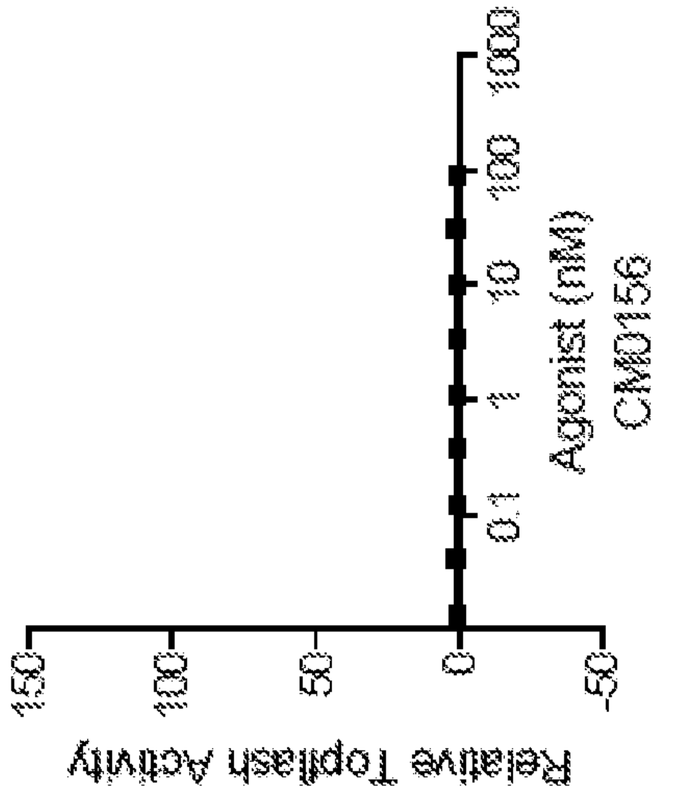
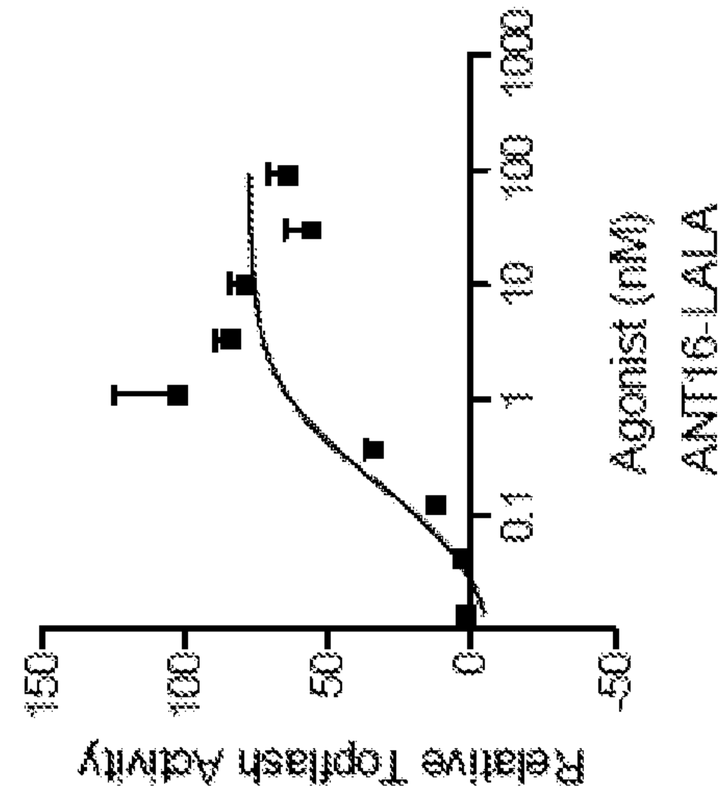
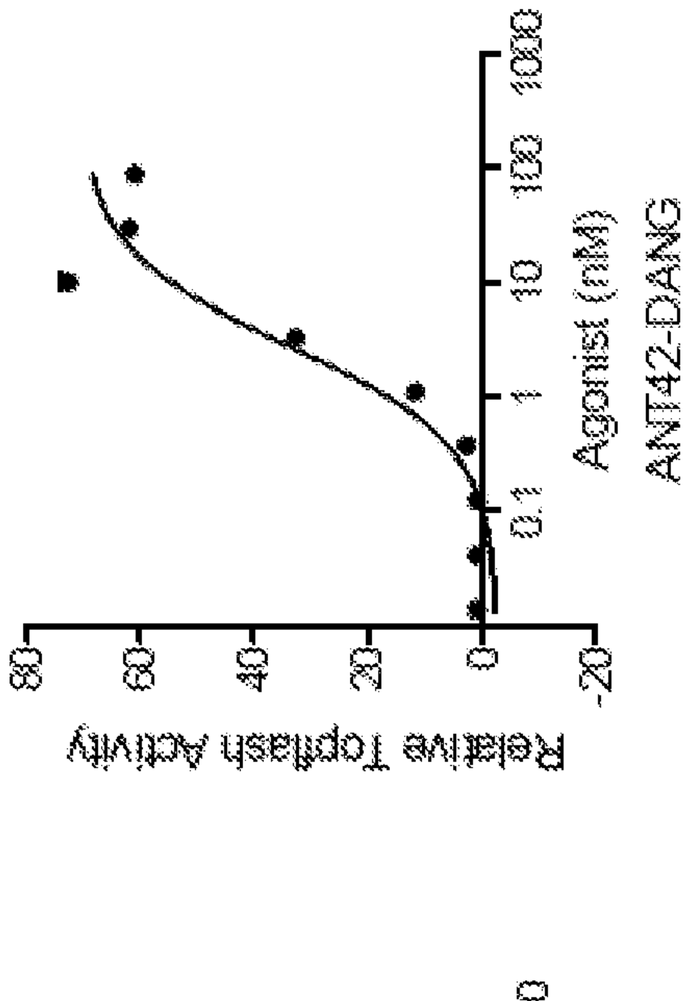
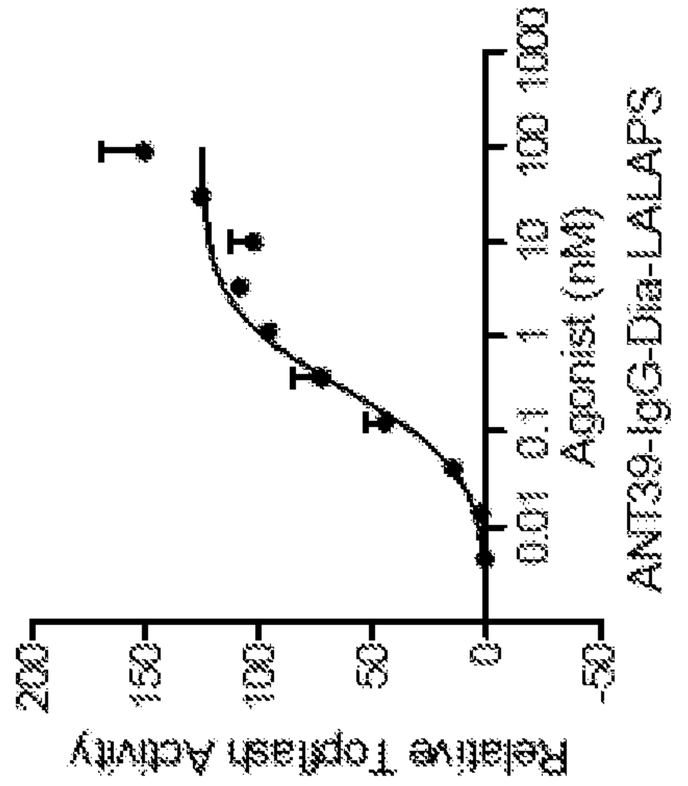

Relative Topflash Activity
150
100
50
0
-50
0.1
1
10
100
1000
Agonist (nM)
ANT39-DAMG

FIG 10 cont.


Relative Topflash Activity
150
100
50
0
-50
0.1
1
10
100
1000
Agonist (nM)
CM0156


Relative Topflash Activity
150
100
50
0
-50
0.1
1
10
100
1000
Agonist (nM)
ANT16-LALA


Relative Topflash Activity
80
60
40
20
0
-20
0.01
0.1
1
10
100
1000
Agonist (nM)
ANT42-DANG


Relative Topflash Activity
200
150
100
50
0
-50
0.01
0.1
1
10
100
1000
Agonist (nM)
ANT39-IgG-Dia-LALAPS

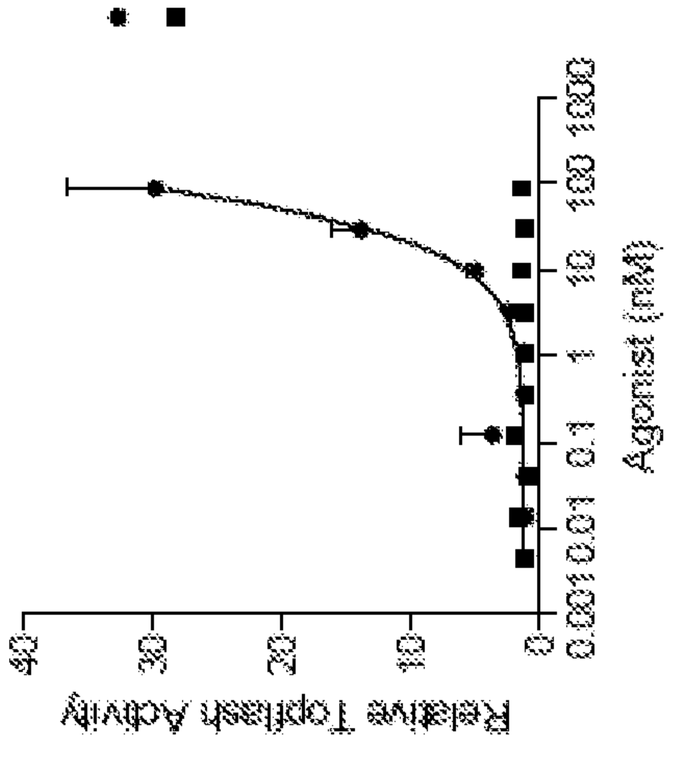
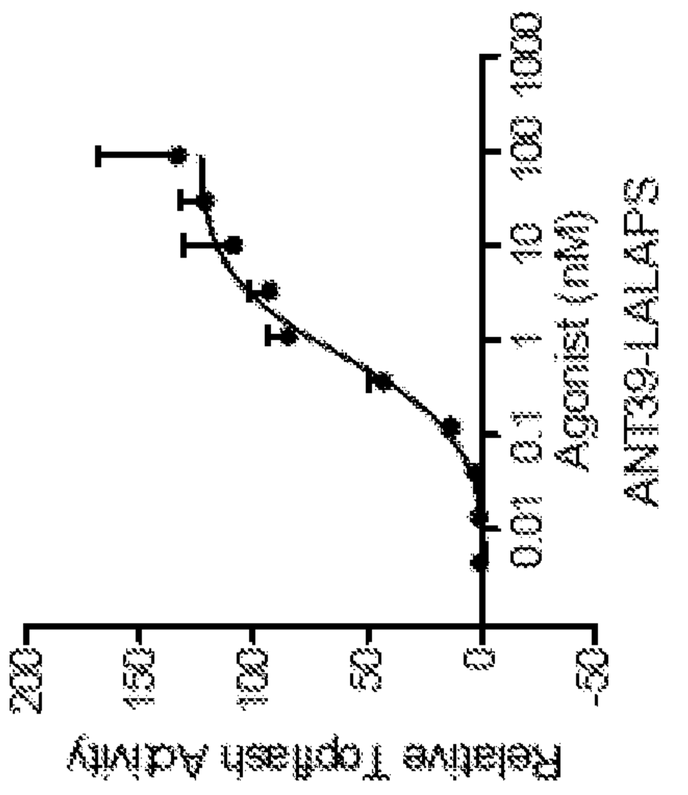
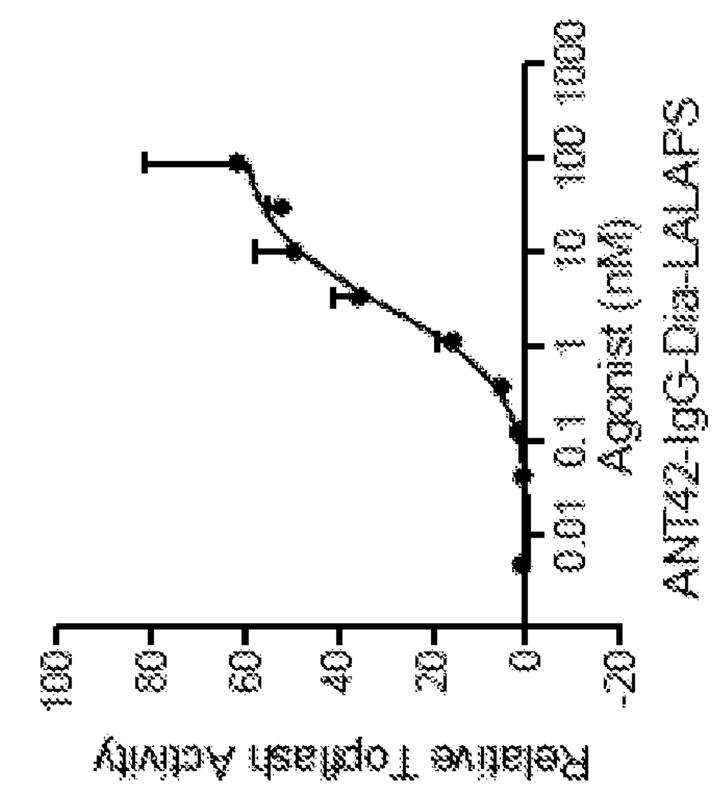

ANT42-LALAPS
CM0156
Relative Topflash Activity
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
Agonist (nM)

FIG 10 cont.


Relative Topflash Activity
200
150
100
50
0
-50
0.01
0.1
1
10
100
1000
Agonist (nM)
ANT39-L-Dia-LALAPS


Relative Topflash Activity
100
80
60
40
20
0
-20
0.01
0.1
1
10
100
1000
Agonist (nM)
ANT42-IgG-Dia-LALAPS

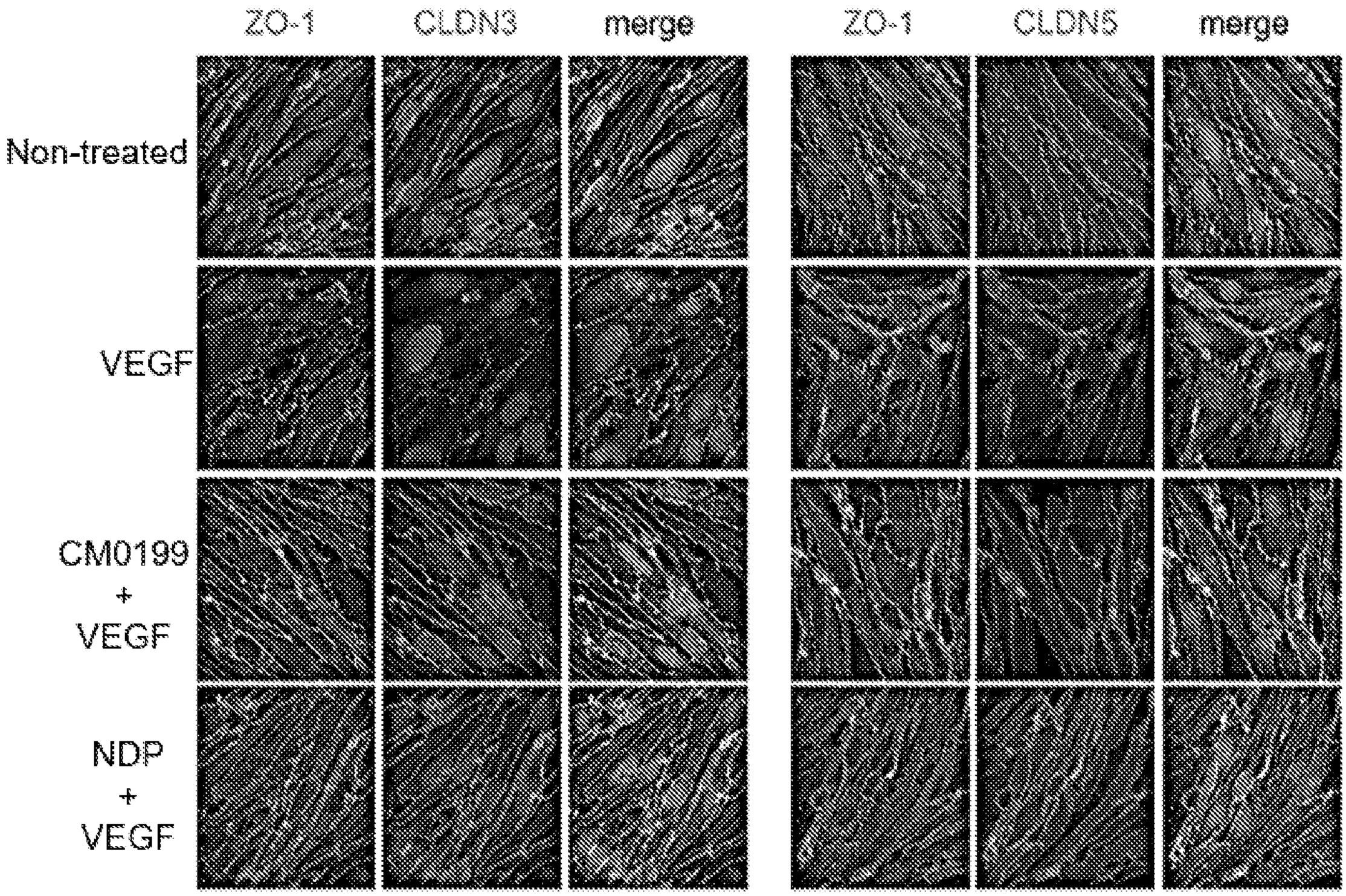

ZO-1
CLDN3
merge
ZO-1
CLDN5
merge
Non-treated
VEGF
CM0199
+
VEGF
NDP
+
VEGF

FIG 11A

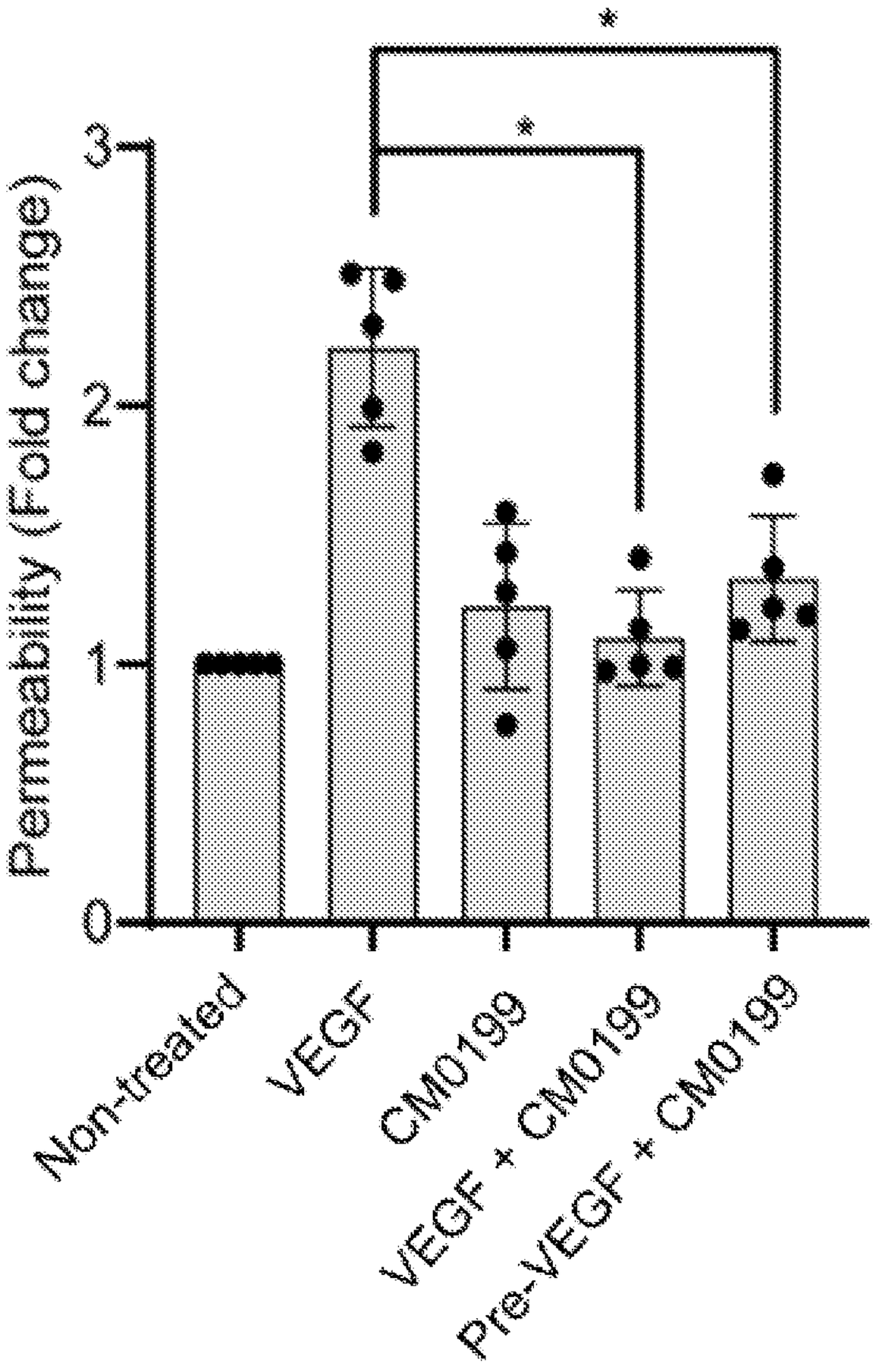

Permeability (Fold change)
0
1
2
3
Non-treated
VEGF
CM0199
VEGF + CM0199
Pre-VEGF + CM0199

FIG 11B

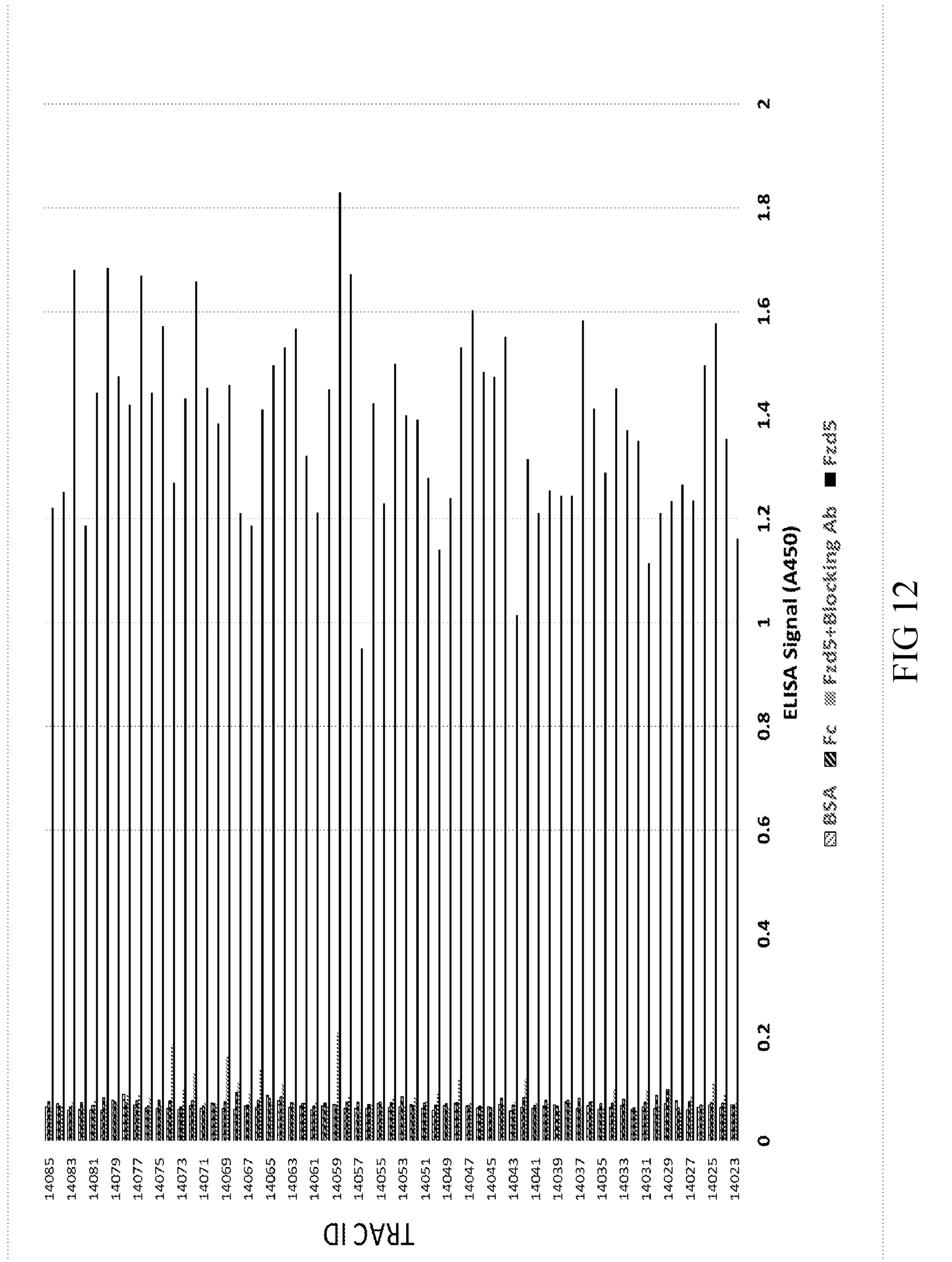

TRAC ID
14085
14083
14081
14079
14077
14075
14073
14071
14069
14067
14065
14063
14061
14059
14057
14055
14053
14051
14049
14047
14045
14043
14041
14039
14037
14035
14033
14031
14029
14027
14025
14023
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
ELISA Signal (A450)
BSA
Fc
Fzd5+Blocking Ab
Fzd5

FIG 12

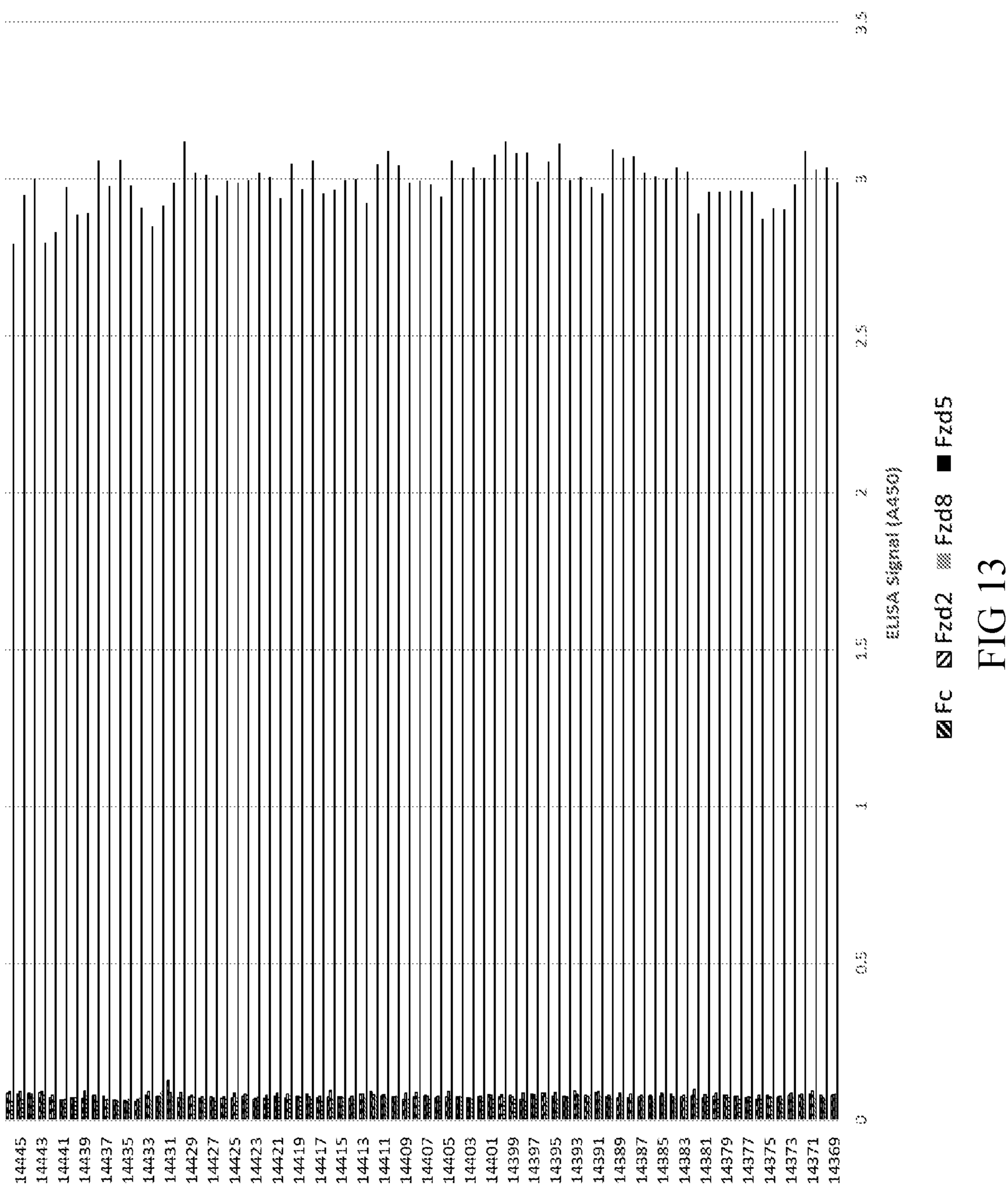

TRAC ID
14445
14443
14441
14439
14437
14435
14433
14431
14429
14427
14425
14423
14421
14419
14417
14415
14413
14411
14409
14407
14405
14403
14401
14399
14397
14395
14393
14391
14389
14387
14385
14383
14381
14379
14377
14375
14373
14371
14369
ELISA Signal (A450)
0
0.5
1
1.5
2
2.5
3
Fc
Fzd2
Fzd8
Fzd5

FIG 13

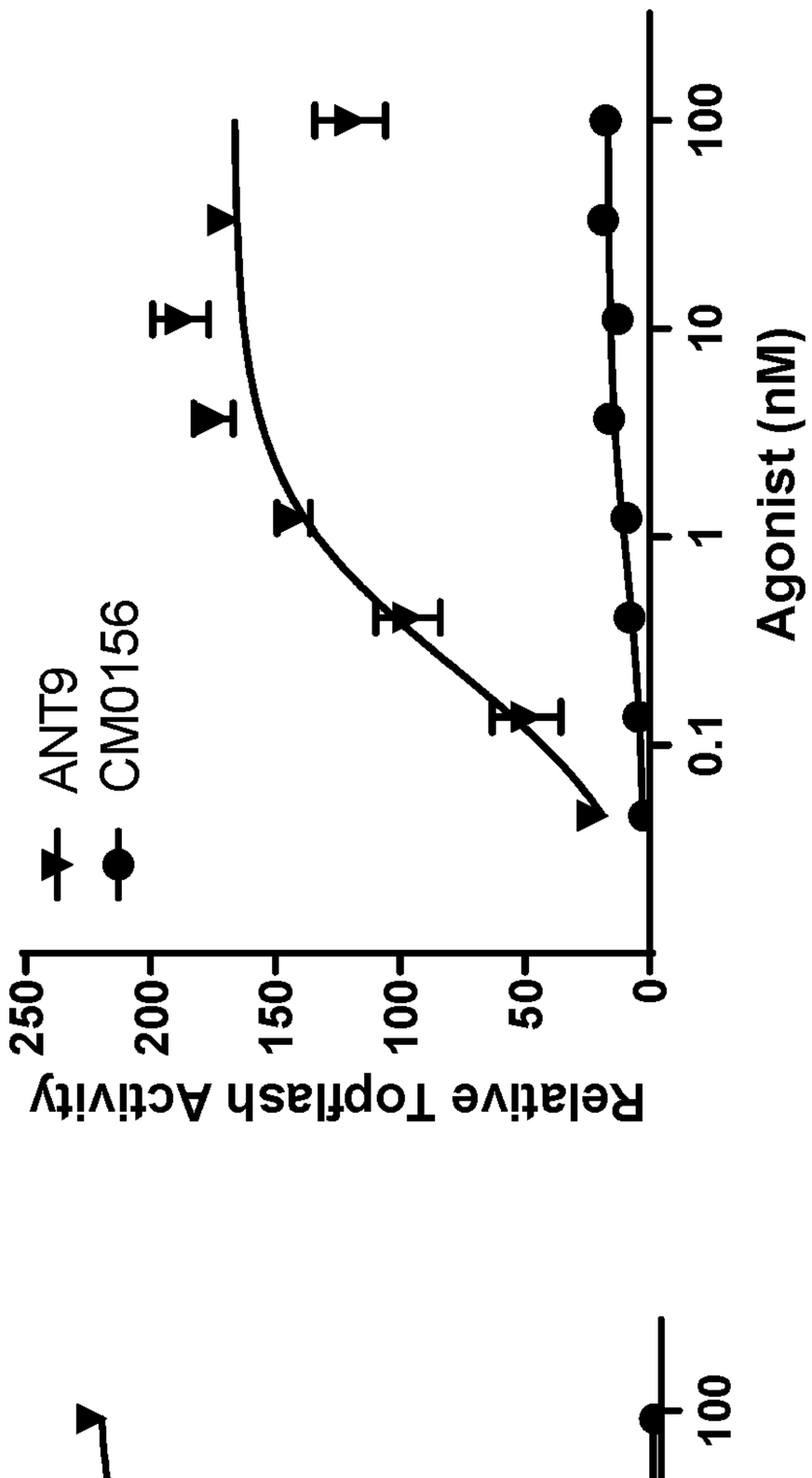

ANT9
CM0156
Relative Topflash Activity
250
200
150
100
50
0
0.1
1
10
100
Agonist (nM)
ANT59
CM0156
Relative Topflash Activity
60
40
20
0
Veh.
0.1
1
10
100
Agonist (nM)

FIG. 14

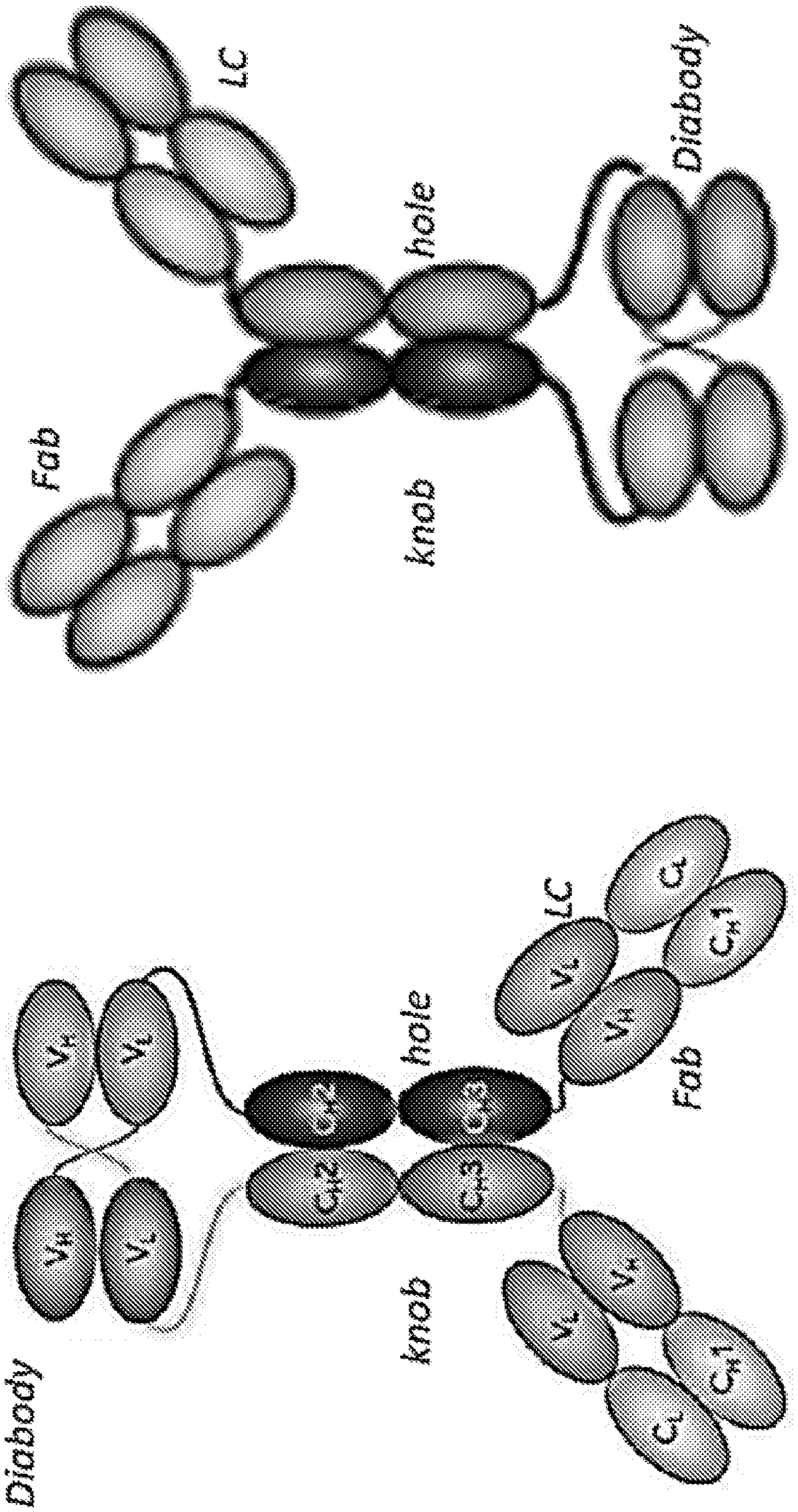


FIG. 15

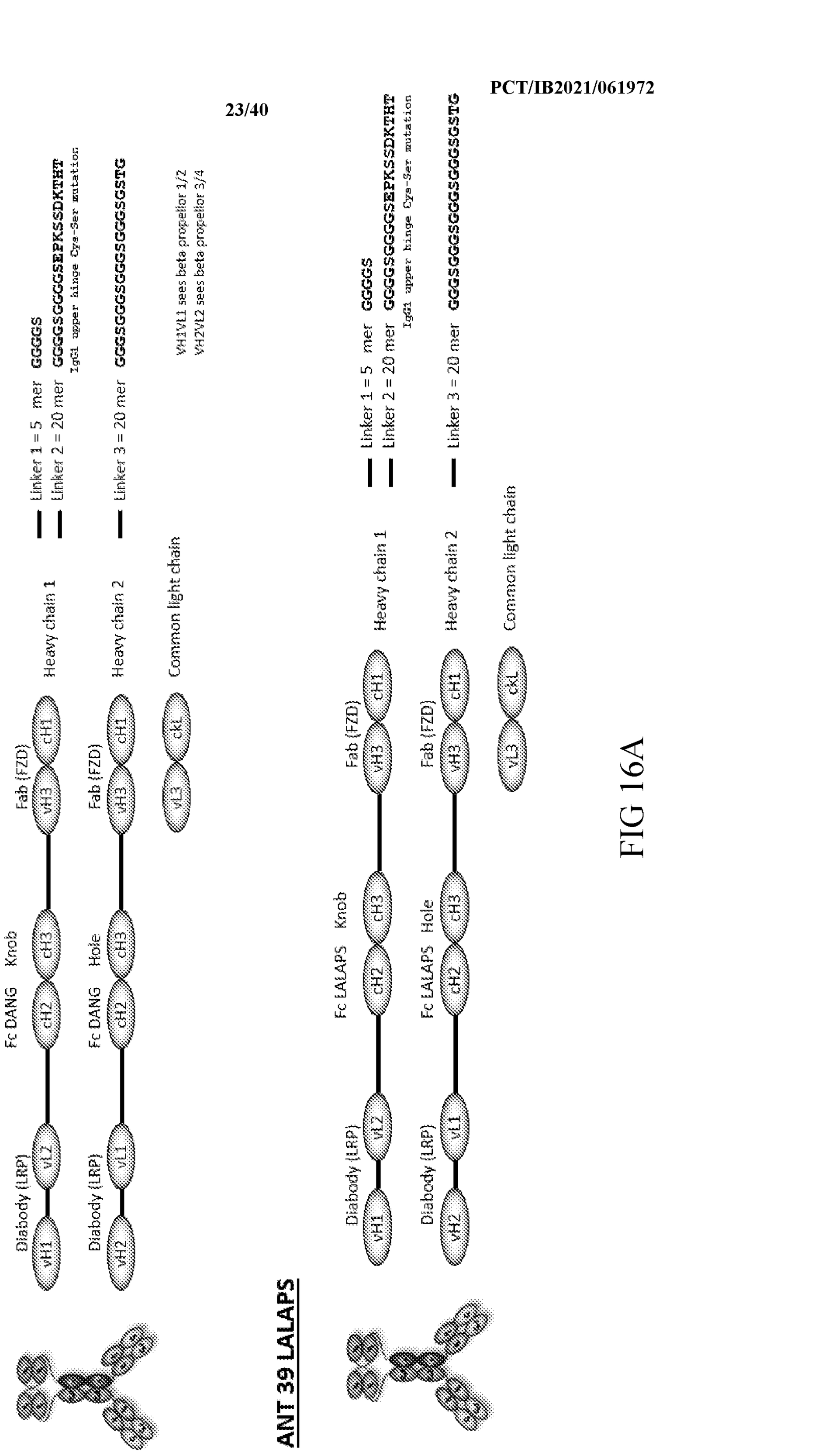

Linker 1 = 5 mer GGGGS
Linker 2 = 20 mer GGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
Linker 3 = 20 mer GGGSGGGGSGGGGSGGGSTG
VH1VL1 sees beta propellor 1/2
VH2VL2 sees beta propellor 3/4
Heavy chain 1
Heavy chain 2
Common light chain
Fab (FZD)
vH3
cH1
vL3
cKL
Fc DANG Knob
Fc DANG Hole
Diabody (LRP)
vL2
vL1
vH1
vH2
ANT 39
Linker 1 = 5 mer GGGGS
Linker 2 = 20 mer GGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
Linker 3 = 20 mer GGGSGGGGSGGGGSGGGSTG
Fc LALAPS Knob
Fc LALAPS Hole
ANT 39 LALAPS

FIG 16A

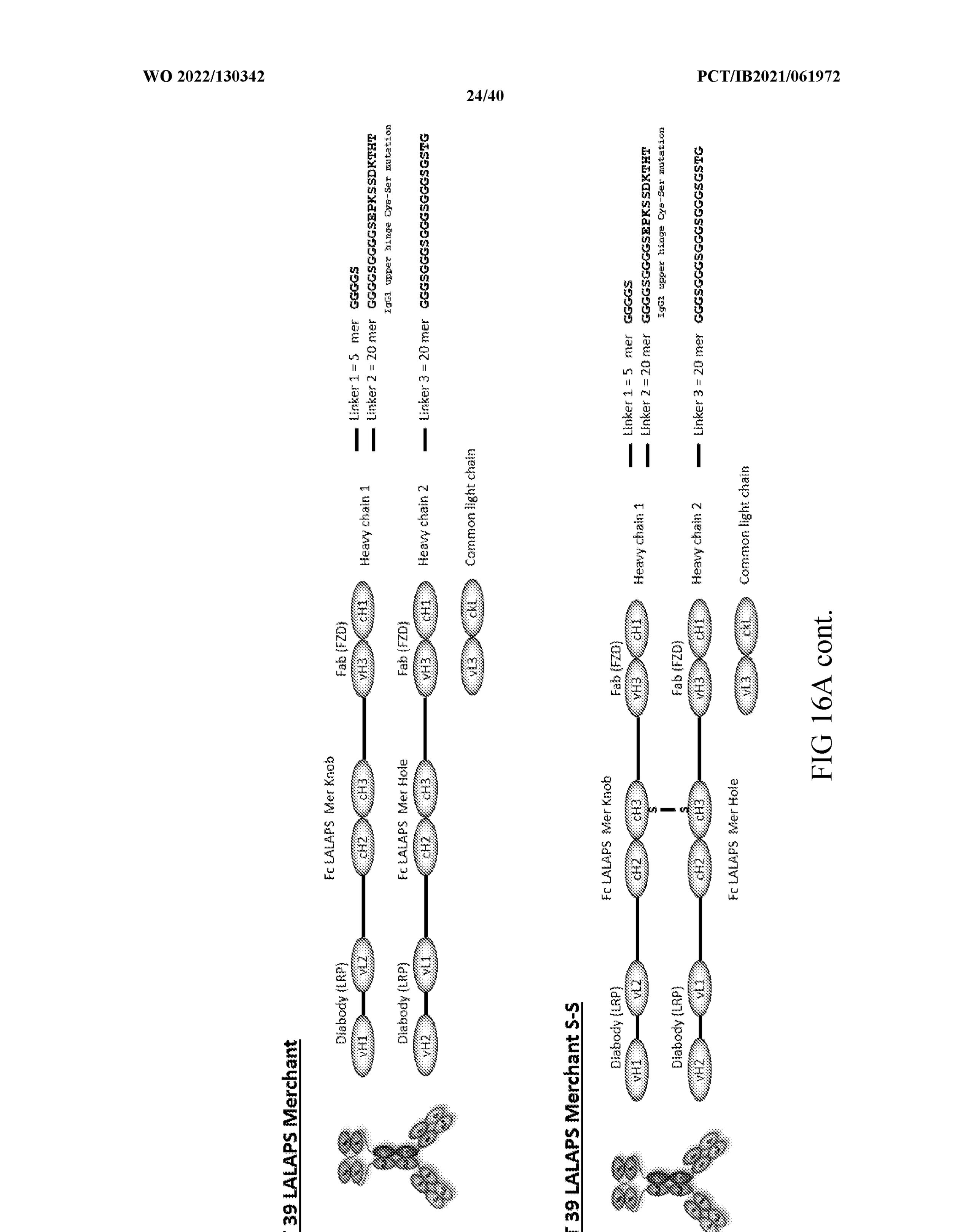
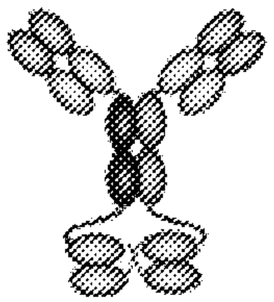
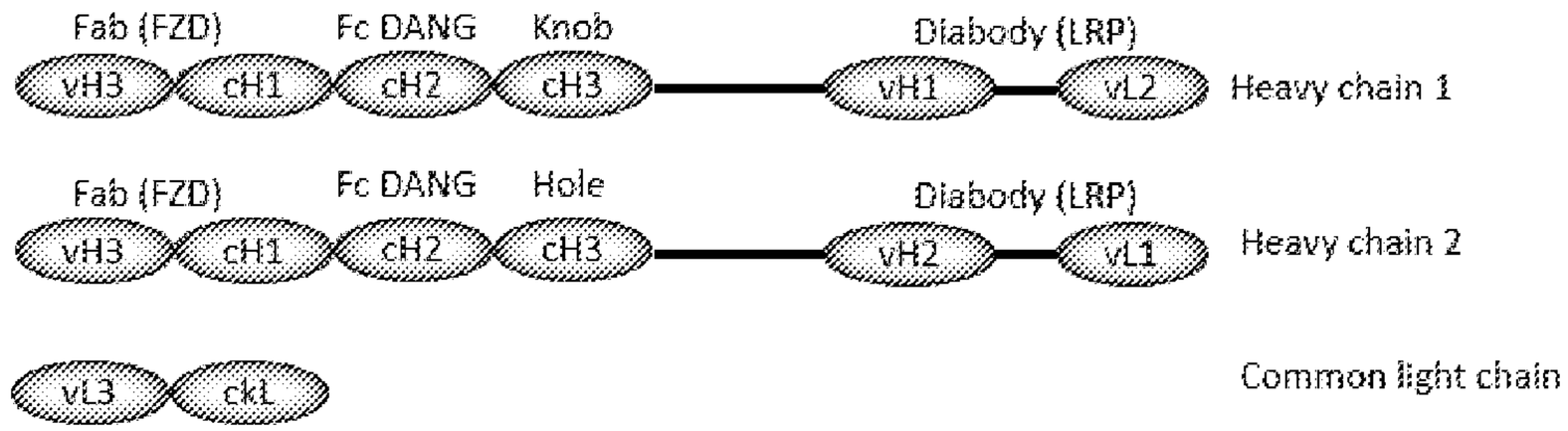

ANT 39 LALAPS Mer Knob
Fab (FZD)
vH3
cH1
Heavy chain 1
Linker 1 = 5 mer GGGGS
Linker 2 = 20 mer GGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
Fab (FZD)
vH3
cH1
Heavy chain 2
Linker 3 = 20 mer GGGSGGGSGGGSGGGSGSTG
vL3
cKL
Common light chain
Fc LALAPS Mer Knob
Diabody (LRP)
vH1
vL2
cH2
cH3
Fc LALAPS Mer Hole
Diabody (LRP)
vH2
vL1
cH2
cH3
ANT 39 LALAPS Mer Hole
Fab (FZD)
vH3
cH1
Heavy chain 1
Linker 1 = 5 mer GGGGS
Linker 2 = 20 mer GGGGSGGGGSEPKSSDKTHT
IgG2 upper hinge Cys-Ser mutation
Fab (FZD)
vH3
cH1
Heavy chain 2
Linker 3 = 20 mer GGGSGGGSGGGSGGGSGSTG
vL3
cKL
Common light chain
Fc LALAPS Mer Knob
Diabody (LRP)
vH1
vL2
cH2
cH3
S
S
Fc LALAPS Mer Hole
Diabody (LRP)
vH2
vL1
cH2
cH3

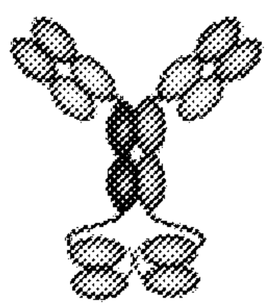
FIG 16A cont.

ANT 39i





ANT 39i LALAPS



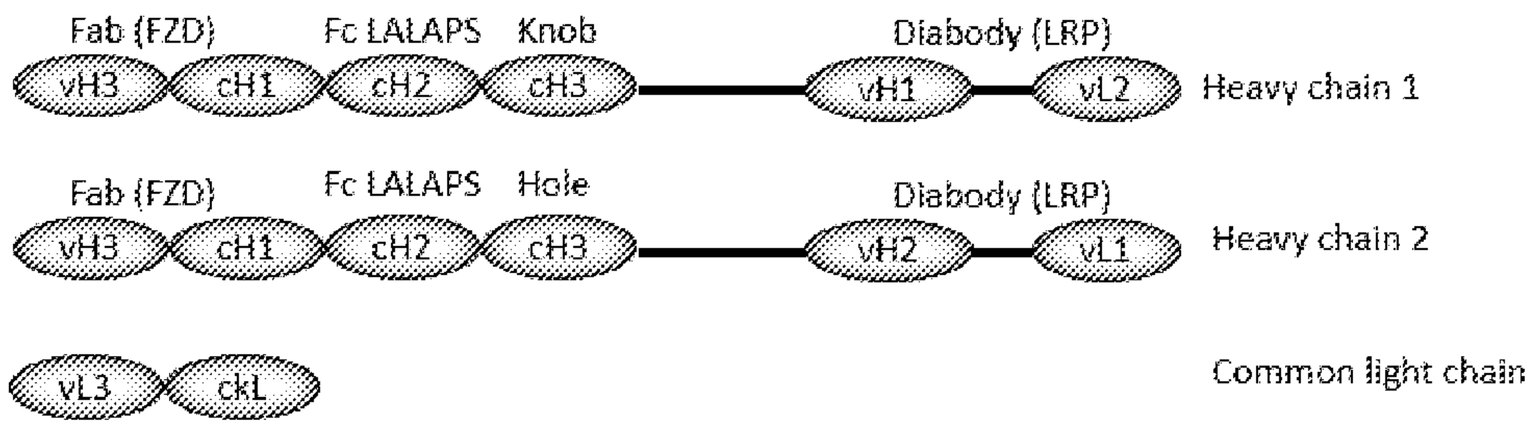
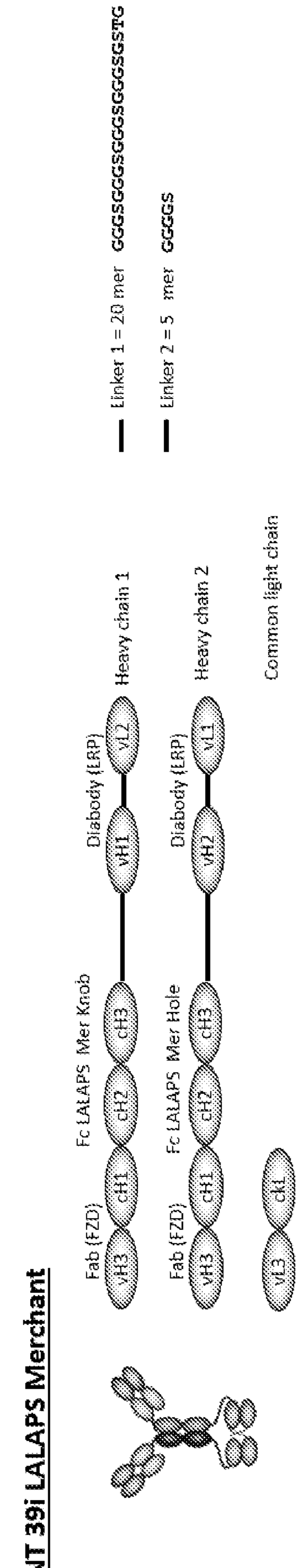


FIG 16B


ANT 39i LALAPS Merchant
Fab (FZD)
vH3
cH1
Fc LALAPS Mer Knob
cH2
cH3
Diabody (LRP)
vH1
vL2
Heavy chain 1
Fab (FZD)
vH3
cH1
Fc LALAPS Mer Hole
cH2
cH3
Diabody (LRP)
vH2
vL1
Heavy chain 2
vL3
cL1
Common light chain
Linker 1 = 20 mer GGGSGGGSGGGSGGGSGGGS
Linker 2 = 5 mer GGGGS

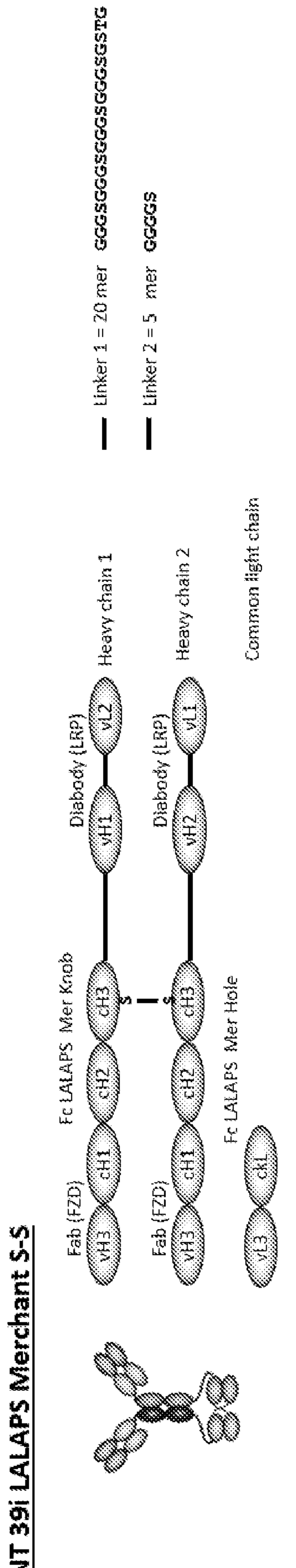

ANT 39i LALAPS Merchant S-S
Fab (FZD)
vH3
cH1
Fc LALAPS Mer Knob
cH2
cH3
S
S
Diabody (LRP)
vH1
vL2
Heavy chain 1
Fab (FZD)
vH3
cH1
Fc LALAPS Mer Hole
cH2
cH3
Diabody (LRP)
vH2
vL1
Heavy chain 2
vL3
cL1
Common light chain
Linker 1 = 20 mer GGGSGGGSGGGSGGGSGGGS
Linker 2 = 5 mer GGGGS

FIG 16B cont.

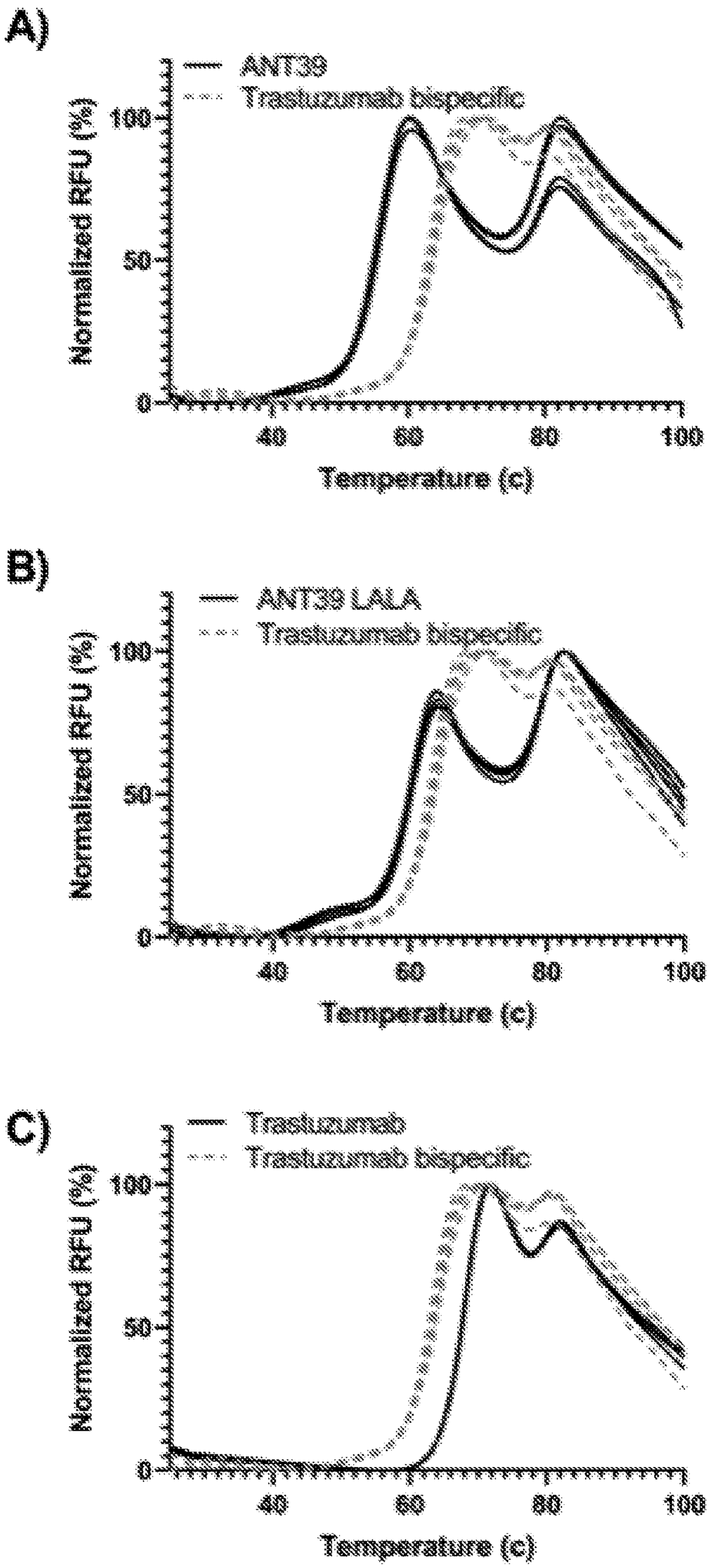

A)
ANT39
Trastuzumab bispecific
Normalized RFU (%)
100
50
0
40
60
80
100
Temperature (c)
B)
ANT39 LALA
Trastuzumab bispecific
Normalized RFU (%)
100
50
0
40
60
80
100
Temperature (c)
C)
Trastuzumab
Trastuzumab bispecific
Normalized RFU (%)
100
50
0
40
60
80
100
Temperature (c)

FIG 17

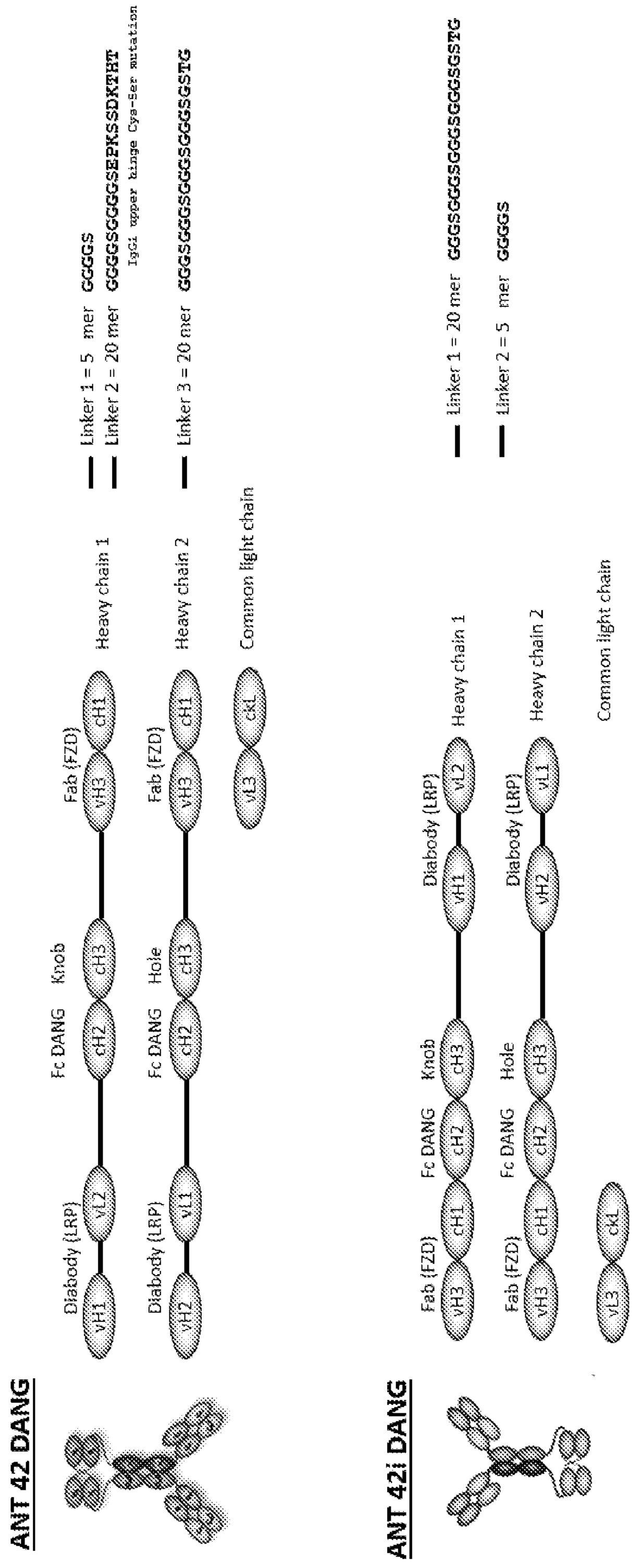

Linker 1 = 5 mer GGGGS
Linker 2 = 20 mer GGGGSGGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
Linker 3 = 20 mer GGGSGGGSGGGSGGGSGSTG
Heavy chain 1
Heavy chain 2
Common light chain
Fab (FZD)
Fc DANG
Knob
Hole
Diabody (LRP)
cH1
cH2
cH3
vH1
vH2
vH3
vL1
vL2
vL3
cKL
ANT 42 DANG
ANT 42i DANG

FIG 18

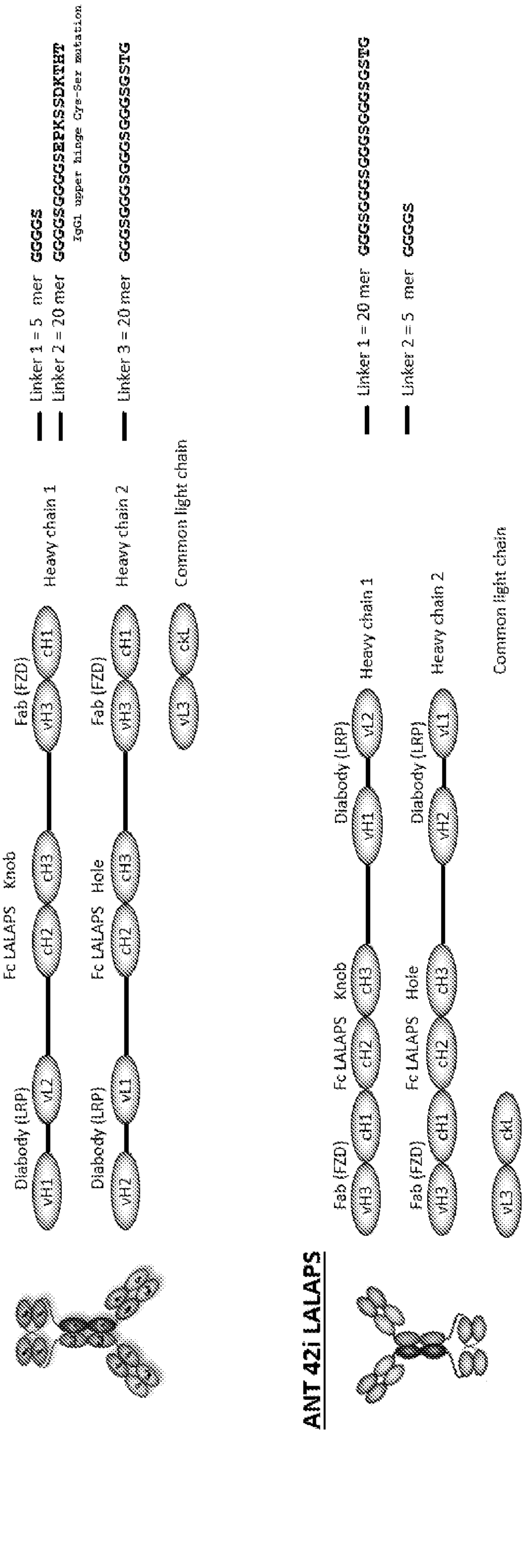

ANT 42 LALAPS
Fab (FZD)
vH3
cH1
Heavy chain 1
Fab (FZD)
vH3
cH1
Heavy chain 2
vL3
cKL
Common light chain
Diabody (LRP)
vL2
Fc LALAPS Knob
cH2
cH3
Diabody (LRP)
vL1
Fc LALAPS Hole
cH2
cH3
Linker 1 = 5 mer
Linker 2 = 20 mer
GGGGS
GGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
GGGSGGGSGGGSGGGSGSTG
ANT 42i LALAPS
Fab (FZD)
vH3
cH1
Heavy chain 1
Fab (FZD)
vH3
cH1
Heavy chain 2
vL3
cKL
Common light chain
Diabody (LRP)
vH1
Fc LALAPS Knob
cH2
cH3
Diabody (LRP)
vH2
Fc LALAPS Hole
cH2
cH3
Linker 1 = 20 mer
Linker 2 = 5 mer
GGGGS
GGGGSGGGGSGGGGSGGGGSGSTG

FIG 18

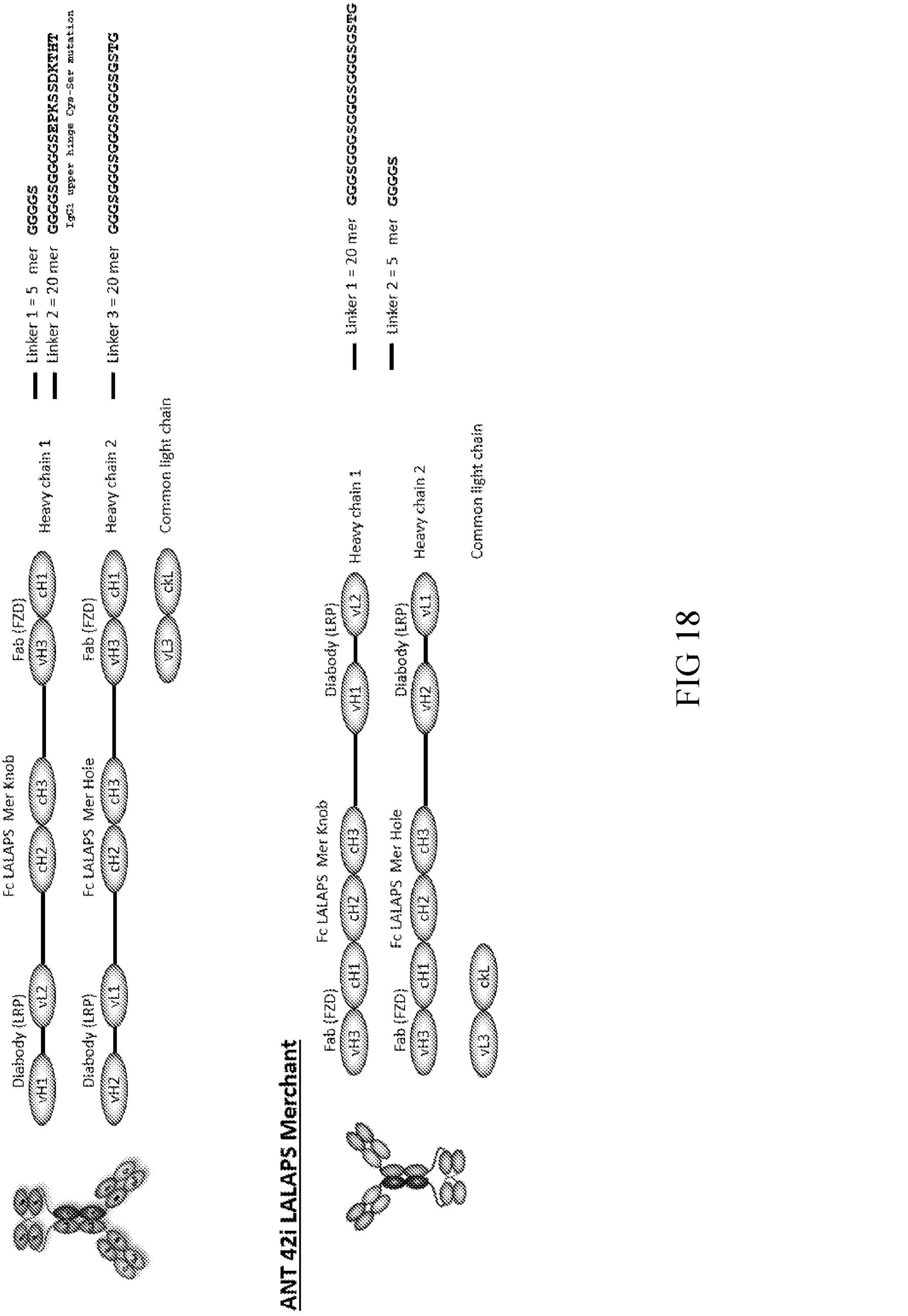

GGGGS
GGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
GGGSGGGSGGGGSGGGSTG
Linker 1 = 5 mer GGGSGGGSGGGGSGGGSTG
Linker 2 = 20 mer GGGGS
Linker 3 = 20 mer
Fab (FZD)
vH3
cH1
Heavy chain 1
Heavy chain 2
Common light chain
vL3
cKL
Diabody (LRP)
vL2
vH1
vH2
vL1
Fc LALAPS Mer Knob
cH2
cH3
Fc LALAPS Mer Hole
ANT 42 LALAPS Merchant
ANT 42i LALAPS Merchant

FIG 18

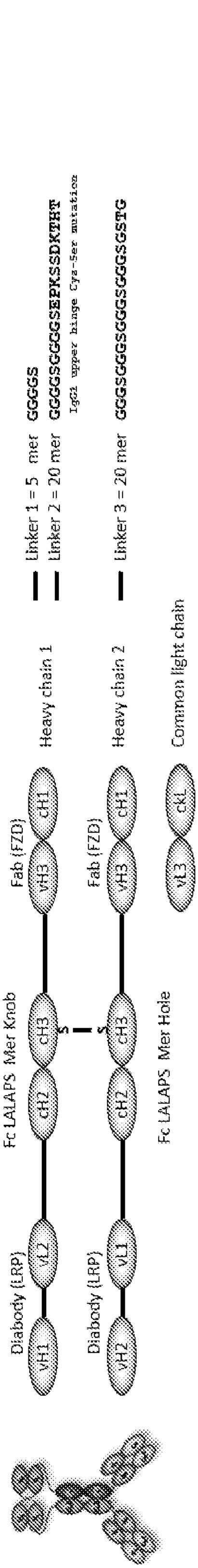

GGGGS
GGGGSGGGGSEPKSSDKTHT
IgG1 upper hinge Cys-Ser mutation
GGGSGGGSGGGSGGGSGSTG
Linker 1 = 5 mer
Linker 2 = 20 mer
Linker 3 = 20 mer
Fab (FZD)
vH3
cH1
Heavy chain 1
Heavy chain 2
Common light chain
vL3
cKL
Diabody (LRP)
vH1
vL2
vH2
vL1
Fc LALAPS Mer Knob
Fc LALAPS Mer Hole
CH2
CH3
S

FIG 18

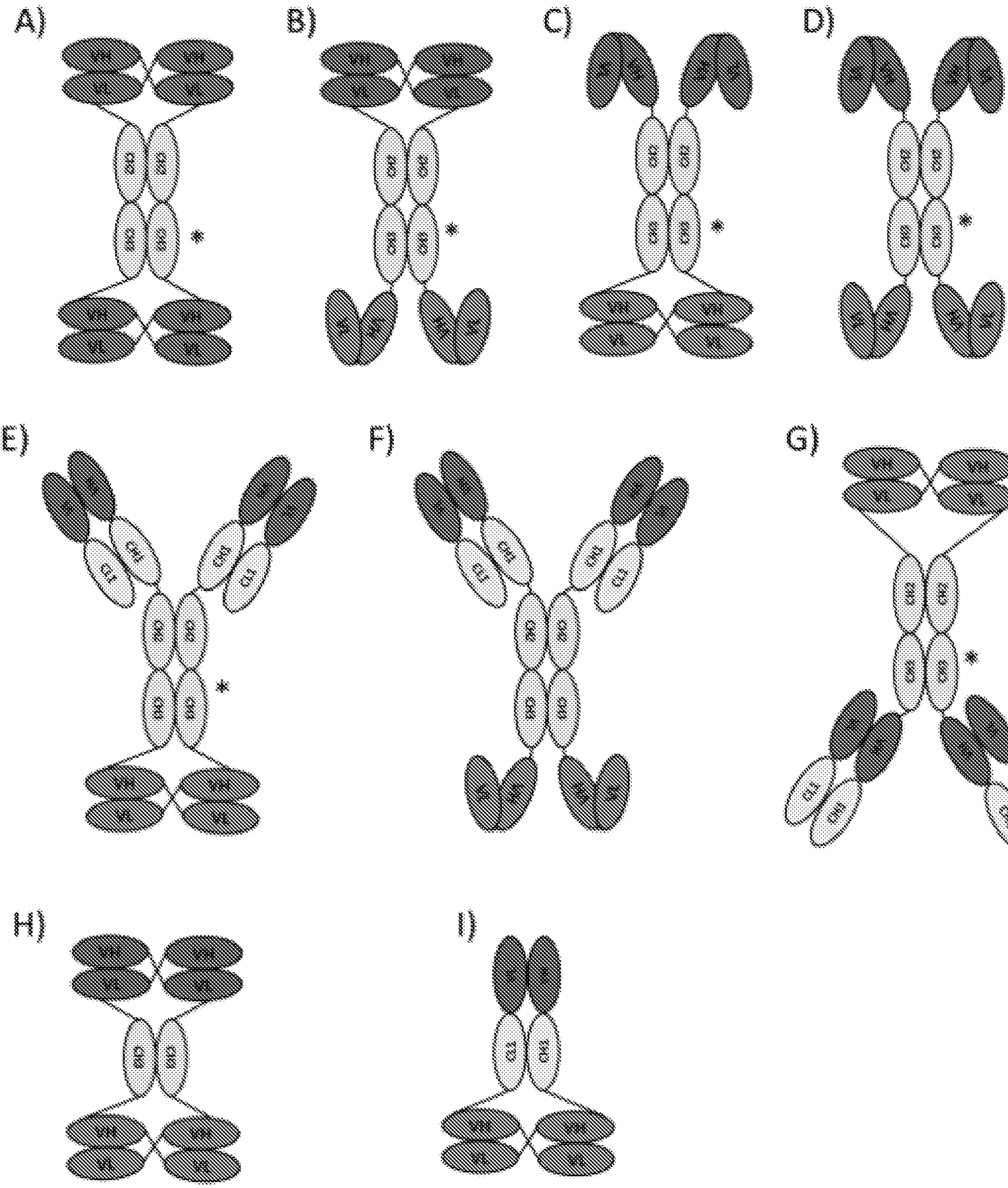


FIG 19

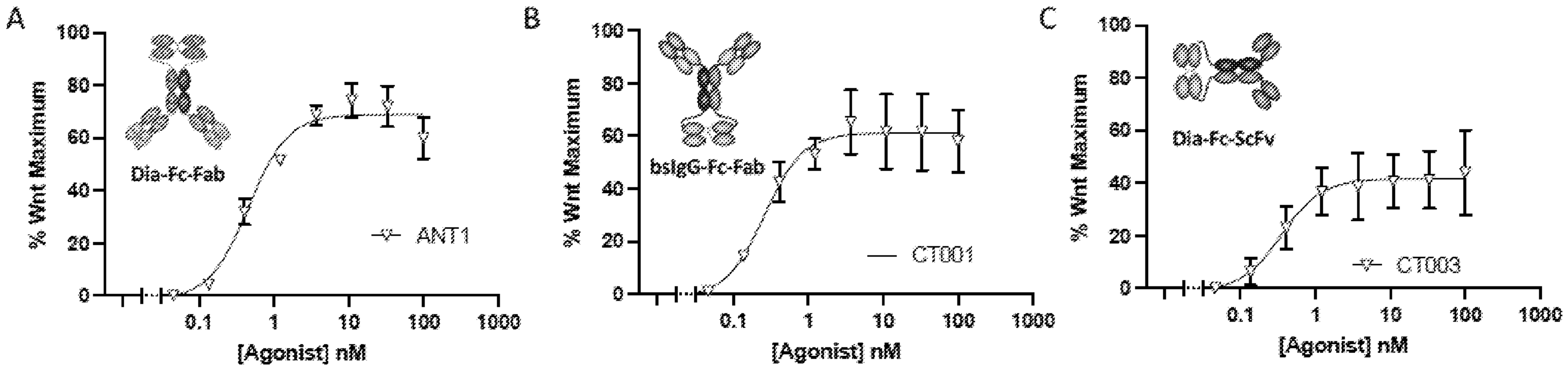
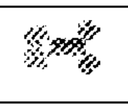
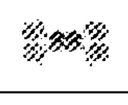

A
% Wnt Maximum
Dia-Fc-Fab
ANT1
[Agonist] nM
B
% Wnt Maximum
bsIgG-Fc-Fab
CT001
[Agonist] nM
C
% Wnt Maximum
Dia-Fc-ScFv
CT003
[Agonist] nM
D
% Wnt Maximum
Dia-Fc-Dia
CM0126
[Agonist] nM
E
% Wnt Maximum
Fab-Dia
Fab-Dia
[Agonist] nM
F
% Wnt Maximum
IgG-ScFv
CM0300
[Agonist] nM

FIG 20

#	Format		Expression [Monomer] (mg/l)*	EC50 (nM)	Alternate Names/Alternate Variant Names
1	Dia-Fc-Fab		97	0.45	ANT#, Ant#, ANT #, Ant #, Diabody-Fc-Fab, ANT#LALAPS, ANT# LALAPS, ANT# LALALPS Merchant, ANT# LALALPS Merchant_S:S, ANT#LALA, ANT# LALA, ANT#DANG, ANT# DANG,
2	bsIgG-Dia		50	0.26	ANT#i, Ant#i, IgG-Diabody, IgG-Dia, bsIgG-Dia, CT#, CM#, ANT#iLALAPS, ANT#i LALAPS, ANT#i LALALPS Merchant, ANT#i LALALPS Merchant_S:S
3	Dia-Fc-ScFv		50	0.60	Diabody-Fc-ScFv, CM#, CT#
4	Dia-Fc-Dia		20	0.31	FLAg, CM#, Diabody-Fc-Diabody, CM#
5	Fab-Dia		25	0.42	Fab-Diabody, CM#
6	IgG-ScFv		100	NA	CM#

- number; Dia = Diabody

FIG 21

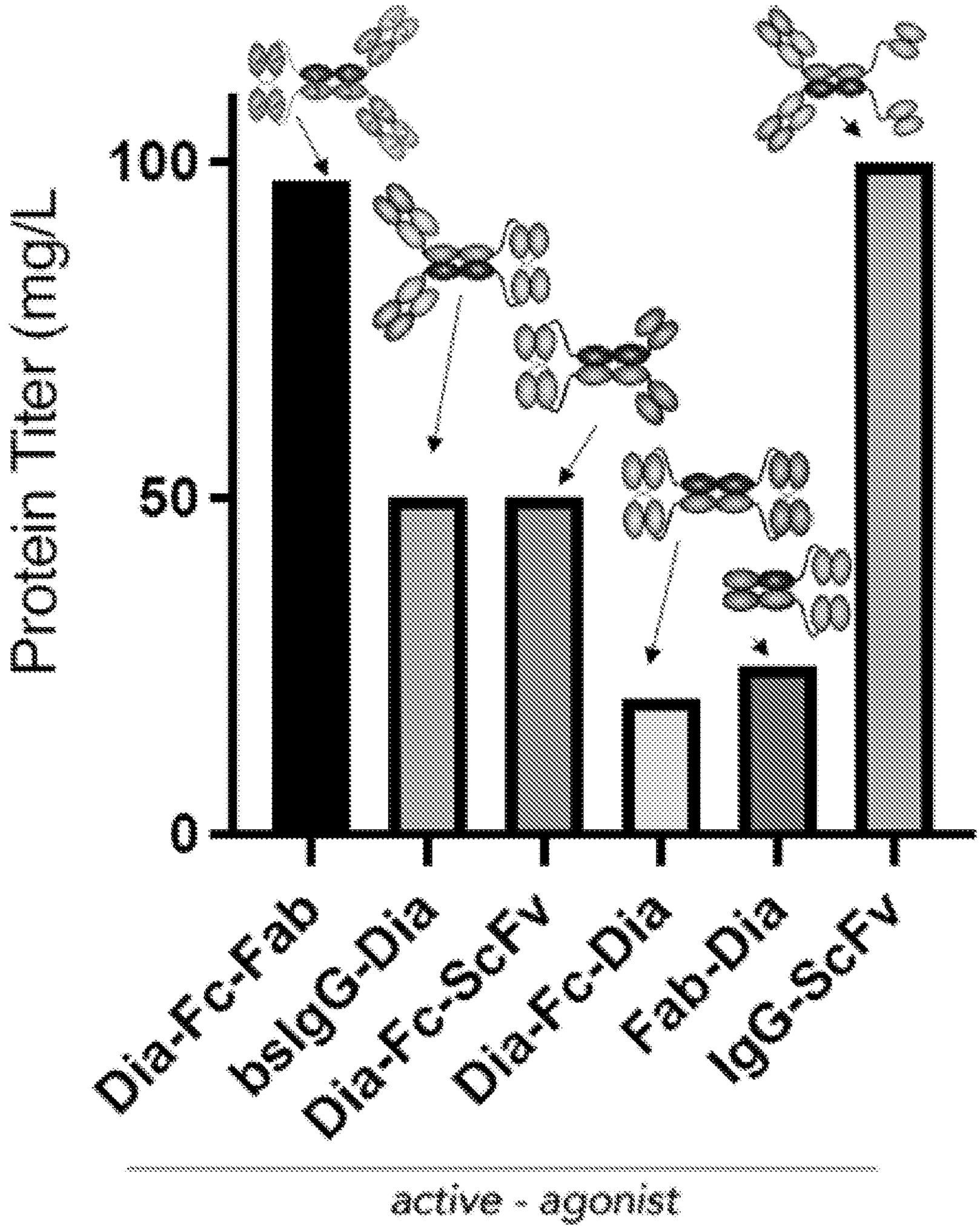

Protein Titer (mg/L
100
50
0
Dia-Fc-Fab
bsIgG-Dia
Dia-Fc-ScFv
Dia-Fc-Dia
Fab-Dia
IgG-ScFv
active - agonist

FIG 21 cont.

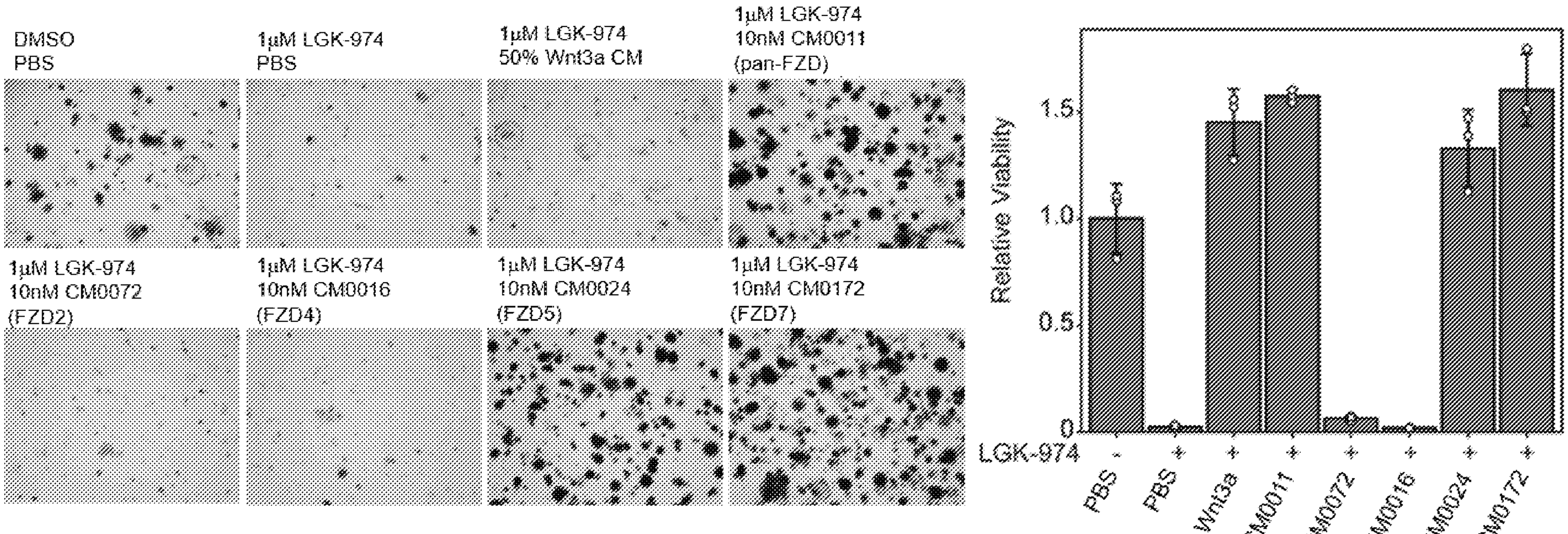

DMSO
PBS
1μM LGK-974
PBS
1μM LGK-974
50% Wnt3a CM
1μM LGK-974
10nM CM0011
(pan-FZD)
1μM LGK-974
10nM CM0072
(FZD2)
1μM LGK-974
10nM CM0016
(FZD4)
1μM LGK-974
10nM CM0024
(FZD5)
1μM LGK-974
10nM CM0172
(FZD7)
Relative Viability
0
0.5
1.0
1.5
LGK-974
PBS
PBS
Wnt3a
CM0011
CM0072
CM0016
CM0024
CM0172

FIG 22

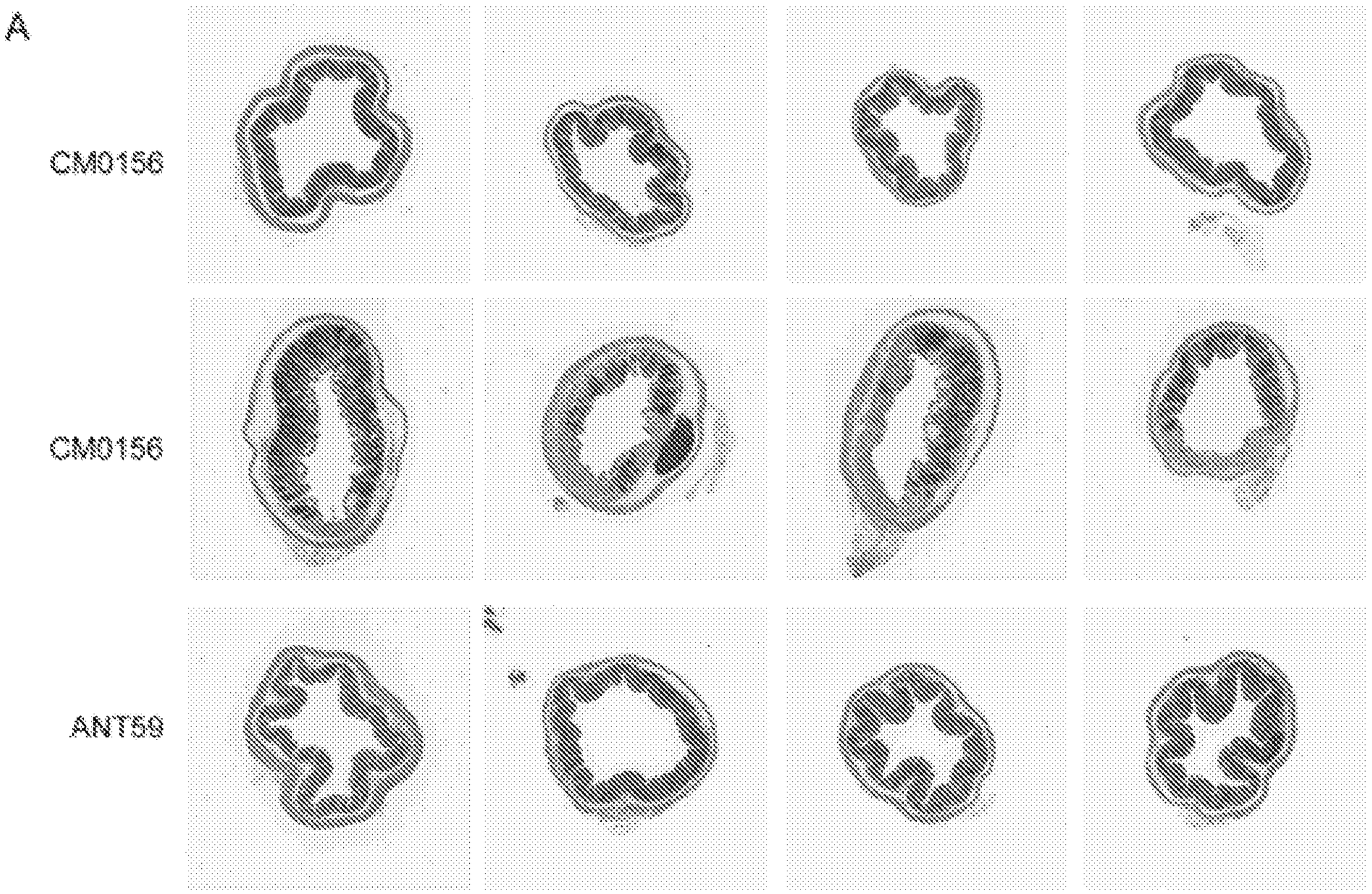


FIG 23

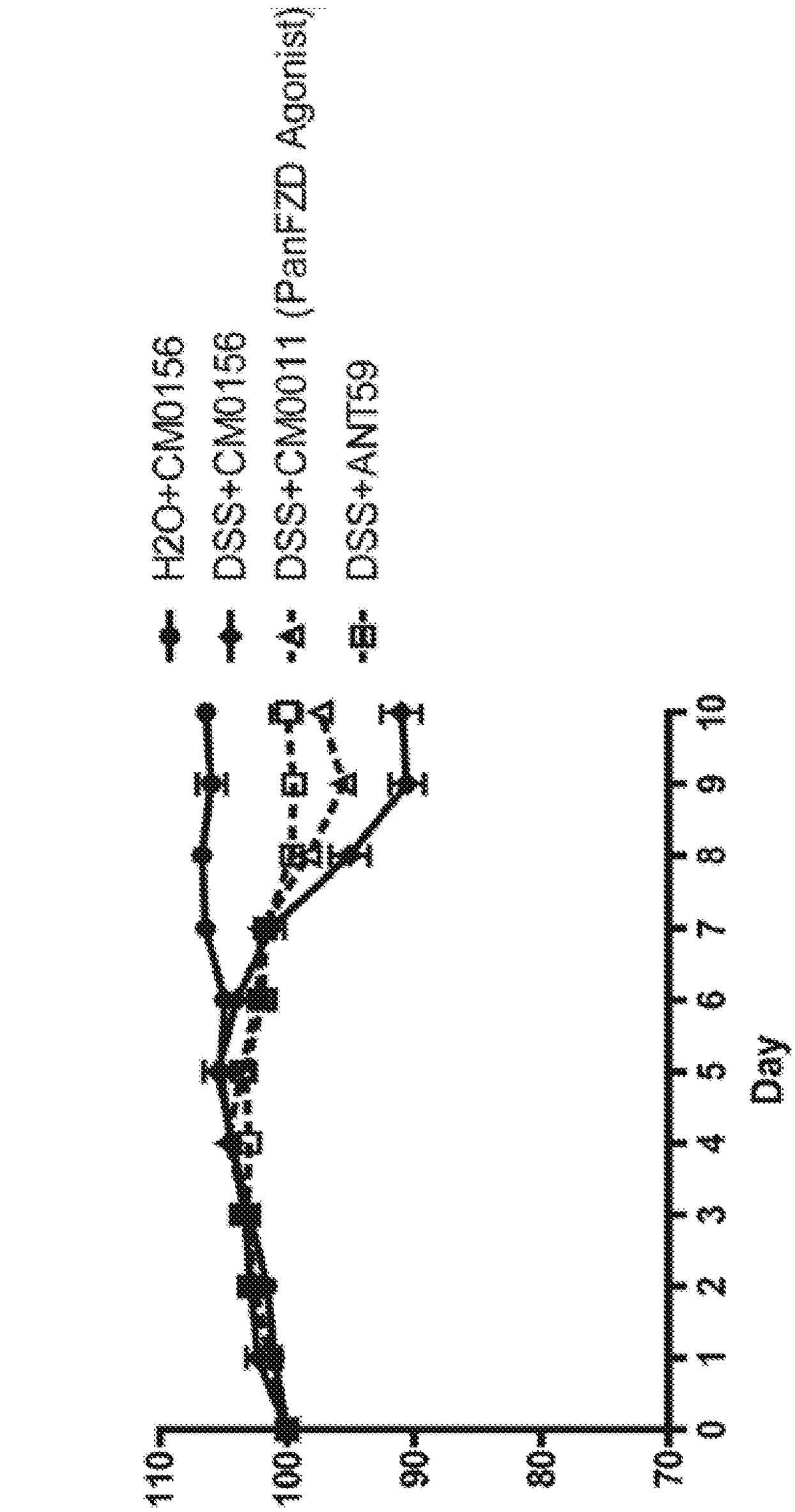
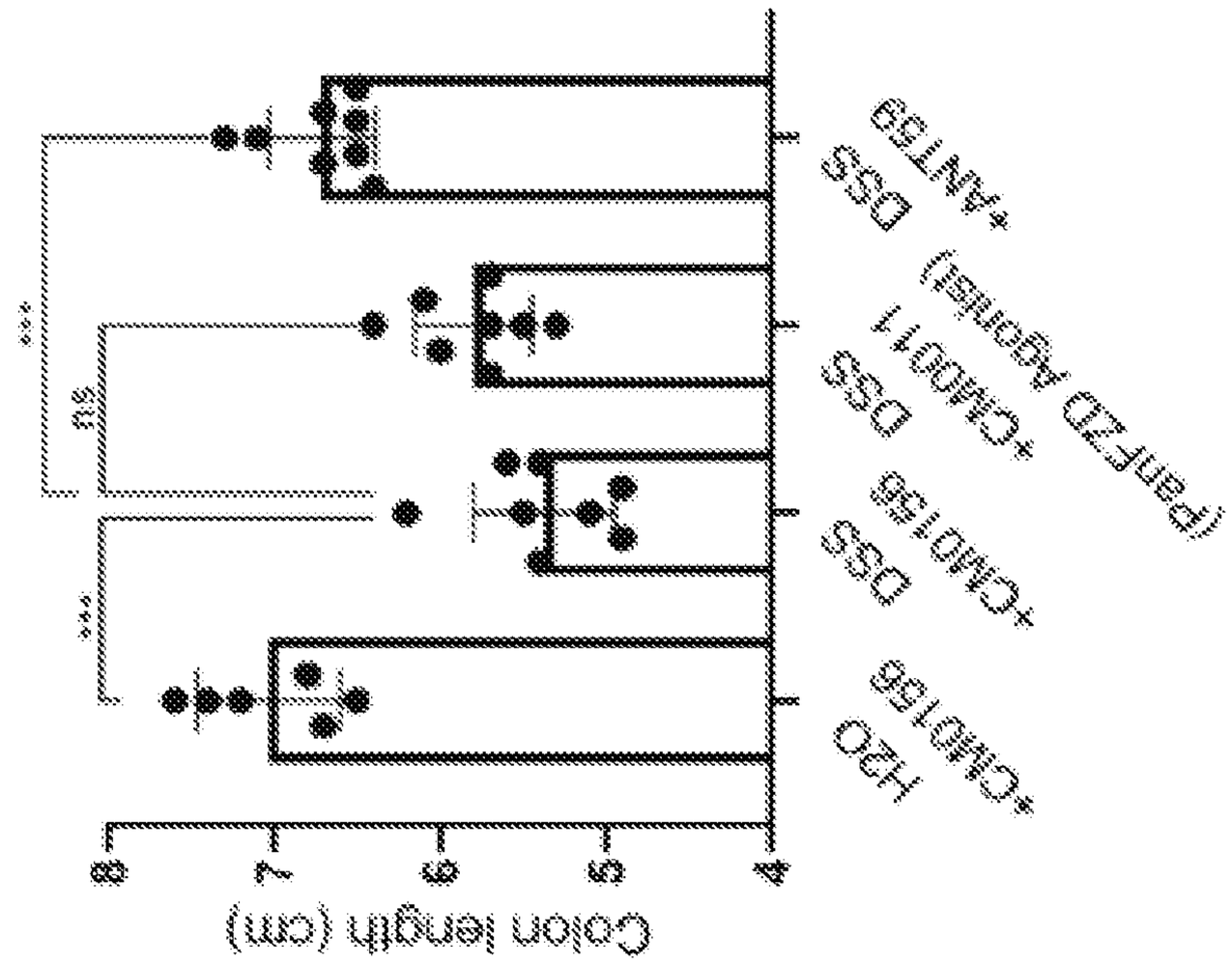

H2O+CM0156
DSS+CM0156
DSS+CM011 (PanFZD Agonist)
DSS+ANT59
Day
0
1
2
3
4
5
6
7
8
9
10
Body weight (%)
110
100
90
80
70
A)

FIG 24


H2O
*CM0156
DSS + CM0156
DSS + PanFZD Ag.)
DSS + ANT59
Colon length (cm)
8
7
6
5
4

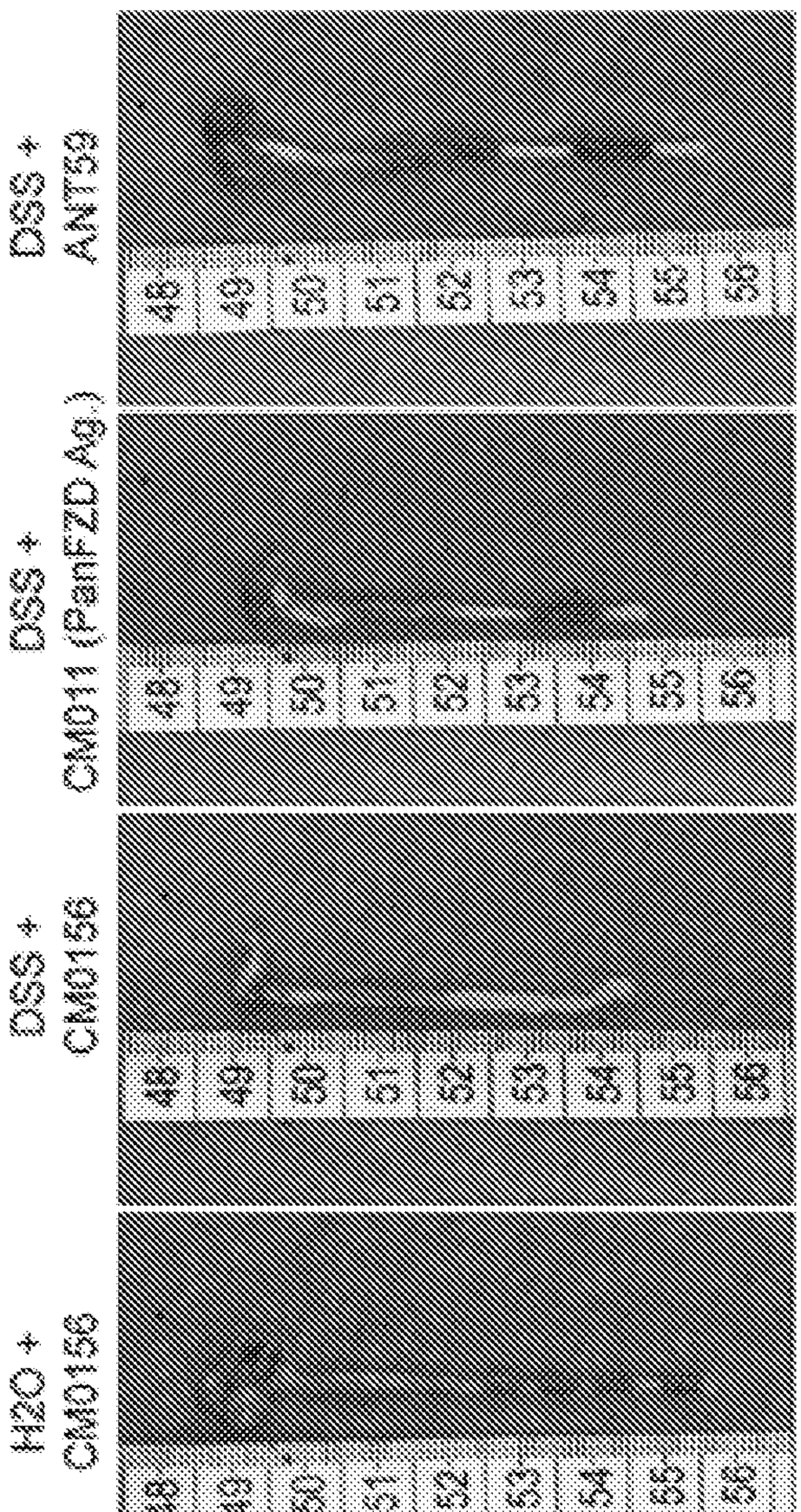
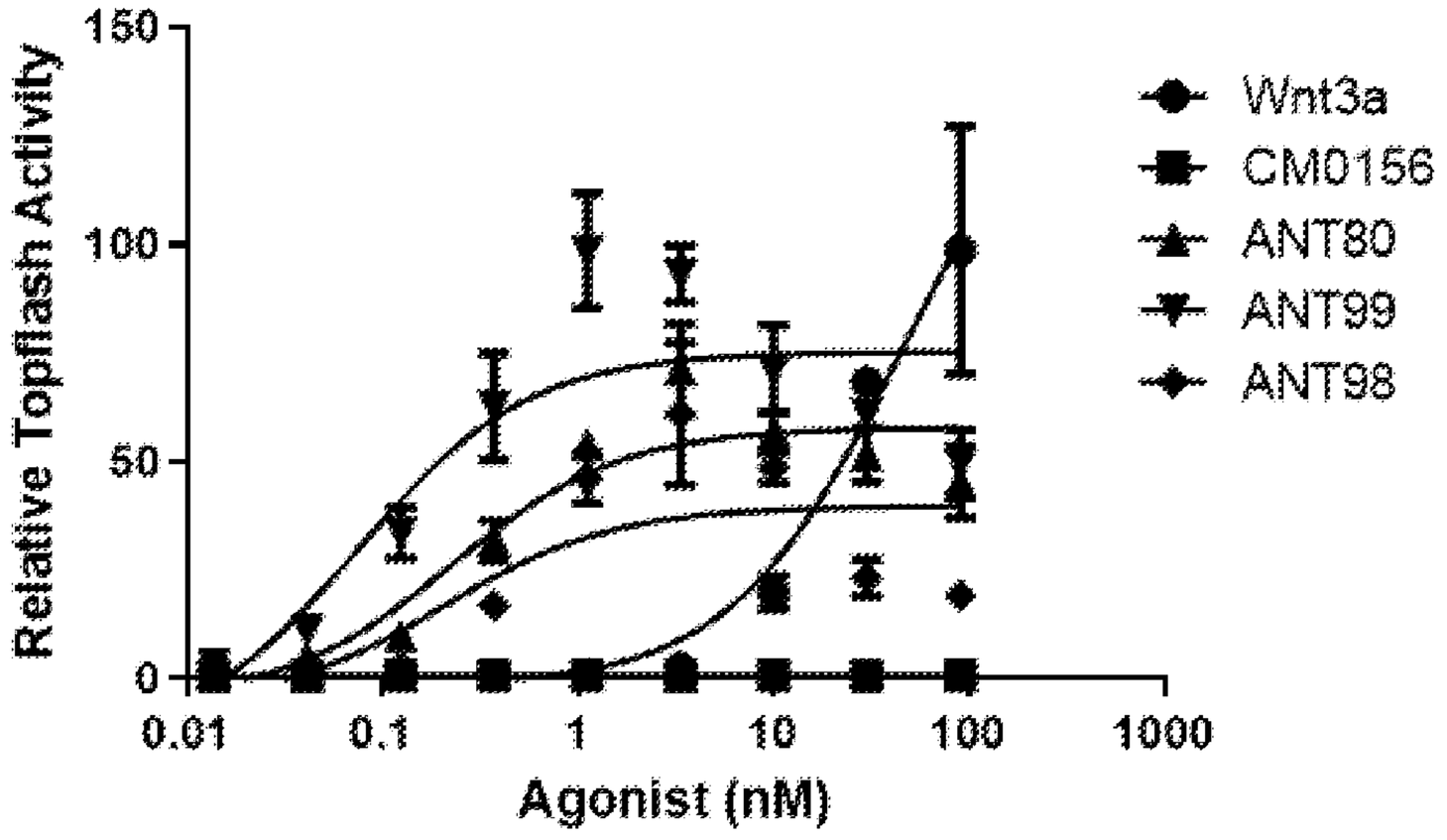

DSS + CM0156
DSS + CM011 (PanFZD Ag.)
DSS + ANT59
H2O + CM0156
48
49
50
51
52
53
54
55
56

FIG 24 cont.

ANT	Exp. Titer (mg/l)	FZD5 avidity (nM)
80	121	0.05
98	81	2
99	234	0.4



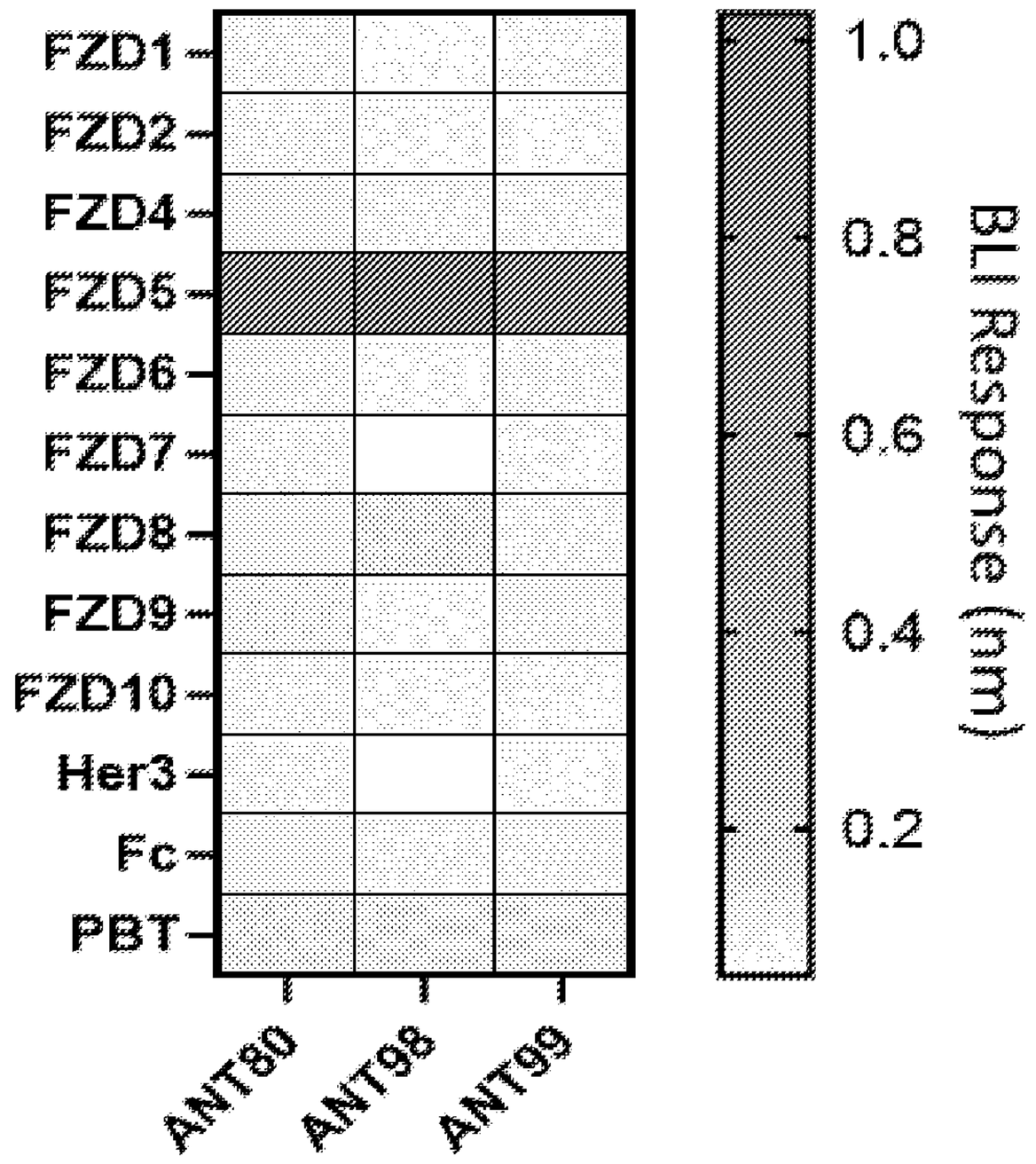


FIG 25

WO 2022/130342 PCT/IB2021/061972

SEQUENCE LISTING

<110> ANTLERA THERAPEUTICS, INC.
ANGERS, STEPHANE
SIDHU, SACHDEV
BLAZER, LEVI
ADAMS, JARRETT
SESHAGIRI, SOMASEKAR

<120> TETRAVALENT FZD AND WNT CO-RECEPTOR BINDING ANTIBODY MOLECULES AND USES THEREOF

<130> 117946.PD606WO

<140>
<141>

<150> 63/127,408
<151> 2020-12-18

<160> 1029

<170> PatentIn version 3.5

<210> 1
<211> 5
<212> PRT
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<220>
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<400> 1
Ser Val Ser Ser Ala
1 5

<210> 2
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
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Ser Ala Ser Ser Leu Tyr Ser
1 5

<210> 3
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<220>
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peptide

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Trp Tyr Tyr Ala Pro Ile
1 5

<210> 4
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peptide

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Gly Asn Tyr Gly Pro Ile
1 5

<210> 5
<211> 6
<212> PRT
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<220>
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1 5

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

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

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Gly Tyr Tyr Ala Leu Ile
1 5

<210> 7
<211> 6
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<213> Artificial Sequence

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

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Trp Tyr Phe Ala Pro Ile
1 5

<210> 8
<211> 6
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<220>
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Gly Tyr Asn Ala Pro Ile
1 5

<210> 9
<211> 6
<212> PRT
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<220>
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peptide

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1 5

<210> 10
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<212> PRT
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<220>
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1 5

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

<220>
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peptide

<400> 11
Ser Asn Tyr Ala Pro Ile
1 5

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

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

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Trp Tyr Asn Ala Pro Ile
1 5

<210> 13
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<213> Artificial Sequence

<220>
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peptide

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Gly Phe Tyr Ala Pro Ile
1   5

<210> 14
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
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      peptide

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Gly Tyr Ser Ala Pro Ile
1   5

<210> 15
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
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      peptide

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Gly Tyr Ala Gly Leu Ile
1   5

<210> 16
<211> 6
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<220>
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      peptide

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Gly Phe Ser Ser Pro Ile
1   5

<210> 17
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<212> PRT
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<220>
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peptide

<400> 17
Gly His Tyr Ala Pro Ile
1 5

<210> 18
<211> 6
<212> PRT
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<220>
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peptide

<400> 18
Ser Phe Tyr Ala Pro Ile
1 5

<210> 19
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<220>
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<400> 19
Gly Tyr Arg Ala Pro Ile
1 5

<210> 20
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<220>
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peptide

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Trp His Arg Ala Pro Ile
1 5

<210> 21
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<220>
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<400> 21
Gly Asp Phe Ala Pro Phe
1 5

<210> 22
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<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 22
Gly Tyr Ser Ser Pro Ile
1 5

<210> 23
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1 5

<210> 24
<211> 6
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<220>
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peptide

<400> 24
Leu Ser Ser Tyr Ser Met
1 5

<210> 25
<211> 6
<212> PRT
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<220>
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peptide

<400> 25
Ile Ala Phe Tyr Ser Ile
1 5

<210> 26
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 26
Ile Tyr Ser Tyr Ser Ile
1 5

<210> 27
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
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peptide

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Ile Ser Ser Tyr Ser Ile
1 5

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

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

<400> 28
Ile Ser Ala Tyr Ser Ile
1 5

<210> 29
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 29
Leu Ser Ser Tyr Ser Ile
1 5

<210> 30
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 30
Leu Tyr Ser Tyr Ser Met
1 5

<210> 31
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 31
Leu Thr Ser Tyr Ser Met
1 5

<210> 32
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 32
Ile Ser Ser Tyr Ser Met
1 5

<210> 33
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 33
Leu Phe Ser Tyr Pro Met
1 5

<210> 34
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 34
Leu Ser Ala Tyr Ser Met
1 5

<210> 35
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 35
Ile Ser Ser His Ser Met
1 5

<210> 36
<211> 6
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 36
Ile Ser Ala Tyr Ala Met
1 5

<210> 37
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 37
Ile Ser Thr Tyr Ser Met
1 5

<210> 38
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 38
Leu His Ala Phe Ser Met
1   5

<210> 39
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 39
Ile Ser Gly Tyr Ser Ile
1   5

<210> 40
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 40
Ile Ser Asn Tyr Ser Ile
1   5

<210> 41
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 41
Ile Ser Ala Tyr Ser Met
1   5

<210> 42
<211> 6

<212> PRT
<213> Artificial Sequence

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

<400> 42
Leu Thr Ser Tyr Ala Met
1 5

<210> 43
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 43
Leu Tyr Ser Tyr Ser Ile
1 5

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

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

<400> 44
Leu Ser Ser Phe Ser Met
1 5

<210> 45
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 45

Ile Ala Ser Tyr Ser Ile
1   5

<210> 46
<211> 6
<212> PRT
<213> Artificial Sequence

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

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Ile His Ser Asn Ser Met
1   5

<210> 47
<211> 6
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 47
Leu Ser Thr Asn Ser Met
1   5

<210> 48
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
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<210> 485
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Ala Leu

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Ala Leu

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Tyr Gly Phe

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Trp Ala Phe

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peptide

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1   5

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1   5

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peptide

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peptide

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peptide

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peptide

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1 5

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peptide

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peptide

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<210> 663
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<210> 664
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1 5

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peptide

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1 5

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1 5

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1 5

<210> 670
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1 5

<210> 671
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1 5

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1   5

<210> 673
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1   5

<210> 674
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1   5

<210> 675
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1   5

<210> 676
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<212> PRT
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peptide

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1 5

<210> 677
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1 5

<210> 678
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1 5

<210> 679
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peptide

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Ser Ala Phe Ser Leu Ile
1   5

<210> 680
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1   5

<210> 682
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      peptide

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1   5

<210> 683
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peptide

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1 5

<210> 684
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1 5

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peptide

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1 5

<210> 686
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peptide

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1 5

<210> 687
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peptide

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1 5

<210> 688
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1 5

<210> 689
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1 5

<210> 690
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peptide

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1 5

<210> 691
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peptide

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1 5

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peptide

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1 5

<210> 693
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1 5

<210> 694
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peptide

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1 5

<210> 695
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1 5

<210> 696
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peptide

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1 5

<210> 697
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peptide

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Ile Ser Phe Tyr Ser Ile
1 5

<210> 698
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1 5

<210> 699
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<220>
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1 5

<210> 700
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1 5

<210> 701
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peptide

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1 5

<210> 702
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peptide

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1 5

<210> 703
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peptide

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1 5

<210> 704
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<220>
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peptide

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Leu Ser Gly Phe Gly Ile
1   5

<210> 705
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      peptide

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1   5

<210> 706
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Leu Ala Tyr Asn Ser Ile
1   5

<210> 707
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1   5

<210> 708
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<400> 708
Ile His Tyr Tyr Ser Ile
1 5

<210> 709
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peptide

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1 5

<210> 710
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1 5

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peptide

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1 5

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peptide

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peptide

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peptide

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1 5

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peptide

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1 5

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peptide

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1 5

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peptide

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1 5

<210> 719
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peptide

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1 5

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peptide

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1 5

<210> 721
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1 5

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peptide

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Leu His Ser Tyr Tyr Ile
1   5

<210> 723
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1   5

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1   5

<210> 726
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peptide

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Ile Ser Thr Tyr Tyr Met
1 5

<210> 727
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peptide

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1 5

<210> 728
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peptide

<400> 728
Ile Phe Ser Thr Ser Ile
1 5

<210> 729
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peptide

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Ile Ser Tyr Ser Thr Met
1 5

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1 5

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1 5

<210> 732
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peptide

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1 5

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peptide

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1 5

<210> 735
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peptide

<400> 735
Phe Ser Ser Ser Thr Ile
1 5

<210> 736
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peptide

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1 5

<210> 737
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Ile Ser Tyr Thr Ser Ile
1 5

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1 5

<210> 739
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Ile Ala Ser Tyr Ser Met
1 5

<210> 740
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peptide

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1 5

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1 5 10

<210> 742
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<220>
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peptide

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1 5 10

<210> 743
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<220>
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peptide

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1 5 10

<210> 744
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<220>
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peptide

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Arg Ile Tyr Pro Ser Gly Gly Thr Thr Asp
1 5 10

<210> 745
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<220>
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peptide

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Gly Ile Ser Thr Ser Gly Gly Tyr Thr Asp
1 5 10

<210> 746
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<220>
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peptide

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Tyr Ile Ser Pro Ser Gly Gly Tyr Thr Asp
1 5 10

<210> 747
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<220>
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peptide

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1   5   10

<210> 748
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<212> PRT
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<220>
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1   5   10

<210> 749
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<220>
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      peptide

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1   5   10

<210> 750
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1   5   10

<210> 751
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<212> PRT
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peptide

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Tyr Ile Ala Ser Phe Tyr Gly Asp Thr Tyr
1 5 10

<210> 752
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peptide

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1 5 10

<210> 753
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peptide

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1 5 10

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peptide

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Gly Ile Ser Ser Tyr Tyr Ser Tyr Thr Tyr
1 5 10

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1 5 10

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1 5 10

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peptide

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1 5 10

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peptide

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1 5 10

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peptide

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1 5 10

<210> 761
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peptide

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1 5 10

<210> 762
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peptide

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1 5 10

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peptide

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1 5 10

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peptide

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peptide

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1 5 10

<210> 766
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peptide

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<210> 767
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peptide

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1 5 10

<210> 768
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peptide

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1 5 10

<210> 769
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peptide

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1 5 10

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peptide

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peptide

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1 5 10

<210> 772
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peptide

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

<210> 773
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<400> 773
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1   5   10

<210> 774
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      peptide

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Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Ser
1   5   10

<210> 775
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<220>
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      peptide

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1   5   10

<210> 776
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<212> PRT
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<220>
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peptide

<400> 776
Ser Ile Tyr Ser Tyr Tyr Ser Phe Thr Asn
1 5 10

<210> 777
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<212> PRT
<213> Artificial Sequence

<220>
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peptide

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1 5 10

<210> 778
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peptide

<400> 778
Thr Ile Ser Pro Tyr Tyr Gly Tyr Thr Ser
1 5 10

<210> 779
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<220>
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peptide

<400> 779

His Ile Ser Ser Tyr Tyr Gly Phe Thr Ser
1 5 10

<210> 780
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Ala Ile His Pro Tyr Tyr Gly Tyr Thr Ser
1 5 10

<210> 781
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<400> 781
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1 5 10

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1 5 10

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peptide

<400> 783
Ser Ile Ser Ser Tyr Tyr Gly Tyr Thr Asp
1 5 10

<210> 784
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peptide

<400> 784
Ser Ile Tyr Ser Tyr Tyr Gly Tyr Thr Thr
1 5 10

<210> 785
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peptide

<400> 785
Ser Ile Ser Ser His Tyr Gly Tyr Thr His
1 5 10

<210> 786
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<212> PRT
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peptide

<400> 786
Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Ala
1 5 10

<210> 787
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<212> PRT
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peptide

<400> 787
Ser Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr
1 5 10

<210> 788
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<220>
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peptide

<400> 788
Ser Ile Tyr Ser Ser Tyr Ser Tyr Thr Ser
1 5 10

<210> 789
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peptide

<400> 789
Ser Ile Tyr Ser Ser Tyr Ser Tyr Thr Ala
1 5 10

<210> 790
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peptide

<400> 790
Ser Ile Tyr Ser Ser Tyr Ser Tyr Thr Gly
1 5 10

<210> 791
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peptide

<400> 791
Ser Ile Tyr Pro Ser Tyr Ser Tyr Thr Ser
1 5 10

<210> 792
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<220>
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peptide

<400> 792
Ser Ile Tyr Ser Arg Phe Ser Tyr Thr Ala
1 5 10

<210> 793
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<220>
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peptide

<400> 793
Asn Ile Tyr Ser Ser Tyr Gly Tyr Thr Ser
1 5 10

<210> 794
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<220>
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peptide

<400> 794
Ala Ile Tyr Ser Pro Tyr Gly Tyr Thr Ser
1 5 10

<210> 795
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peptide

<400> 795
Thr Ile Tyr Ser Tyr Tyr Ser Tyr Thr Ser
1 5 10

<210> 796
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peptide

<400> 796
Ser Ile Tyr Ser Ser Phe Gly Tyr Thr Ser
1 5 10

<210> 797
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<220>
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peptide

<400> 797
Ser Ile Ser Pro Ser Tyr Ser Tyr Thr Tyr
1   5   10

<210> 798
<211> 10
<212> PRT
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<220>
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      peptide

<400> 798
Ser Ile Thr Ser Ala Tyr Ser Tyr Thr Tyr
1   5   10

<210> 799
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<212> PRT
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<220>
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      peptide

<400> 799
Ser Ile Val Ser Ser Tyr Ser Arg Thr Tyr
1   5   10

<210> 800
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<212> PRT
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<220>
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      peptide

<400> 800
Ala Ile Tyr Pro Phe Asp Gly Tyr Thr Tyr
1   5   10

<210> 801
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<212> PRT
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<220>
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peptide

<400> 801
Gly Ile Phe Ser Tyr Phe Ser Tyr Thr Tyr
1 5 10

<210> 802
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<212> PRT
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<220>
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peptide

<400> 802
Ser Ile Ser Pro Phe Cys Gly Phe Thr Tyr
1 5 10

<210> 803
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<212> PRT
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<220>
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peptide

<400> 803
Ser Ile Thr Pro Ser Tyr Gly Tyr Thr Asn
1 5 10

<210> 804
<211> 10
<212> PRT
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<220>
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peptide

<400> 804

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

<210> 805
<211> 10
<212> PRT
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<220>
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<400> 805
Ser Ile Phe Pro Cys Cys Ser Asn Thr Tyr
1 5 10

<210> 806
<211> 10
<212> PRT
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<220>
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<400> 806
Ser Ile Ala Pro Ser Phe Gly His Thr Tyr
1 5 10

<210> 807
<211> 10
<212> PRT
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<220>
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<400> 807
Ser Ile Ser Pro Tyr Tyr Ser Tyr Thr Arg
1 5 10

<210> 808
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 808
Ser Ile Phe Ser Thr Tyr Ser Tyr Thr Tyr
1 5 10

<210> 809
<211> 10
<212> PRT
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<220>
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peptide

<400> 809
Ser Ile Ala Pro Ser Tyr Ser Phe Thr Tyr
1 5 10

<210> 810
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 810
Ser Ile Thr Pro Tyr Tyr Ser Thr Thr Ser
1 5 10

<210> 811
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 811
Phe Ile Ser Pro Tyr His Ser Tyr Thr Asp
1 5 10

<210> 812
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 812
Ser Ile Ser Ser Arg Tyr Gly Tyr Thr Tyr
1 5 10

<210> 813
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 813
Ala His Tyr Phe Pro Trp Ala Gly Ala Met
1 5 10

<210> 814
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 814
Thr Val Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met
1 5 10 15

<210> 815
<211> 10
<212> PRT
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<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 815
Ser Ser Tyr Phe Pro Trp Phe Ser Ala Met
1 5 10

<210> 816
<211> 13
<212> PRT
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<220>
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peptide

<400> 816
Ala Ser Tyr Tyr Ser Asn Tyr Tyr Tyr Gly Pro Ala Met
1 5 10

<210> 817
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 817
Gly Trp Phe Ser Phe Arg Ser Tyr Tyr Arg Ser Tyr Tyr Tyr Tyr Ser
1 5 10 15

Ala Leu

<210> 818
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 818

Ser Gly His Pro Arg Tyr Tyr Ser Arg Arg His Ser Tyr Gly Met
1   5   10   15

<210> 819
<211> 13
<212> PRT
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<220>
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      peptide

<400> 819
Ser Tyr Tyr Ser Asn Tyr Tyr Tyr Tyr Tyr Asp Ala Met
1   5   10

<210> 820
<211> 10
<212> PRT
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<220>
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      peptide

<400> 820
Ala His Tyr Phe Pro Trp Ala Gly Ala Leu
1   5   10

<210> 821
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<212> PRT
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<220>
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      peptide

<400> 821
Ala His Tyr Phe Arg Arg Ala Arg Gly Leu
1   5   10

<210> 822
<211> 10
<212> PRT
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<220>
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peptide

<400> 822
Ser His Tyr Phe Pro Trp Ala Gly Ala Met
1 5 10

<210> 823
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<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 823
Ala His Tyr Phe Pro Trp Ala Gly Gly Met
1 5 10

<210> 824
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<212> PRT
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<220>
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peptide

<400> 824
Ser Tyr Tyr Tyr Pro Arg Ser Arg Gly Met
1 5 10

<210> 825
<211> 10
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<220>
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peptide

<400> 825
Ser His Tyr Phe Pro Trp Ala Val Ala Met
1 5 10

<210> 826
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<212> PRT
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<220>
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peptide

<400> 826
Ser His Tyr Phe Pro Trp Phe Ala Ala Met
1 5 10

<210> 827
<211> 10
<212> PRT
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peptide

<400> 827
Ala Asn Tyr Phe Pro Trp Ala Tyr Ala Met
1 5 10

<210> 828
<211> 10
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peptide

<400> 828
Ala His Tyr Phe Pro Trp Val Val Gly Met
1 5 10

<210> 829
<211> 10
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peptide

<400> 829
Ser His Tyr Phe Pro Trp Ala Gly Ala Leu
1 5 10

<210> 830
<211> 10
<212> PRT
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peptide

<400> 830
Ser Ser Tyr Phe Pro Trp Phe Ser Ala Leu
1 5 10

<210> 831
<211> 10
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peptide

<400> 831
Ser Ser Tyr Phe Pro Trp Leu Ser Asp Met
1 5 10

<210> 832
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<220>
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peptide

<400> 832
Ser Ser Tyr Phe Pro Trp Val Ser Gly Met
1 5 10

<210> 833
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<212> PRT
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<220>
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peptide

<400> 833
Ser Ser Tyr Leu Pro Trp Phe Ser Ala Leu
1 5 10

<210> 834
<211> 10
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<220>
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peptide

<400> 834
Ser Ser Tyr Phe Pro Trp Phe Thr Ala Leu
1 5 10

<210> 835
<211> 10
<212> PRT
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peptide

<400> 835
Ser Ser Tyr Phe Pro Trp Val Gly Gly Phe
1 5 10

<210> 836
<211> 10
<212> PRT
<213> Artificial Sequence

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peptide

<400> 836
Ser Ser Arg Phe Pro Trp Phe Tyr Gly Leu
1 5 10

<210> 837
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<400> 837
Ser Ser Tyr Phe Pro Trp Ser Ser Ala Met
1 5 10

<210> 838
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<400> 838
Ser His Tyr Phe Pro Trp Leu Ser Ala Leu
1 5 10

<210> 839
<211> 10
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<400> 839
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1 5 10

<210> 840
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<212> PRT
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<220>
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peptide

<400> 840
Ser Ser Tyr Ile Pro Trp Arg Tyr Ala Ile
1 5 10

<210> 841
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 841
Ser Ser Tyr Phe Pro Trp Ile Ser Ala Met
1 5 10

<210> 842
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peptide

<400> 842
Ser Ser Tyr Phe Pro Trp Ile Ser Ala Leu
1 5 10

<210> 843
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<220>
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peptide

<400> 843

Ser Ser Arg Phe Pro Trp Ile Ser Gly Met
1   5   10

<210> 844
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      peptide

<400> 844
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1   5   10

<210> 845
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      peptide

<400> 845
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1   5   10

<210> 846
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      peptide

<400> 846
Ser Ser Tyr Leu Pro Trp Ile Thr Ala Met
1   5   10

<210> 847
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<220>
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peptide

<400> 847
Ser Ala Tyr Phe Pro Trp Phe Ala Ala Leu
1 5 10

<210> 848
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<212> PRT
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peptide

<400> 848
Ser Ser Tyr Phe Pro Trp Phe Phe Ala Met
1 5 10

<210> 849
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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 849
Ser Ser His Phe Pro Trp Val Ser Ala Leu
1 5 10

<210> 850
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 850
Ser Ser Tyr Phe Pro Trp Val Ser Ala Met
1 5 10

<210> 851
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 851
Ser Ser His Phe Pro Trp Phe Ser Ala Met
1 5 10

<210> 852
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 852
Ser Ser Tyr Phe Pro Trp Phe Ser Ala Ile
1 5 10

<210> 853
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 853
Ser Ser Arg Phe Pro Trp Phe Pro Ala Met
1 5 10

<210> 854
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 854
Ser Ser Tyr Val Pro Trp Phe Tyr Ala Leu
1 5 10

<210> 855
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 855
Ala Ser Tyr Phe Pro Trp Phe Pro Ala Met
1 5 10

<210> 856
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 856
Ser Ser Tyr Phe Pro Trp Phe Phe Ala Leu
1 5 10

<210> 857
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 857
Ser Ser Tyr Tyr Pro Trp Phe Ser Ala Leu
1 5 10

<210> 858
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 858
Ser Ser Tyr Leu Pro Trp Val Ser Ala Leu
1 5 10

<210> 859
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 859
Ser Phe Asn Gly Ala Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met
1 5 10 15

<210> 860
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 860
Asn Val Val Val Ser Arg Lys Pro Tyr Phe Phe Arg Ser Ala Met
1 5 10 15

<210> 861
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 861
Thr Val Pro Gly Ser Lys Arg Pro Tyr Phe Ala Ser Leu Ala Ile
1 5 10 15

<210> 862
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 862
Asn Val Arg Gly Phe Arg Lys Pro Tyr Phe Ser Arg Trp Ala Met
1 5 10 15

<210> 863
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 863
Asn Val Pro Gly Ile Lys Arg Pro Tyr Phe Thr Ala Trp Ala Met
1 5 10 15

<210> 864
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 864
Thr Ile Arg Gly Ser Lys Arg Pro Tyr Phe Ala Ala Ser Gly Leu
1 5 10 15

<210> 865
<211> 15

<212> PRT
<213> Artificial Sequence

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

<400> 865
Thr Ala Arg Glu Asn Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met
1 5 10 15

<210> 866
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 866
Thr Leu Pro Leu Ser Lys Lys Pro Tyr Phe Ser Leu Trp Ala Phe
1 5 10 15

<210> 867
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 867
Thr Phe His Gly Ser Lys Lys Pro Tyr Phe Ser Gly Arg Ala Met
1 5 10 15

<210> 868
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 868

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

<210> 869
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 869
Ser Val Arg Gly Ser Lys Lys Pro Tyr Phe Ser His Trp Ala Met
1 5 10 15

<210> 870
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 870
Asn Val Arg Thr Ser Lys Lys Pro Tyr Phe Pro Leu Trp Ala Met
1 5 10 15

<210> 871
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 871
Gly Val Ser Gly Gly Ser Asn Tyr Ile Ser Ile Phe Arg Asn Ser Ser
1 5 10 15

Gly Met

<210> 872
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 872
Gly Gly Leu Ser Val Ser His Tyr Asn Tyr Val His Ser Phe Lys Trp
1 5 10 15

Gly Leu

<210> 873
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 873
Ser Cys Ser Ser Phe Cys Asn Tyr Val Ser Asn Tyr Asn Ala Arg Arg
1 5 10 15

Ala Leu

<210> 874
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 874
Gly Asn Ala Arg Val Ser Asn Tyr Ile Ser Ser Tyr Tyr Ala Trp Arg
1 5 10 15

Ala Met

<210> 875
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 875
Gly Gly Tyr Gly Phe Ser Tyr Tyr Asn Ser Val Thr Phe Tyr Arg Trp
1 5 10 15

Ala Phe

<210> 876
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 876
Val Gly Ser Gly Val Cys Asn Ser Leu His Asn Tyr Phe Tyr Lys Arg
1 5 10 15

Gly Met

<210> 877
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 877

Ser Ser Ser Asp Ile Ser Ile Asp Asn Ser Ile Arg Tyr Thr Trp Gly
1 5 10 15

Ala Met

<210> 878
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 878
Gly His Ser Gly Val Thr Asn Phe Ile Ser Phe Tyr Tyr Arg Arg Arg
1 5 10 15

Ala Met

<210> 879
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 879
Gly Val Ser Gly Leu Asp Asn Asn Arg Thr Ala Ser Tyr Ser Arg Met
1 5 10 15

Gly Met

<210> 880
<211> 18
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 880
Gly Ala Ala Ser Val Asn His Ile Gly Ser Leu Tyr Val Ser Trp Arg
1 5 10 15

Gly Leu

<210> 881
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 881
His Gly Ser Gly Leu Ser His Asn Ala Thr Thr Ser Tyr Tyr Arg Ser
1 5 10 15

Ala Ile

<210> 882
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 882
Ser Ser Ser Ala Val Ser Arg Asn Ser Ile Val Tyr Tyr Ser Arg Thr
1 5 10 15

Ala Met

<210> 883
<211> 18

<212> PRT
<213> Artificial Sequence

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

<400> 883
Gly Val Cys Arg Val Ser Asn Tyr Ser Ser Tyr Phe Tyr Ser Arg Gly
1 5 10 15

Ala Met

<210> 884
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 884
Ala Ile Ser His Val Ala His Tyr Asp Asn Val Ile Tyr Ser Lys Trp
1 5 10 15

Gly Ile

<210> 885
<211> 18
<212> PRT
<213> Artificial Sequence

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

<400> 885
Gly His Ser Val Leu Ser Asn Tyr Val Ser Ile His Tyr Tyr Trp Ala
1 5 10 15

Gly Phe

<210> 886
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 886
Gly Gly Gly Gly Ser
1 5

<210> 887
<211> 14
<212> PRT
<213> Artificial Sequence

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

<400> 887
Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys Ser Ser
1 5 10

<210> 888
<211> 19
<212> PRT
<213> Artificial Sequence

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

<400> 888
Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
1 5 10 15

Gly Gly Gly

<210> 889
<211> 16

<212> PRT
<213> Artificial Sequence

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

<400> 889
Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala
1 5 10 15

<210> 890
<211> 15
<212> PRT
<213> Artificial Sequence

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

<400> 890
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Ser Ser
1 5 10 15

<210> 891
<211> 20
<212> PRT
<213> Artificial Sequence

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

<400> 891
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

Gly Ser Thr Gly
20

<210> 892
<211> 20
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 892
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp
1 5 10 15

Lys Thr His Thr
20

<210> 893
<211> 6
<212> PRT
<213> Artificial Sequence

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

<400> 893
Ile His Ser Ser Ser Ile
1 5

<210> 894
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 894
Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr
1 5 10

<210> 895
<211> 9
<212> PRT
<213> Artificial Sequence

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

<400> 895

Tyr His His Pro Phe Gly Tyr Ala Leu
1 5

<210> 896
<211> 5
<212> PRT
<213> Artificial Sequence

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

<400> 896
Gly Val Tyr Leu Phe
1 5

<210> 897
<211> 721
<212> PRT
<213> Artificial Sequence

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

<400> 897
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 Asp Phe Thr Ala Tyr
20 25 30

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

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

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

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

```
Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285
```

```
Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495
```

```
Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr
    530                 535                 540

Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Pro Ala Pro Gly His Trp Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu
        595                 600                 605

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    610                 615                 620

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
625                 630                 635                 640

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                645                 650                 655

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            660                 665                 670

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        675                 680                 685
```

```
Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    690                 695                 700

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
705                 710                 715                 720

Thr
```

<210> 898
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 898

```
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 Asp Phe Ser Ser Ser
            20                  25                  30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110
```

```
Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
        115                 120                 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly
305                 310                 315                 320
```

```
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510
```

```
Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr
    530                 535                 540

Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Pro Gly
            580                 585                 590

His Trp Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        595                 600                 605

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    610                 615                 620

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
625                 630                 635                 640

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
                645                 650                 655

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            660                 665                 670

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        675                 680                 685

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    690                 695                 700

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715
```

<210> 899
<211> 214
<212> PRT
<213> Artificial Sequence

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

<400> 899
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 Val Ser Ser Ala
20 25 30

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

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Arg 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 Trp Tyr Tyr Ala Pro Ile
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

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

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

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

Phe Asn Arg Gly Glu Cys
210

<210> 900
<211> 745
<212> PRT
<213> Artificial Sequence

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

<400> 900
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Met Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Gly Gly Ser Gly Val Ser His Tyr Gly Ser Val Tyr Tyr Ser Trp
        115                 120                 125

Trp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
145                 150                 155                 160

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
                165                 170                 175

Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
            180                 185                 190

Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro
        195                 200                 205

Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile
    210                 215                 220

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala
225                 230                 235                 240

Ser Tyr Ala Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                245                 250                 255

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Thr Ser Asp
            260                 265                 270

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
        275                 280                 285
```

```
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
    290                 295                 300

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
305                 310                 315                 320

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
                325                 330                 335

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg
            340                 345                 350

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
        355                 360                 365

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
    370                 375                 380

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe
385                 390                 395                 400

Asp Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
                405                 410                 415

Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
            420                 425                 430

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
        435                 440                 445

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
    450                 455                 460

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
465                 470                 475                 480

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
                485                 490                 495
```

```
Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
            500                 505                 510

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
        515                 520                 525

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
    530                 535                 540

Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln Ala Pro Gly
545                 550                 555                 560

Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr
                565                 570                 575

Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
            580                 585                 590

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
        595                 600                 605

Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Pro Gly His Trp Gly Phe
    610                 615                 620

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
625                 630                 635                 640

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
                645                 650                 655

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
            660                 665                 670

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
        675                 680                 685
```

```
Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
    690                 695                 700

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
705                 710                 715                 720

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
                725                 730                 735

Pro Lys Ser Cys Asp Lys Thr His Thr
            740                 745
```

<210> 901
<211> 738
<212> PRT
<213> Artificial Sequence

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

<400> 901

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Leu Ser Tyr Tyr Tyr
        35                  40                  45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95
```

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Trp Ser His Val Ser Gly His Tyr Ser Gly Met Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr Phe
225                 230                 235                 240

Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly
                245                 250                 255

Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro
            260                 265                 270

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
        275                 280                 285

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
    290                 295                 300
```

```
Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
305                 310                 315                 320

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
                325                 330                 335

Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
            340                 345                 350

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
        355                 360                 365

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
    370                 375                 380

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu
385                 390                 395                 400

Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe
                405                 410                 415

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
            420                 425                 430

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
        435                 440                 445

Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
    450                 455                 460

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
465                 470                 475                 480

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly
                485                 490                 495
```

```
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu
            500                 505                 510

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
        515                 520                 525

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
    530                 535                 540

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
545                 550                 555                 560

Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
                565                 570                 575

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
            580                 585                 590

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
        595                 600                 605

Arg Pro Ala Pro Gly His Trp Gly Phe Asp Tyr Trp Gly Gln Gly Thr
    610                 615                 620

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
625                 630                 635                 640

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
                645                 650                 655

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
            660                 665                 670

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
        675                 680                 685

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
    690                 695                 700
```

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
705 710 715 720

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
725 730 735

His Thr

<210> 902
<211> 229
<212> PRT
<213> Artificial Sequence

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

<400> 902
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Asp
1 5 10 15

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
20 25 30

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
35 40 45

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
50 55 60

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
65 70 75 80

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
85 90 95

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Tyr Tyr Ala Pro Ile Thr
100 105 110

```
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
        115                 120                 125


Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
    130                 135                 140


Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
145                 150                 155                 160


Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                165                 170                 175


Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
            180                 185                 190


Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
        195                 200                 205


Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
    210                 215                 220


Asn Arg Gly Glu Cys
225


<210> 903
<211> 734
<212> PRT
<213> Artificial Sequence

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

<400> 903
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30
```

```
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
        35                  40                  45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220
```

```
Tyr Cys Gln Gln Ala Ser Tyr Ala Pro Ile Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
                245                 250                 255

Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
            260                 265                 270

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        275                 280                 285

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    290                 295                 300

Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
305                 310                 315                 320

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                325                 330                 335

Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            340                 345                 350

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
        355                 360                 365

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    370                 375                 380

Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
385                 390                 395                 400

Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp
                405                 410                 415

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            420                 425                 430
```

```
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        435                 440                 445

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
    450                 455                 460

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
465                 470                 475                 480

Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly
                485                 490                 495

Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val
            500                 505                 510

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
        515                 520                 525

Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val
    530                 535                 540

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser
545                 550                 555                 560

Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
                565                 570                 575

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
            580                 585                 590

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Pro
        595                 600                 605

Gly His Trp Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
    610                 615                 620
```

```
Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
625                 630                 635                 640


Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
                645                 650                 655


Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            660                 665                 670


Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        675                 680                 685


Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    690                 695                 700


Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
705                 710                 715                 720


Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730


<210> 904
<211> 739
<212> PRT
<213> Artificial Sequence

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

<400> 904
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Leu Ser Tyr Tyr Tyr
        35                  40                  45
```

```
Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Trp Ser His Val Ser Gly His Tyr Ser Gly Met Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
                245                 250                 255
```

```
Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
        275                 280                 285

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    290                 295                 300

Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe
305                 310                 315                 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                325                 330                 335

Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr
            340                 345                 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
        355                 360                 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
    370                 375                 380

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg
385                 390                 395                 400

Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly
                405                 410                 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
            420                 425                 430

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
        435                 440                 445
```

```
Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    450                 455                 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465                 470                 475                 480

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser
                485                 490                 495

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly
            500                 505                 510

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
        515                 520                 525

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
    530                 535                 540

Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
545                 550                 555                 560

Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
                565                 570                 575

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
            580                 585                 590

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
        595                 600                 605

Ala Arg Pro Ala Pro Gly His Trp Gly Phe Asp Tyr Trp Gly Gln Gly
    610                 615                 620

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
625                 630                 635                 640

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
                645                 650                 655
```

```
Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
            660                 665                 670

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
        675                 680                 685

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
    690                 695                 700

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
705                 710                 715                 720

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
                725                 730                 735

Thr His Thr
```

<210> 905
<211> 747
<212> PRT
<213> Artificial Sequence

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

<400> 905

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Ser Ser Ser Ser
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60
```

```
Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Gly Gly Ser Gly Val Ser His Tyr Gly Ser Val Tyr Tyr Ser Trp
        115                 120                 125

Trp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
145                 150                 155                 160

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
                165                 170                 175

Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
            180                 185                 190

Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro
        195                 200                 205

Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile
    210                 215                 220

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr
225                 230                 235                 240

Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu
                245                 250                 255
```

```
Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Thr
            260                 265                 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
        275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
    290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
                325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr
            340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
        355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
    370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met
385                 390                 395                 400

Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
                405                 410                 415

Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
            420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
        435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
    450                 455                 460
```

```
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480


Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
                485                 490                 495


Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
            500                 505                 510


Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly
        515                 520                 525


Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
    530                 535                 540


Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln Ala
545                 550                 555                 560


Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly
                565                 570                 575


Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala
            580                 585                 590


Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala
        595                 600                 605


Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Pro Gly His Trp
    610                 615                 620


Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
625                 630                 635                 640


Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
                645                 650                 655
```

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
660 665 670

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
675 680 685

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
690 695 700

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
705 710 715 720

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
725 730 735

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
740 745

<210> 906
<211> 731
<212> PRT
<213> Artificial Sequence

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

<400> 906
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

```
Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Ser Ser Tyr Ser Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Ser
                245                 250                 255

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
            260                 265                 270
```

```
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
        275                 280                 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser
    290                 295                 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305                 310                 315                 320

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr
                325                 330                 335

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
            340                 345                 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
        355                 360                 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
    370                 375                 380

Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val
385                 390                 395                 400

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
                405                 410                 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
            420                 425                 430

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
        435                 440                 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
    450                 455                 460
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465                 470                 475                 480

Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
                485                 490                 495

Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly
            500                 505                 510

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
        515                 520                 525

Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln Ala
    530                 535                 540

Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly
545                 550                 555                 560

Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala
                565                 570                 575

Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala
            580                 585                 590

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Pro Gly His Trp
        595                 600                 605

Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
    610                 615                 620

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
625                 630                 635                 640

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                645                 650                 655

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            660                 665                 670
```

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
675 680 685

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
690 695 700

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
705 710 715 720

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730

<210> 907
<211> 736
<212> PRT
<213> Artificial Sequence

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

<400> 907
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285
```

```
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495
```

```
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile
545                 550                 555                 560

Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro
        595                 600                 605

Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
625                 630                 635                 640

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                645                 650                 655

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            660                 665                 670

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        675                 680                 685
```

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
690 695 700

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
705 710 715 720

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730 735

<210> 908
<211> 732
<212> PRT
<213> Artificial Sequence

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

<400> 908
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

```
Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
            260                 265                 270

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320
```

```
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510
```

```
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Asp
545                 550                 555                 560

Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly His
        595                 600                 605

Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    610                 615                 620

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
625                 630                 635                 640

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
                645                 650                 655

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
            660                 665                 670

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
        675                 680                 685

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
    690                 695                 700

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
705                 710                 715                 720
```

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730

<210> 909
<211> 229
<212> PRT
<213> Artificial Sequence

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

<400> 909
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Asp
1 5 10 15

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
20 25 30

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
35 40 45

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
50 55 60

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
65 70 75 80

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
85 90 95

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Tyr Asn Ala Pro Ile Thr
100 105 110

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
115 120 125

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
130 135 140

```
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
145                 150                 155                 160


Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                165                 170                 175


Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
            180                 185                 190


Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
        195                 200                 205


Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
    210                 215                 220


Asn Arg Gly Glu Cys
225


<210> 910
<211> 737
<212> PRT
<213> Artificial Sequence

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

<400> 910
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
        35                  40                  45


Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60
```

```
Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255
```

```
Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
            260                 265                 270

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460
```

```
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile
545                 550                 555                 560

Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala
        595                 600                 605

Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
625                 630                 635                 640

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
                645                 650                 655
```

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
660 665 670

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
675 680 685

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
690 695 700

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
705 710 715 720

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
725 730 735

Thr

<210> 911
<211> 733
<212> PRT
<213> Artificial Sequence

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

<400> 911
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

```
Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
            260                 265                 270
```

```
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460
```

```
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe Ile
545                 550                 555                 560

Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly Ser
        595                 600                 605

Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            660                 665                 670
```

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
675 680 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
690 695 700

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705 710 715 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730

<210> 912
<211> 229
<212> PRT
<213> Artificial Sequence

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

<400> 912
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Asp
1 5 10 15

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
20 25 30

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
35 40 45

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
50 55 60

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
65 70 75 80

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
85 90 95

```
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Thr Gly Ser Leu Ile Thr
            100                 105                 110


Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
        115                 120                 125


Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
    130                 135                 140


Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
145                 150                 155                 160


Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                165                 170                 175


Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
            180                 185                 190


Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
        195                 200                 205


Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
    210                 215                 220


Asn Arg Gly Glu Cys
225
```

<210> 913
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 913

```
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 Asp Leu Ser His Ser
            20                  25                  30

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

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

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

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

Ala Arg Ser Ser Tyr Phe Pro Trp Phe Phe Ala Leu Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
        115                 120                 125

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
    130                 135                 140

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
145                 150                 155                 160

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
                165                 170                 175

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
            180                 185                 190

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
        195                 200                 205
```

```
Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415
```

```
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser Ser Met
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
    530                 535                 540

Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        595                 600                 605
```

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
610 615 620

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
625 630 635 640

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
645 650 655

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
660 665 670

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
675 680 685

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
690 695 700

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705 710 715

<210> 914
<211> 722
<212> PRT
<213> Artificial Sequence

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

<400> 914
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 Asp Ile Ser Ser Tyr
20 25 30

Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ala Ser Ile Tyr Pro Ser Tyr Ser Tyr Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Asn Val Arg Gly Phe Arg Lys Pro Tyr Phe Ser Arg Trp Ala
            100                 105                 110

Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
    130                 135                 140

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val
145                 150                 155                 160

Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                165                 170                 175

Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg
            180                 185                 190

Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
        195                 200                 205

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Phe Phe
    210                 215                 220

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly
225                 230                 235                 240

Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His
                245                 250                 255
```

```
Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
            260                 265                 270

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
        275                 280                 285

Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu
    290                 295                 300

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
305                 310                 315                 320

Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser
                325                 330                 335

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
            340                 345                 350

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
        355                 360                 365

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
    370                 375                 380

Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala
385                 390                 395                 400

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
                405                 410                 415

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
            420                 425                 430

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
        435                 440                 445
```

```
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
    450                 455                 460

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly
465                 470                 475                 480

Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
                485                 490                 495

Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
            500                 505                 510

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile
        515                 520                 525

Ala Tyr Ser Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    530                 535                 540

Glu Trp Val Ala Thr Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala
545                 550                 555                 560

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
                565                 570                 575

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
            580                 585                 590

Tyr Tyr Cys Ala Arg Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
        595                 600                 605

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    610                 615                 620

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
625                 630                 635                 640

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                645                 650                 655
```

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
660 665 670

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
675 680 685

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
690 695 700

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
705 710 715 720

His Thr

<210> 915
<211> 214
<212> PRT
<213> Artificial Sequence

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

<400> 915
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 Val Ser Ser Ala
20 25 30

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

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Arg 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 His Tyr Phe Pro Ile
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

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

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

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

Phe Asn Arg Gly Glu Cys
    210
```

<210> 916
<211> 722
<212> PRT
<213> Artificial Sequence

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

<400> 916

```
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 Asp Leu Ser His Ser
            20                  25                  30

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

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

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

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

Ala Arg Ser Ser Tyr Phe Pro Trp Phe Phe Ala Leu Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
        115                 120                 125

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
    130                 135                 140

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
145                 150                 155                 160

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
                165                 170                 175

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
            180                 185                 190

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
        195                 200                 205
```

```
Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415
```

```
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser Ile
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala
    530                 535                 540

Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly Thr
        595                 600                 605
```

```
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    610                 615                 620


Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
625                 630                 635                 640


Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                645                 650                 655


Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            660                 665                 670


Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        675                 680                 685


Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    690                 695                 700


Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
705                 710                 715                 720


His Thr
```

<210> 917
<211> 727
<212> PRT
<213> Artificial Sequence

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

<400> 917

```
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 Asp Ile Ser Ser Tyr
            20                  25                  30
```

```
Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Ser Ile Tyr Pro Ser Tyr Ser Tyr Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Asn Val Arg Gly Phe Arg Lys Pro Tyr Phe Ser Arg Trp Ala
            100                 105                 110

Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
    130                 135                 140

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val
145                 150                 155                 160

Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                165                 170                 175

Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg
            180                 185                 190

Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
        195                 200                 205

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Phe Phe
    210                 215                 220

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly
225                 230                 235                 240
```

```
Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His
                245                 250                 255

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
            260                 265                 270

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
        275                 280                 285

Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu
    290                 295                 300

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
305                 310                 315                 320

Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser
                325                 330                 335

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
            340                 345                 350

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
        355                 360                 365

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
    370                 375                 380

Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala
385                 390                 395                 400

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
                405                 410                 415

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
            420                 425                 430
```

```
Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
        435                 440                 445

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
    450                 455                 460

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly
465                 470                 475                 480

Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
                485                 490                 495

Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
            500                 505                 510

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile
        515                 520                 525

His Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    530                 535                 540

Glu Trp Val Ala Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala
545                 550                 555                 560

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
                565                 570                 575

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
            580                 585                 590

Tyr Tyr Cys Ala Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr
        595                 600                 605

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
    610                 615                 620

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
625                 630                 635                 640
```

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
645 650 655

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
660 665 670

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
675 680 685

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
690 695 700

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
705 710 715 720

Ser Cys Asp Lys Thr His Thr
725

<210> 918
<211> 213
<212> PRT
<213> Artificial Sequence

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

<400> 918
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 Val Ser Ser Ala
20 25 30

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

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

```
Ser Arg 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 Gly Val Tyr Leu Phe Thr
                85                  90                  95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160

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

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

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205

Asn Arg Gly Glu Cys
    210
```

<210> 919
<211> 735
<212> PRT
<213> Artificial Sequence

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

<400> 919

```
Glu Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
1               5                  10                  15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ser Ser
            20                  25                  30

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

Trp Val Ala Thr Val Tyr Pro Tyr Leu Asp Tyr Thr Tyr Tyr Ala Asp
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr
65                  70                  75                  80

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

Tyr Cys Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Met Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
        115                 120                 125

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    130                 135                 140

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
145                 150                 155                 160

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                165                 170                 175

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
            180                 185                 190
```

```
Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
        195                 200                 205

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr
    210                 215                 220

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His
225                 230                 235                 240

Thr Lys Val Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
            340                 345                 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
        355                 360                 365

Gly Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu
    370                 375                 380

Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe
385                 390                 395                 400
```

```
Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
                405                 410                 415

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
            420                 425                 430

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
        435                 440                 445

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
    450                 455                 460

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr
465                 470                 475                 480

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Ser Ser Ser Ser Ile
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser
    530                 535                 540

Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590
```

```
Gly Gly Ser Gly Val Ser His Tyr Gly Ser Val Tyr Tyr Ser Trp Trp
        595                 600                 605

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
    610                 615                 620

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
625                 630                 635                 640

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
                645                 650                 655

Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            660                 665                 670

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
        675                 680                 685

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
    690                 695                 700

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Ser
705                 710                 715                 720

Tyr Ala Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                725                 730                 735
```

<210> 920
<211> 728
<212> PRT
<213> Artificial Sequence

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

<400> 920

```
Glu Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
1               5                   10                  15
```

```
Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ser Ser
            20                  25                  30

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

Trp Val Ala Thr Val Tyr Pro Tyr Leu Asp Tyr Thr Tyr Tyr Ala Asp
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr
65                  70                  75                  80

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

Tyr Cys Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Met Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
        115                 120                 125

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    130                 135                 140

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
145                 150                 155                 160

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                165                 170                 175

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
            180                 185                 190

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
        195                 200                 205

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr
    210                 215                 220
```

```
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His
225                 230                 235                 240

Thr Lys Val Glu Pro Lys Ser Ser Asp Lys Thr His Asn Cys Pro Pro
                245                 250                 255

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            260                 265                 270

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        275                 280                 285

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    290                 295                 300

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
305                 310                 315                 320

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                325                 330                 335

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
            340                 345                 350

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
        355                 360                 365

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu
    370                 375                 380

Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe
385                 390                 395                 400

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
                405                 410                 415
```

```
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
            420                 425                 430

Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
        435                 440                 445

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
    450                 455                 460

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr
465                 470                 475                 480

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Leu Ser Tyr Tyr Tyr Met
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser
    530                 535                 540

Ile Tyr Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Trp Ser His Val Ser Gly His Tyr Ser Gly Met Asp Tyr Trp Gly Gln
        595                 600                 605

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
    610                 615                 620
```

```
Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
625                 630                 635                 640


Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
                645                 650                 655


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
            660                 665                 670


Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
        675                 680                 685


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    690                 695                 700


Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr Phe Gly
705                 710                 715                 720


Gln Gly Thr Lys Val Glu Ile Lys
                725
```

<210> 921
<211> 712
<212> PRT
<213> Artificial Sequence

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

<400> 921

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
        35                  40                  45
```

```
Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240
```

```
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys
    370                 375                 380

Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445
```

```
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly
            580                 585                 590

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
        595                 600                 605

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
    610                 615                 620

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
625                 630                 635                 640
```

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
645 650 655

Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
660 665 670

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
675 680 685

Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly
690 695 700

Gln Gly Thr Lys Val Glu Ile Lys
705 710

<210> 922
<211> 712
<212> PRT
<213> Artificial Sequence

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

<400> 922
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

```
Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285
```

```
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys
    370                 375                 380

Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480
```

```
Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly
            580                 585                 590

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
        595                 600                 605

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
    610                 615                 620

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
625                 630                 635                 640

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
                645                 650                 655

Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
            660                 665                 670

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
        675                 680                 685
```

Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly
690 695 700

Gln Gly Thr Lys Val Glu Ile Lys
705 710

<210> 923
<211> 712
<212> PRT
<213> Artificial Sequence

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

<400> 923
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
115 120 125

```
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    130                 135                 140

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320
```

```
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys
    370                 375                 380

Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525
```

```
Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly
            580                 585                 590

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
        595                 600                 605

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
    610                 615                 620

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
625                 630                 635                 640

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
                645                 650                 655

Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
            660                 665                 670

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
        675                 680                 685

Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly
    690                 695                 700

Gln Gly Thr Lys Val Glu Ile Lys
705                 710
```

<210> 924
<211> 712
<212> PRT
<213> Artificial Sequence

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

<400> 924
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
115 120 125

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145 150 155 160

```
Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu
        355                 360                 365
```

```
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys
    370                 375                 380

Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560
```

```
Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575


Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly
            580                 585                 590


Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
        595                 600                 605


Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
    610                 615                 620


Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
625                 630                 635                 640


Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
                645                 650                 655


Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
            660                 665                 670


Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
        675                 680                 685


Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly
    690                 695                 700


Gln Gly Thr Lys Val Glu Ile Lys
705                 710


<210> 925
<211> 697
<212> PRT
<213> Artificial Sequence

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

<400> 925
```

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
            20                  25                  30

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

Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
    50                  55                  60

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
                565                 570                 575

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
            580                 585                 590

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
        595                 600                 605
```

```
Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
    610                 615                 620

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
625                 630                 635                 640

Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
                645                 650                 655

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
            660                 665                 670

Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
        675                 680                 685

Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695
```

<210> 926
<211> 697
<212> PRT
<213> Artificial Sequence

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

<400> 926

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
            20                  25                  30

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

Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
    50                  55                  60
```

```
Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65                  70                  75                  80

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460
```

```
Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
                565                 570                 575

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
            580                 585                 590

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
        595                 600                 605

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
    610                 615                 620

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
625                 630                 635                 640

Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
                645                 650                 655
```

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
660 665 670

Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
675 680 685

Gly Gln Gly Thr Lys Val Glu Ile Lys
690 695

<210> 927
<211> 697
<212> PRT
<213> Artificial Sequence

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

<400> 927
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
20 25 30

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

Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
50 55 60

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510
```

```
Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
                565                 570                 575

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
            580                 585                 590

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
        595                 600                 605

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
    610                 615                 620

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
625                 630                 635                 640

Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
                645                 650                 655

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
            660                 665                 670

Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
        675                 680                 685

Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695
```

<210> 928
<211> 697

<212> PRT
<213> Artificial Sequence

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

<400> 928
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
20 25 30

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

Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
50 55 60

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
                565                 570                 575
```

```
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
            580                 585                 590


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
        595                 600                 605


Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
    610                 615                 620


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
625                 630                 635                 640


Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
                645                 650                 655


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
            660                 665                 670


Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
        675                 680                 685


Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695


<210> 929
<211> 716
<212> PRT
<213> Artificial Sequence

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

<400> 929
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30
```

```
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
        35                  40                  45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220
```

```
Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp Leu
        355                 360                 365

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys
    370                 375                 380

Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430
```

```
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp
            580                 585                 590

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620
```

```
Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
625                 630                 635                 640


Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                645                 650                 655


Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
            660                 665                 670


Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
        675                 680                 685


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro
    690                 695                 700


Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705                 710                 715


<210> 930
<211> 716
<212> PRT
<213> Artificial Sequence

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

<400> 930
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
        35                  40                  45


Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60
```

```
Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270
```

```
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp Leu
        355                 360                 365

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys
    370                 375                 380

Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460
```

```
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp
            580                 585                 590

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
625                 630                 635                 640

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                645                 650                 655

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
            660                 665                 670
```

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
675 680 685

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro
690 695 700

Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710 715

<210> 931
<211> 716
<212> PRT
<213> Artificial Sequence

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

<400> 931
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

```
Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300
```

```
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys
    370                 375                 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510
```

```
Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp
            580                 585                 590

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
625                 630                 635                 640

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                645                 650                 655

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
            660                 665                 670

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
        675                 680                 685

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro
    690                 695                 700
```

Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710 715

<210> 932
<211> 716
<212> PRT
<213> Artificial Sequence

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

<400> 932
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr
115 120 125

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

```
Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr
            340                 345                 350
```

```
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys
    370                 375                 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
465                 470                 475                 480

Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
            500                 505                 510

Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr
    530                 535                 540
```

```
Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560


Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575


Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp
            580                 585                 590


Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605


Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
625                 630                 635                 640


Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                645                 650                 655


Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
            660                 665                 670


Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
        675                 680                 685


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro
    690                 695                 700


Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705                 710                 715
```

<210> 933
<211> 701
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 933

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


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
            20                  25                  30


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


Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
    50                  55                  60


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


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


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


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


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


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


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


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

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

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

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

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

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

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

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

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

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

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp
            340                 345                 350

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

Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380
```

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
                565                 570                 575

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590
```

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
        595                 600                 605


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
    610                 615                 620


Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
625                 630                 635                 640


Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
                645                 650                 655


Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
            660                 665                 670


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
        675                 680                 685


Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695                 700


<210> 934
<211> 701
<212> PRT
<213> Artificial Sequence

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

<400> 934
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
            20                  25                  30


Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
    50                  55                  60

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

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

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

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

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

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

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

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

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

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

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
225                 230                 235                 240
```

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

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

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

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

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

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

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp
            340                 345                 350

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

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

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

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

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

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

```
Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
                565                 570                 575

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
        595                 600                 605

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
    610                 615                 620

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
625                 630                 635                 640
```

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
645 650 655

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
660 665 670

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
675 680 685

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
690 695 700

<210> 935
<211> 701
<212> PRT
<213> Artificial Sequence

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

<400> 935
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
20 25 30

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

Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
50 55 60

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

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

```
Ala Arg Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495
```

```
Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560

Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
                565                 570                 575

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
        595                 600                 605

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
    610                 615                 620

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
625                 630                 635                 640

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
                645                 650                 655

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
            660                 665                 670

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
        675                 680                 685

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695                 700
```

<210> 936
<211> 701
<212> PRT
<213> Artificial Sequence

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

<400> 936
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
20 25 30

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

Ala Tyr Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val
50 55 60

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
        515                 520                 525

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
    530                 535                 540

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
545                 550                 555                 560
```

```
Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
                565                 570                 575


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590


Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
        595                 600                 605


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
    610                 615                 620


Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
625                 630                 635                 640


Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
                645                 650                 655


Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
            660                 665                 670


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
        675                 680                 685


Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695                 700


<210> 937
<211> 732
<212> PRT
<213> Artificial Sequence

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

<400> 937
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15
```

```
Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205
```

```
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
            260                 265                 270

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415
```

```
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Asp
545                 550                 555                 560

Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly His
        595                 600                 605
```

```
Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    610                 615                 620


Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
625                 630                 635                 640


Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
                645                 650                 655


Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
            660                 665                 670


Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
        675                 680                 685


Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
    690                 695                 700


Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
705                 710                 715                 720


Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730


<210> 938
<211> 732
<212> PRT
<213> Artificial Sequence

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

<400> 938
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30
```

```
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240
```

```
Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
            260                 265                 270

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430
```

```
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Asp
545                 550                 555                 560

Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly His
        595                 600                 605

Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    610                 615                 620

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
625                 630                 635                 640
```

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
645 650 655

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
660 665 670

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
675 680 685

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
690 695 700

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
705 710 715 720

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730

<210> 939
<211> 732
<212> PRT
<213> Artificial Sequence

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

<400> 939
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

```
Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255
```

```
Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
            260                 265                 270

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460
```

```
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Asp
545                 550                 555                 560

Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly His
        595                 600                 605

Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    610                 615                 620

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
625                 630                 635                 640

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
                645                 650                 655
```

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
            660   665   670

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
        675   680   685

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
    690   695   700

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
705   710   715   720

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725   730

<210> 940
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 940
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 Asp Phe Ser Ser Ser
            20   25   30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
        115                 120                 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
        275                 280                 285
```

```
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480
```

```
Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr
    530                 535                 540

Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly
            580                 585                 590

His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        595                 600                 605

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    610                 615                 620

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
625                 630                 635                 640

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
                645                 650                 655

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            660                 665                 670

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        675                 680                 685
```

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
690 695 700

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705 710 715

<210> 941
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 941
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 Asp Phe Ser Ser Ser
20 25 30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
115 120 125

```
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320
```

```
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg
        515                 520                 525
```

```
Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr
    530                 535                 540

Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly
            580                 585                 590

His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        595                 600                 605

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    610                 615                 620

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
625                 630                 635                 640

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
                645                 650                 655

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            660                 665                 670

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        675                 680                 685

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    690                 695                 700

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715
```

<210> 942
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 942
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 Asp Phe Ser Ser Ser
20 25 30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
115 120 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
130 135 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145 150 155 160

```
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365
```

```
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr
    530                 535                 540

Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560
```

```
Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575


Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly
            580                 585                 590


His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        595                 600                 605


Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    610                 615                 620


Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
625                 630                 635                 640


Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
                645                 650                 655


Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            660                 665                 670


Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        675                 680                 685


Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    690                 695                 700


Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715
```

<210> 943
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 943

```
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 Asp Phe Ser Ser Ser
            20                  25                  30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
        115                 120                 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205
```

```
Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400
```

```
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr
    530                 535                 540

Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro Ala Val Gly
            580                 585                 590

His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        595                 600                 605
```

```
Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    610                 615                 620

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
625                 630                 635                 640

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
                645                 650                 655

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            660                 665                 670

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        675                 680                 685

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    690                 695                 700

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715
```

<210> 944
<211> 736
<212> PRT
<213> Artificial Sequence

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

<400> 944

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
        35                  40                  45
```

```
Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240
```

```
Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445
```

```
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile
545                 550                 555                 560

Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro
        595                 600                 605

Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
625                 630                 635                 640
```

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
645 650 655

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
660 665 670

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
675 680 685

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
690 695 700

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
705 710 715 720

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730 735

<210> 945
<211> 736
<212> PRT
<213> Artificial Sequence

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

<400> 945
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

```
Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110


Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125


Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190


Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220


Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240


Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255


Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
            260                 265                 270
```

```
Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460
```

```
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile
545                 550                 555                 560

Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro
        595                 600                 605

Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
625                 630                 635                 640

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                645                 650                 655

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            660                 665                 670
```

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
675 680 685

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
690 695 700

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
705 710 715 720

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730 735

<210> 946
<211> 736
<212> PRT
<213> Artificial Sequence

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

<400> 946
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285
```

```
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495
```

```
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile
545                 550                 555                 560

Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro
        595                 600                 605

Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
625                 630                 635                 640

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                645                 650                 655

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            660                 665                 670

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        675                 680                 685
```

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
690 695 700

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
705 710 715 720

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730 735

<210> 947
<211> 736
<212> PRT
<213> Artificial Sequence

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

<400> 947
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

```
Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320
```

```
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510
```

```
Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile
545                 550                 555                 560

Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Pro
        595                 600                 605

Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
625                 630                 635                 640

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                645                 650                 655

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            660                 665                 670

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        675                 680                 685

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
    690                 695                 700

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
705                 710                 715                 720
```

```
Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730                 735


<210> 948
<211> 721
<212> PRT
<213> Artificial Sequence

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

<400> 948
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 Asp Phe Thr Ala Tyr
            20                  25                  30


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


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


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


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


Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125


Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140
```

```
Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335
```

```
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr
    530                 535                 540
```

```
Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu
        595                 600                 605

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    610                 615                 620

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
625                 630                 635                 640

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                645                 650                 655

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            660                 665                 670

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        675                 680                 685

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    690                 695                 700

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
705                 710                 715                 720

Thr
```

<210> 949
<211> 721
<212> PRT
<213> Artificial Sequence

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

<400> 949
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 Asp Phe Thr Ala Tyr
20 25 30

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

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

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

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

Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
115 120 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
130 135 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145 150 155 160

```
Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365
```

```
Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr
    530                 535                 540

Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560
```

```
Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu
        595                 600                 605

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    610                 615                 620

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
625                 630                 635                 640

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                645                 650                 655

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            660                 665                 670

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        675                 680                 685

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    690                 695                 700

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
705                 710                 715                 720

Thr
```

<210> 950
<211> 721
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 950

```
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 Asp Phe Thr Ala Tyr
            20                  25                  30


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


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


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


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


Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125


Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140


Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160


Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175


Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr
            180                 185                 190
```

```
Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380
```

```
Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400


Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415


Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430


Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445


Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460


Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480


Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495


Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510


Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met
        515                 520                 525


His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr
    530                 535                 540


Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560


Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575


Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590
```

```
Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu
        595                 600                 605


Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    610                 615                 620


Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
625                 630                 635                 640


Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                645                 650                 655


Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            660                 665                 670


Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        675                 680                 685


Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    690                 695                 700


Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
705                 710                 715                 720


Thr
```

<210> 951
<211> 721
<212> PRT
<213> Artificial Sequence

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

<400> 951

```
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 Asp Phe Thr Ala Tyr
            20                  25                  30

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

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

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

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

Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205
```

```
Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415
```

```
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr Ser Met
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr
    530                 535                 540

Ile Ser Ser Tyr Asp Ser Ile Thr Asp Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Pro Ala Val Gly His Met Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu
        595                 600                 605
```

```
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    610                 615                 620

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
625                 630                 635                 640

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                645                 650                 655

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            660                 665                 670

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        675                 680                 685

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    690                 695                 700

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
705                 710                 715                 720

Thr
```

<210> 952
<211> 214
<212> PRT
<213> Artificial Sequence

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

<400> 952

```
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 Val Ser Ser Ala
            20                  25                  30
```

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

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Arg 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 Trp Tyr Asn Ala Pro Ile
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

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

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

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

Phe Asn Arg Gly Glu Cys
    210
```

<210> 953
<211> 713

<212> PRT
<213> Artificial Sequence

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

<400> 953
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
115 120 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145 150 155 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
165 170 175

```
Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365
```

```
Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser
    370                 375                 380

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575
```

```
Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
            580                 585                 590


Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
        595                 600                 605


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    610                 615                 620


Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
625                 630                 635                 640


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
                645                 650                 655


Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
            660                 665                 670


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
        675                 680                 685


Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
    690                 695                 700


Gly Gln Gly Thr Lys Val Glu Ile Lys
705                 710
```

<210> 954
<211> 713
<212> PRT
<213> Artificial Sequence

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

<400> 954

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15
```

```
Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205
```

```
Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser
    370                 375                 380

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415
```

```
Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
            580                 585                 590

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
        595                 600                 605
```

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
610 615 620

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
625 630 635 640

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
645 650 655

Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
660 665 670

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
675 680 685

Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
690 695 700

Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710

<210> 955
<211> 713
<212> PRT
<213> Artificial Sequence

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

<400> 955
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
35 40 45

```
Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
                245                 250                 255
```

```
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser
    370                 375                 380

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445
```

```
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
            580                 585                 590

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
        595                 600                 605

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    610                 615                 620

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
625                 630                 635                 640

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
                645                 650                 655
```

```
Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
            660                 665                 670


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
        675                 680                 685


Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
    690                 695                 700


Gly Gln Gly Thr Lys Val Glu Ile Lys
705                 710


<210> 956
<211> 713
<212> PRT
<213> Artificial Sequence

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

<400> 956
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
        35                  40                  45


Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60


Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95
```

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285
```

```
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser
    370                 375                 380

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495
```

```
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575

Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln
            580                 585                 590

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
        595                 600                 605

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    610                 615                 620

Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp
625                 630                 635                 640

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
                645                 650                 655

Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
            660                 665                 670

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
        675                 680                 685
```

Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe
690 695 700

Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710

<210> 957
<211> 698
<212> PRT
<213> Artificial Sequence

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

<400> 957
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
20 25 30

Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
100 105 110

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

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

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

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

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

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

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

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

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

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
            260                 265                 270

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

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

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

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

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

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

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

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

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

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

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

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr
        515                 520                 525
```

```
Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
            580                 585                 590

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
        595                 600                 605

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
    610                 615                 620

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
625                 630                 635                 640

Ala Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
                645                 650                 655

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
            660                 665                 670

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr
        675                 680                 685

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695
```

<210> 958
<211> 698
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 958

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


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
            20                  25                  30


Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


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


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


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


Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
            100                 105                 110


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


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


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


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


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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

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

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

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

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

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

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

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

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

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

```
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

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

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

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

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr
        515                 520                 525

Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
            580                 585                 590
```

```
Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
        595                 600                 605


Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
    610                 615                 620


Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
625                 630                 635                 640


Ala Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
                645                 650                 655


Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
            660                 665                 670


Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr
        675                 680                 685


Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695


<210> 959
<211> 698
<212> PRT
<213> Artificial Sequence

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

<400> 959
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
            20                  25                  30


Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

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

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

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

Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
            100                 105                 110

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

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

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

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240
```

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

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

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

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

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

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

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

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

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

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

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

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

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445
```

```
Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr
        515                 520                 525

Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
            580                 585                 590

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
        595                 600                 605

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
    610                 615                 620

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
625                 630                 635                 640
```

Ala Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
645 650 655

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
660 665 670

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr
675 680 685

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
690 695

<210> 960
<211> 698
<212> PRT
<213> Artificial Sequence

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

<400> 960
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
20 25 30

Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

```
Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
            100                 105                 110

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

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

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

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

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

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

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

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

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

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

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

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

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

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

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

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

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

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495
```

```
Phe Asp Phe Ser Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr
        515                 520                 525

Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
            580                 585                 590

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
        595                 600                 605

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
    610                 615                 620

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
625                 630                 635                 640

Ala Ser Asp Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
                645                 650                 655

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
            660                 665                 670

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr
        675                 680                 685

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695
```

<210> 961
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 961
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
115 120 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145 150 155 160

```
Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350
```

```
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
    370                 375                 380

Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560
```

```
Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575


Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
            580                 585                 590


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        595                 600                 605


Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
    610                 615                 620


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
625                 630                 635                 640


Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                645                 650                 655


Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
            660                 665                 670


Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
        675                 680                 685


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
    690                 695                 700


Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705                 710                 715


<210> 962
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 962
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1   5   10   15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20   25   30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
        35   40   45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50   55   60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65   70   75   80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85   90   95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100   105   110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
        115   120   125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145   150   155   160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165   170   175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180   185   190

```
Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
    370                 375                 380

Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400
```

```
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575

Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
            580                 585                 590
```

```
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        595                 600                 605

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
    610                 615                 620

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
625                 630                 635                 640

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                645                 650                 655

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
            660                 665                 670

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
        675                 680                 685

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
    690                 695                 700

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705                 710                 715
```

<210> 963
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 963

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30
```

```
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240
```

```
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
               245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
               325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
    370                 375                 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
               405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430
```

```
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480

Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575

Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
            580                 585                 590

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        595                 600                 605

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
    610                 615                 620

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
625                 630                 635                 640
```

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
645 650 655

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
660 665 670

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
675 680 685

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
690 695 700

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710 715

<210> 964
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 964
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Thr Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

```
Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270
```

```
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
    370                 375                 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
465                 470                 475                 480
```

```
Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
                485                 490                 495

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
            500                 505                 510

Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
        515                 520                 525

Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala
    530                 535                 540

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser
545                 550                 555                 560

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                565                 570                 575

Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr
            580                 585                 590

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        595                 600                 605

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
    610                 615                 620

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
625                 630                 635                 640

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                645                 650                 655

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
            660                 665                 670
```

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
675 680 685

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser
690 695 700

Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710 715

<210> 965
<211> 702
<212> PRT
<213> Artificial Sequence

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

<400> 965
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
20 25 30

Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
100 105 110

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

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

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

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

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

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

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

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

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

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
            260                 265                 270

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

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

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

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

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe
            340                 345                 350

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

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

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

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

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

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

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510
```

```
Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr
        515                 520                 525

Ala Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp
                565                 570                 575

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
            580                 585                 590

Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
        595                 600                 605

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
    610                 615                 620

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
625                 630                 635                 640

Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
                645                 650                 655

Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
            660                 665                 670

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr
        675                 680                 685

Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695                 700
```

<210> 966
<211> 702

<212> PRT
<213> Artificial Sequence

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

<400> 966
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
20 25 30

Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
100 105 110

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

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

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

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

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

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

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

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

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

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

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe
            340                 345                 350

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

```
Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

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

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

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

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

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr
        515                 520                 525

Ala Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp
                565                 570                 575
```

```
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
            580                 585                 590


Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
        595                 600                 605


Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
    610                 615                 620


Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
625                 630                 635                 640


Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
                645                 650                 655


Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
            660                 665                 670


Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr
        675                 680                 685


Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695                 700


<210> 967
<211> 702
<212> PRT
<213> Artificial Sequence

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

<400> 967
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
            20                  25                  30
```

```
Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

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

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

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

Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
            100                 105                 110

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

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

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

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

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

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

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

```
Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

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

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

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

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

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

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

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

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

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

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

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

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430
```

```
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr
        515                 520                 525

Ala Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp
                565                 570                 575

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
            580                 585                 590

Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
        595                 600                 605

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
    610                 615                 620
```

```
Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
625                 630                 635                 640


Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
                645                 650                 655


Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
            660                 665                 670


Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr
        675                 680                 685


Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    690                 695                 700


<210> 968
<211> 702
<212> PRT
<213> Artificial Sequence

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

<400> 968
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr
            20                  25                  30


Phe Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


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


Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65                  70                  75                  80
```

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

Ala Arg Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln
            100                 105                 110

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

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

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

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

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

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

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

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

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

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

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

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

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

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

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

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

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

Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
    450                 455                 460

Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
465                 470                 475                 480
```

```
Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                485                 490                 495

Phe Asp Phe Thr Ala Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly
            500                 505                 510

Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr
        515                 520                 525

Ala Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp
                565                 570                 575

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
            580                 585                 590

Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
        595                 600                 605

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
    610                 615                 620

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
625                 630                 635                 640

Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
                645                 650                 655

Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
            660                 665                 670

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr
        675                 680                 685
```

Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
690 695 700

<210> 969
<211> 733
<212> PRT
<213> Artificial Sequence

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

<400> 969
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
115 120 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
130 135 140

```
Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
            260                 265                 270

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335
```

```
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg Gln
    530                 535                 540
```

```
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe Ile
545                 550                 555                 560

Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly Ser
        595                 600                 605

Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            660                 665                 670

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        675                 680                 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
    690                 695                 700

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705                 710                 715                 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730
```

<210> 970
<211> 733
<212> PRT
<213> Artificial Sequence

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

<400> 970
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
115 120 125

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
130 135 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145 150 155 160

```
Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
            260                 265                 270

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365
```

```
Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe Ile
545                 550                 555                 560
```

```
Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly Ser
        595                 600                 605

Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            660                 665                 670

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        675                 680                 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
    690                 695                 700

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705                 710                 715                 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730
```

<210> 971
<211> 733
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 971

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                  10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Ser Ser Ser
        35                  40                  45


Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60


Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110


Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        115                 120                 125


Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    130                 135                 140


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160


Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175


Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser Gly
            180                 185                 190
```

```
Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys Val
225                 230                 235                 240

Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
            260                 265                 270

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380
```

```
Gln Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu Ser
            500                 505                 510

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
        515                 520                 525

Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg Gln
    530                 535                 540

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe Ile
545                 550                 555                 560

Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                565                 570                 575

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
            580                 585                 590
```

```
Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly Ser
        595                 600                 605

Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            660                 665                 670

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        675                 680                 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
    690                 695                 700

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705                 710                 715                 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730
```

<210> 972
<211> 718
<212> PRT
<213> Artificial Sequence

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

<400> 972

```
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 Asp Phe Ser Ser Ser
            20                  25                  30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
        115                 120                 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205
```

```
Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415
```

```
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe
    530                 535                 540

Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly
            580                 585                 590

Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        595                 600                 605
```

```
Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
    610                 615                 620

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
625                 630                 635                 640

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
                645                 650                 655

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
            660                 665                 670

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
        675                 680                 685

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
    690                 695                 700

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715
```

<210> 973
<211> 718
<212> PRT
<213> Artificial Sequence

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

<400> 973

```
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 Asp Phe Ser Ser Ser
            20                  25                  30

Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
        115                 120                 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255
```

```
Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445
```

```
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe
    530                 535                 540

Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly
            580                 585                 590

Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        595                 600                 605

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
    610                 615                 620

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
625                 630                 635                 640

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
                645                 650                 655
```

```
Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
            660                 665                 670


Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
        675                 680                 685


Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
    690                 695                 700


Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715


<210> 974
<211> 718
<212> PRT
<213> Artificial Sequence

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

<400> 974
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 Asp Phe Ser Ser Ser
            20                  25                  30


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


Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


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


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

```
Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
        115                 120                 125

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285
```

```
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495
```

```
Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg
        515                 520                 525

Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe
    530                 535                 540

Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly
            580                 585                 590

Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        595                 600                 605

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
    610                 615                 620

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
625                 630                 635                 640

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
                645                 650                 655

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
            660                 665                 670

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
        675                 680                 685
```

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
690 695 700

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705 710 715

<210> 975
<211> 718
<212> PRT
<213> Artificial Sequence

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

<400> 975
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 Asp Phe Ser Ser Ser
20 25 30

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

Ala Ser Ile Ser Ser Ser Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Arg Ser Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
115 120 125

```
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
    130                 135                 140

Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro
145                 150                 155                 160

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asp Leu Tyr Ser
                165                 170                 175

Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
            180                 185                 190

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
        195                 200                 205

Gln Gln Tyr Ala Gly Ala Gly Leu Ile Thr Phe Gly Gln Gly Thr Lys
    210                 215                 220

Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Pro
225                 230                 235                 240

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335
```

```
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
    370                 375                 380

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
            420                 425                 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        435                 440                 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    450                 455                 460

Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln Leu Val Glu
                485                 490                 495

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
            500                 505                 510

Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His Trp Val Arg
        515                 520                 525
```

```
Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile Tyr Pro Phe
    530                 535                 540

Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
545                 550                 555                 560

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
                565                 570                 575

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Phe Pro Gly
            580                 585                 590

Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        595                 600                 605

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
    610                 615                 620

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
625                 630                 635                 640

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
                645                 650                 655

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
            660                 665                 670

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
        675                 680                 685

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
    690                 695                 700

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
705                 710                 715
```

<210> 976
<211> 737

<212> PRT
<213> Artificial Sequence

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

<400> 976
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
115 120 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
165 170 175

```
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365
```

```
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile
545                 550                 555                 560

Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575
```

```
Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala
        595                 600                 605

Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
625                 630                 635                 640

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
                645                 650                 655

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
            660                 665                 670

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
        675                 680                 685

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
    690                 695                 700

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
705                 710                 715                 720

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
                725                 730                 735

Thr
```

<210> 977
<211> 737
<212> PRT
<213> Artificial Sequence

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

<400> 977
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
35 40 45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
115 120 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
165 170 175

```
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380
```

```
Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile
545                 550                 555                 560

Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575
```

```
Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala
        595                 600                 605

Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
625                 630                 635                 640

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
                645                 650                 655

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
            660                 665                 670

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
        675                 680                 685

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
    690                 695                 700

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
705                 710                 715                 720

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
                725                 730                 735

Thr
```

<210> 978
<211> 737
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 978

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                  10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
        35                  40                  45


Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60


Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110


Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125


Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160


Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190
```

```
Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380
```

```
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile
545                 550                 555                 560

Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590
```

```
Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala
        595                 600                 605

Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
625                 630                 635                 640

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
                645                 650                 655

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
            660                 665                 670

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
        675                 680                 685

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
    690                 695                 700

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
705                 710                 715                 720

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
                725                 730                 735

Thr
```

<210> 979
<211> 737
<212> PRT
<213> Artificial Sequence

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

<400> 979

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                  10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Thr Ala Tyr Ala
        35                  40                  45

Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
            180                 185                 190
```

```
Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
                245                 250                 255

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

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met
385                 390                 395                 400
```

```
Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile His
    530                 535                 540

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr Ile
545                 550                 555                 560

Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590
```

```
Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala
        595                 600                 605

Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
625                 630                 635                 640

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
                645                 650                 655

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
            660                 665                 670

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
        675                 680                 685

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
    690                 695                 700

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
705                 710                 715                 720

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
                725                 730                 735

Thr
```

<210> 980
<211> 722
<212> PRT
<213> Artificial Sequence

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

<400> 980

```
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 Asp Phe Thr Ala Tyr
            20                  25                  30

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

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

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

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

Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205
```

```
Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400
```

```
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
    530                 535                 540

Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr
        595                 600                 605
```

```
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    610                 615                 620


Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
625                 630                 635                 640


Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                645                 650                 655


Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            660                 665                 670


Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        675                 680                 685


Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    690                 695                 700


Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
705                 710                 715                 720


His Thr



<210> 981
<211> 722
<212> PRT
<213> Artificial Sequence

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

<400> 981
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 Asp Phe Thr Ala Tyr
            20                  25                  30
```

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

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

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

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

Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220
```

```
Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240


Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255


Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270


Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285


Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300


Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320


Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335


His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350


Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365


Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380


Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
385                 390                 395                 400


Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415


Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430
```

```
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
    530                 535                 540

Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr
        595                 600                 605

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    610                 615                 620
```

```
Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
625                 630                 635                 640


Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                645                 650                 655


Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            660                 665                 670


Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        675                 680                 685


Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    690                 695                 700


Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
705                 710                 715                 720


His Thr
```

<210> 982
<211> 722
<212> PRT
<213> Artificial Sequence

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

<400> 982

```
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 Asp Phe Thr Ala Tyr
            20                  25                  30


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

```
Ala Ser Ile Tyr Pro Ser Gly Gly Tyr Thr Ala Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255
```

```
Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445
```

```
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
                485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
    530                 535                 540

Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
                565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr
        595                 600                 605

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    610                 615                 620

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
625                 630                 635                 640

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                645                 650                 655
```

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
660 665 670

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
675 680 685

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
690 695 700

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
705 710 715 720

His Thr

<210> 983
<211> 722
<212> PRT
<213> Artificial Sequence

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

<400> 983
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 Asp Phe Thr Ala Tyr
20 25 30

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

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

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

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

Ala Arg Arg Ser Tyr Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
        115                 120                 125

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
    130                 135                 140

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
145                 150                 155                 160

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
                165                 170                 175

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

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
        195                 200                 205

Tyr Tyr Cys Gln Gln Tyr Trp Ala Tyr Tyr Ser Pro Ile Thr Phe Gly
    210                 215                 220

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
225                 230                 235                 240

Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270
```

```
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu
    370                 375                 380

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
465                 470                 475                 480
```

```
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
               485                 490                 495

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
            500                 505                 510

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asp Phe Tyr Phe Ile
        515                 520                 525

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
    530                 535                 540

Ile Tyr Pro Phe Ile Gly Asn Thr Tyr Tyr Ala Asp Ser Val Lys Gly
545                 550                 555                 560

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
               565                 570                 575

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            580                 585                 590

Ala Phe Pro Gly Ser Tyr His Pro Phe Asp Tyr Trp Gly Gln Gly Thr
        595                 600                 605

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    610                 615                 620

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
625                 630                 635                 640

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
               645                 650                 655

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            660                 665                 670
```

```
Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        675                 680                 685


Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    690                 695                 700


Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
705                 710                 715                 720


His Thr
```

<210> 984
<211> 214
<212> PRT
<213> Artificial Sequence

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

<400> 984

```
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 Val Ser Ser Ala
            20                  25                  30


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


Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Arg 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 Thr Gly Ser Leu Ile
                85                  90                  95
```

```
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160


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


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


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


Phe Asn Arg Gly Glu Cys
    210


<210> 985
<211> 10
<212> PRT
<213> Artificial Sequence

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

<400> 985
Thr Val Tyr Pro Tyr Leu Asp Tyr Thr Tyr
1               5                   10


<210> 986
<211> 735
<212> PRT
<213> Artificial Sequence
```

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

<400> 986
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Tyr Ser Tyr
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Ser Tyr Thr Gly Ala Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Tyr Trp Ser Thr Asn Arg Ile Leu Ser Tyr Gly Gly Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
145 150 155 160

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
165 170 175

```
Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
            180                 185                 190

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
        195                 200                 205

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
    210                 215                 220

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Phe Asp Pro Ile Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
                245                 250                 255

Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
        275                 280                 285

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    290                 295                 300

Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe
305                 310                 315                 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                325                 330                 335

Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr
            340                 345                 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
        355                 360                 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
    370                 375                 380
```

```
Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg
385                 390                 395                 400

Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly
                405                 410                 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
            420                 425                 430

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
        435                 440                 445

Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    450                 455                 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465                 470                 475                 480

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser
                485                 490                 495

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly
            500                 505                 510

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
        515                 520                 525

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser
    530                 535                 540

Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
545                 550                 555                 560

Ala Thr Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val
                565                 570                 575
```

```
Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
            580                 585                 590

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
        595                 600                 605

Ala Arg Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
    610                 615                 620

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
625                 630                 635                 640

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                645                 650                 655

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            660                 665                 670

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        675                 680                 685

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    690                 695                 700

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
705                 710                 715                 720

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730                 735
```

<210> 987
<211> 733
<212> PRT
<213> Artificial Sequence

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

<400> 987

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                  10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Leu Ser His Ser Ser
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Ser Ser His Tyr Gly Tyr Thr His Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Ser Tyr Phe Pro Trp Phe Phe Ala Leu Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala Val Ala Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
            180                 185                 190

Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
        195                 200                 205
```

```
Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
                245                 250                 255

Gly Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys
            260                 265                 270

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        275                 280                 285

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    290                 295                 300

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
305                 310                 315                 320

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                325                 330                 335

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            340                 345                 350

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        355                 360                 365

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    370                 375                 380

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
385                 390                 395                 400
```

```
Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
                405                 410                 415

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            420                 425                 430

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        435                 440                 445

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    450                 455                 460

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
465                 470                 475                 480

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
                485                 490                 495

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
            500                 505                 510

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
        515                 520                 525

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser Ser Met
    530                 535                 540

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
545                 550                 555                 560

Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
                565                 570                 575

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
            580                 585                 590

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
        595                 600                 605
```

```
Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            660                 665                 670

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        675                 680                 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
    690                 695                 700

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705                 710                 715                 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730
```

<210> 988
<211> 735
<212> PRT
<213> Artificial Sequence

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

<400> 988

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30
```

```
Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Tyr Ser Tyr
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Tyr Ser Tyr Thr Gly Ala Thr Asp Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Tyr Trp Ser Thr Asn Arg Ile Leu Ser Tyr Gly Gly Met Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
145                 150                 155                 160

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
                165                 170                 175

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
            180                 185                 190

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
        195                 200                 205

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
    210                 215                 220
```

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Phe Asp Pro Ile Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
                245                 250                 255

Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
        275                 280                 285

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    290                 295                 300

Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe
305                 310                 315                 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                325                 330                 335

Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr
            340                 345                 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
        355                 360                 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
    370                 375                 380

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg
385                 390                 395                 400

Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly
                405                 410                 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
            420                 425                 430
```

```
Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
        435                 440                 445

Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    450                 455                 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465                 470                 475                 480

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser
                485                 490                 495

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly
            500                 505                 510

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
        515                 520                 525

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser
    530                 535                 540

Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
545                 550                 555                 560

Ala Thr Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val
                565                 570                 575

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
            580                 585                 590

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
        595                 600                 605

Ala Arg Asp Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
    610                 615                 620
```

```
Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
625                 630                 635                 640


Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                645                 650                 655


Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            660                 665                 670


Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        675                 680                 685


Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    690                 695                 700


Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
705                 710                 715                 720


Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730                 735


<210> 989
<211> 733
<212> PRT
<213> Artificial Sequence

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

<400> 989
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Leu Ser His Ser Ser
        35                  40                  45
```

```
Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ser Ile Ser Ser His Tyr Gly Tyr Thr His Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Ser Tyr Phe Pro Trp Phe Phe Ala Leu Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala Val Ala Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
            180                 185                 190

Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
                245                 250                 255
```

```
Gly Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys
            260                 265                 270

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        275                 280                 285

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    290                 295                 300

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
305                 310                 315                 320

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                325                 330                 335

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            340                 345                 350

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        355                 360                 365

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    370                 375                 380

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
385                 390                 395                 400

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
                405                 410                 415

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            420                 425                 430

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        435                 440                 445
```

```
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    450                 455                 460

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
465                 470                 475                 480

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
                485                 490                 495

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
            500                 505                 510

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
        515                 520                 525

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser Ser Met
    530                 535                 540

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
545                 550                 555                 560

Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
                565                 570                 575

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
            580                 585                 590

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
        595                 600                 605

Asp Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655
```

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
660 665 670

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
675 680 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
690 695 700

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705 710 715 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730

<210> 990
<211> 735
<212> PRT
<213> Artificial Sequence

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

<400> 990
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Tyr Ser Tyr
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ser Ile Tyr Ser Tyr Thr Gly Ala Thr Asp Tyr Ala Asp Ser Val Lys
65 70 75 80

```
Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Tyr Trp Ser Thr Asn Arg Ile Leu Ser Tyr Gly Gly Met Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
145                 150                 155                 160

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala
                165                 170                 175

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
            180                 185                 190

Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
        195                 200                 205

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
    210                 215                 220

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Phe Asp Pro Ile Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly
                245                 250                 255

Gly Gly Gly Ser Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270
```

```
Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
        275                 280                 285

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    290                 295                 300

Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe
305                 310                 315                 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                325                 330                 335

Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr
            340                 345                 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
        355                 360                 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
    370                 375                 380

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg
385                 390                 395                 400

Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly
                405                 410                 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
            420                 425                 430

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
        435                 440                 445

Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    450                 455                 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465                 470                 475                 480
```

```
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser
                485                 490                 495

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly
            500                 505                 510

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
        515                 520                 525

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser
    530                 535                 540

Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
545                 550                 555                 560

Ala Thr Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val
                565                 570                 575

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
            580                 585                 590

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
        595                 600                 605

Ala Arg Tyr Tyr Asp Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
    610                 615                 620

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
625                 630                 635                 640

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                645                 650                 655

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            660                 665                 670
```

```
Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        675                 680                 685


Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    690                 695                 700


Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
705                 710                 715                 720


Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                725                 730                 735


<210> 991
<211> 733
<212> PRT
<213> Artificial Sequence

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

<400> 991
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Leu Ser His Ser Ser
        35                  40                  45


Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60


Ser Ile Ser Ser His Tyr Gly Tyr Thr His Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95
```

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Ser Ser Tyr Phe Pro Trp Phe Phe Ala Leu Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala Val Ala Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala
            180                 185                 190

Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
                245                 250                 255

Gly Ser Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys
            260                 265                 270

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        275                 280                 285

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    290                 295                 300
```

```
Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
305                 310                 315                 320

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                325                 330                 335

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            340                 345                 350

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        355                 360                 365

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    370                 375                 380

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
385                 390                 395                 400

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
                405                 410                 415

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            420                 425                 430

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        435                 440                 445

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    450                 455                 460

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
465                 470                 475                 480

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly
                485                 490                 495
```

```
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Thr Gly Glu Val
            500                 505                 510

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
        515                 520                 525

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ala Tyr Ser Ser Met
    530                 535                 540

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Thr
545                 550                 555                 560

Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly
                565                 570                 575

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
            580                 585                 590

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
        595                 600                 605

Tyr Tyr Asp Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
625                 630                 635                 640

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                645                 650                 655

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            660                 665                 670

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        675                 680                 685

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
    690                 695                 700
```

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
705 710 715 720

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
725 730

<210> 992
<211> 229
<212> PRT
<213> Artificial Sequence

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

<400> 992
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Asp
1 5 10 15

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
20 25 30

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
35 40 45

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
50 55 60

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
65 70 75 80

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
85 90 95

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala His Tyr Phe Pro Ile Thr
100 105 110

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
115 120 125

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
130 135 140

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
145 150 155 160

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
165 170 175

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
180 185 190

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
195 200 205

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
210 215 220

Asn Arg Gly Glu Cys
225

<210> 993
<211> 741
<212> PRT
<213> Artificial Sequence

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

<400> 993
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

```
Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240
```

```
Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445
```

```
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
545                 550                 555                 560

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
        595                 600                 605

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
625                 630                 635                 640
```

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
645 650 655

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
660 665 670

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
675 680 685

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
690 695 700

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
705 710 715 720

Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr
725 730 735

Lys Val Glu Ile Lys
740

<210> 994
<211> 746
<212> PRT
<213> Artificial Sequence

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

<400> 994
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

```
Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255
```

```
Val Glu Pro Lys Ser Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro
            260                 265                 270

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445
```

```
Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr
545                 550                 555                 560

Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val
        595                 600                 605

Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp
    610                 615                 620

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
625                 630                 635                 640

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                645                 650                 655
```

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
660 665 670

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
675 680 685

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
690 695 700

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
705 710 715 720

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr
725 730 735

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
740 745

<210> 995
<211> 740
<212> PRT
<213> Artificial Sequence

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

<400> 995
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

```
Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255
```

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460
```

```
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
545                 550                 555                 560

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
        595                 600                 605

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
625                 630                 635                 640

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
                645                 650                 655
```

```
Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
            660                 665                 670

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
        675                 680                 685

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
    690                 695                 700

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
705                 710                 715                 720

Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys
                725                 730                 735

Val Glu Ile Lys
            740
```

<210> 996
<211> 746
<212> PRT
<213> Artificial Sequence

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

<400> 996

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser
        35                  40                  45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60
```

```
Val Ala Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

Val Glu Pro Lys Ser Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro
            260                 265                 270
```

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460
```

```
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr
545                 550                 555                 560

Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val
        595                 600                 605

Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp
    610                 615                 620

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
625                 630                 635                 640

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                645                 650                 655

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
            660                 665                 670
```

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        675   680   685

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    690   695   700

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
705   710   715   720

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr
                725   730   735

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            740   745

<210> 997
<211> 740
<212> PRT
<213> Artificial Sequence

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

<400> 997
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1   5   10   15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20   25   30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser
        35   40   45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50   55   60

Val Ala Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser
65   70   75   80

```
Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480
```

```
Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
545                 550                 555                 560

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
        595                 600                 605

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
625                 630                 635                 640

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
                645                 650                 655

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
            660                 665                 670
```

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
675 680 685

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
690 695 700

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
705 710 715 720

Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys
725 730 735

Val Glu Ile Lys
740

<210> 998
<211> 752
<212> PRT
<213> Artificial Sequence

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

<400> 998
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65 70 75 80

```
Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285
```

```
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480
```

```
Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Asp Ile Gln Met
            500                 505                 510

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
        515                 520                 525

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
    530                 535                 540

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
545                 550                 555                 560

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
                565                 570                 575

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
            580                 585                 590

Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln
        595                 600                 605

Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser
    610                 615                 620

Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly
625                 630                 635                 640

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
                645                 650                 655

Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala Pro
            660                 665                 670

Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr
        675                 680                 685
```

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp
690 695 700

Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
705 710 715 720

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp Ala
725 730 735

Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
740 745 750

<210> 999
<211> 752
<212> PRT
<213> Artificial Sequence

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

<400> 999
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65 70 75 80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

```
Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285
```

```
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495
```

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Asp Ile Gln Met
            500                 505                 510

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
        515                 520                 525

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
    530                 535                 540

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
545                 550                 555                 560

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
                565                 570                 575

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
            580                 585                 590

Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln
        595                 600                 605

Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser
    610                 615                 620

Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly
625                 630                 635                 640

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
                645                 650                 655

Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala Pro
            660                 665                 670

Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr
        675                 680                 685
```

```
Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp
    690                 695                 700

Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
705                 710                 715                 720

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp Ala
                725                 730                 735

Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
            740                 745                 750
```

<210> 1000
<211> 756
<212> PRT
<213> Artificial Sequence

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

<400> 1000

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
        35                  40                  45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95
```

```
Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300
```

```
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495
```

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Asp Ile Gln Met
            500                 505                 510

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
        515                 520                 525

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
    530                 535                 540

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
545                 550                 555                 560

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
                565                 570                 575

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
            580                 585                 590

Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly
        595                 600                 605

Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly
    610                 615                 620

Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly
625                 630                 635                 640

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                645                 650                 655

Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly
            660                 665                 670

Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr
        675                 680                 685

Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    690                 695                 700
```

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
705 710 715 720

Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val Arg Gly Ser Lys Lys Pro
725 730 735

Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
740 745 750

Thr Val Ser Ser
755

<210> 1001
<211> 756
<212> PRT
<213> Artificial Sequence

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

<400> 1001
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65 70 75 80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

```
Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285
```

```
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495
```

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Asp Ile Gln Met
            500                 505                 510

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
        515                 520                 525

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
    530                 535                 540

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
545                 550                 555                 560

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
                565                 570                 575

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
            580                 585                 590

Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly
        595                 600                 605

Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly
    610                 615                 620

Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly
625                 630                 635                 640

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                645                 650                 655

Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly
            660                 665                 670

Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr
        675                 680                 685
```

```
Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
    690                 695                 700

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
705                 710                 715                 720

Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val Arg Gly Ser Lys Lys Pro
                725                 730                 735

Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
            740                 745                 750

Thr Val Ser Ser
        755
```

<210> 1002
<211> 757
<212> PRT
<213> Artificial Sequence

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

<400> 1002

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser
        35                  40                  45

Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser
65                  70                  75                  80
```

```
Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Thr Val Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp
        115                 120                 125

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
145                 150                 155                 160

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
                165                 170                 175

Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            180                 185                 190

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
        195                 200                 205

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
    210                 215                 220

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser
225                 230                 235                 240

Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Leu
                245                 250                 255

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

His Asn Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
        275                 280                 285
```

```
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
    290                 295                 300

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
305                 310                 315                 320

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
                325                 330                 335

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
            340                 345                 350

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
        355                 360                 365

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
    370                 375                 380

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
385                 390                 395                 400

Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys
                405                 410                 415

Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
            420                 425                 430

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
        435                 440                 445

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
    450                 455                 460

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
465                 470                 475                 480
```

```
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                485                 490                 495

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
            500                 505                 510

Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
        515                 520                 525

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile
    530                 535                 540

His Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
545                 550                 555                 560

Glu Trp Val Ala Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala
                565                 570                 575

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
            580                 585                 590

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
        595                 600                 605

Tyr Tyr Cys Ala Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr
    610                 615                 620

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr Thr Ala Ala
625                 630                 635                 640

Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Asp Ile Gln Met Thr
                645                 650                 655

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
            660                 665                 670

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
        675                 680                 685
```

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
690 695 700

Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr
705 710 715 720

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
725 730 735

Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly Gln Gly Thr
740 745 750

Lys Val Glu Ile Lys
755

<210> 1003
<211> 750
<212> PRT
<213> Artificial Sequence

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

<400> 1003
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

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

```
Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
               85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Ala His Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp
        115                 120                 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480
```

```
Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Thr Tyr
545                 550                 555                 560

Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr His
        595                 600                 605

His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser
625                 630                 635                 640

Ser Ser Gly Ala Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
                645                 650                 655

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
            660                 665                 670
```

```
Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
        675                 680                 685

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
    690                 695                 700

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
705                 710                 715                 720

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val
                725                 730                 735

Tyr Leu Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            740                 745                 750
```

<210> 1004
<211> 757
<212> PRT
<213> Artificial Sequence

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

<400> 1004

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
            20                  25                  30

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
        35                  40                  45

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
    50                  55                  60

Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
65                  70                  75                  80
```

```
Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
                85                  90                  95

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe
            100                 105                 110

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala
        115                 120                 125

Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val
    130                 135                 140

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
145                 150                 155                 160

Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser Ser Ser Ile His Trp Val
                165                 170                 175

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser
            180                 185                 190

Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
        195                 200                 205

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
    210                 215                 220

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr His Phe
225                 230                 235                 240

Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
                245                 250                 255

Val Ser Ser Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys Ser
            260                 265                 270

Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
        275                 280                 285
```

```
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
    290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
                325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
            340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
        355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
    370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val
                405                 410                 415

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
            420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
        435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
    450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
                485                 490                 495

Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
            500                 505                 510

Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly
        515                 520                 525

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
    530                 535                 540

Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp Val Arg Gln Ala Pro
545                 550                 555                 560

Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser Ser Tyr Gly Tyr
                565                 570                 575

Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp
            580                 585                 590

Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
        595                 600                 605

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val Arg Gly Ser Lys Lys
    610                 615                 620

Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
625                 630                 635                 640

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
                645                 650                 655

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
            660                 665                 670

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
        675                 680                 685
```

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
690 695 700

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
705 710 715 720

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
725 730 735

Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr
740 745 750

Lys Val Glu Ile Lys
755

<210> 1005
<211> 751
<212> PRT
<213> Artificial Sequence

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

<400> 1005
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
20 25 30

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
35 40 45

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
50 55 60

Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
65 70 75 80

```
Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
                85                  90                  95

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe
            100                 105                 110

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala
        115                 120                 125

Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val
    130                 135                 140

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
145                 150                 155                 160

Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser Ser Ser Ile His Trp Val
                165                 170                 175

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser
            180                 185                 190

Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
        195                 200                 205

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
    210                 215                 220

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr His Phe
225                 230                 235                 240

Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
                245                 250                 255

Val Ser Ser Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys Thr
            260                 265                 270
```

```
Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
        275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
    290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
                325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
            340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
        355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
    370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met
385                 390                 395                 400

Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
                405                 410                 415

Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
            420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
        435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
    450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
                485                 490                 495

Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
            500                 505                 510

Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly
        515                 520                 525

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
    530                 535                 540

Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala Pro
545                 550                 555                 560

Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr
                565                 570                 575

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp
            580                 585                 590

Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
        595                 600                 605

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp Ala
    610                 615                 620

Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
625                 630                 635                 640

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
                645                 650                 655

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
            660                 665                 670
```

```
Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        675                 680                 685

Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro
    690                 695                 700

Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile
705                 710                 715                 720

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr
                725                 730                 735

Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            740                 745                 750
```

<210> 1006
<211> 767
<212> PRT
<213> Artificial Sequence

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

<400> 1006

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
            20                  25                  30

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
        35                  40                  45

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
    50                  55                  60

Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
65                  70                  75                  80
```

```
Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
                85                  90                  95

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe
            100                 105                 110

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala
        115                 120                 125

Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val
    130                 135                 140

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
145                 150                 155                 160

Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser Ser Ser Ile His Trp Val
                165                 170                 175

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser
            180                 185                 190

Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
        195                 200                 205

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
    210                 215                 220

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr His Phe
225                 230                 235                 240

Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
                245                 250                 255

Val Ser Ser Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys Ser
            260                 265                 270

Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
        275                 280                 285
```

```
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
    290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
                325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
            340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
        355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
    370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val
                405                 410                 415

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
            420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
        435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
    450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
                485                 490                 495

Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
            500                 505                 510

Thr Pro Glu Ser Gly Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
        515                 520                 525

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
    530                 535                 540

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
545                 550                 555                 560

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly
                565                 570                 575

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
            580                 585                 590

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
        595                 600                 605

Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
    610                 615                 620

Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly
625                 630                 635                 640

Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
                645                 650                 655

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser
            660                 665                 670

Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        675                 680                 685
```

```
Val Ala Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser
    690                 695                 700

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
705                 710                 715                 720

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
                725                 730                 735

Cys Ala Arg Thr Val Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp
            740                 745                 750

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        755                 760                 765
```

<210> 1007
<211> 763
<212> PRT
<213> Artificial Sequence

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

<400> 1007

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
            20                  25                  30

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser
        35                  40                  45

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
    50                  55                  60

Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
65                  70                  75                  80
```

```
Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
                85                  90                  95

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe
            100                 105                 110

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala
        115                 120                 125

Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val
    130                 135                 140

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
145                 150                 155                 160

Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser Ser Ser Ile His Trp Val
                165                 170                 175

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser
            180                 185                 190

Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
        195                 200                 205

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
    210                 215                 220

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr His Phe
225                 230                 235                 240

Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
                245                 250                 255

Val Ser Ser Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys Thr
            260                 265                 270
```

```
Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
        275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
    290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
                325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
            340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
        355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
    370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met
385                 390                 395                 400

Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
                405                 410                 415

Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
            420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
        435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
    450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
               485                 490                 495

Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
            500                 505                 510

Thr Pro Glu Ser Gly Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser
        515                 520                 525

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
    530                 535                 540

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
545                 550                 555                 560

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly
               565                 570                 575

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
            580                 585                 590

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
        595                 600                 605

Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu
    610                 615                 620

Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser
625                 630                 635                 640

Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
               645                 650                 655

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser
            660                 665                 670
```

Tyr Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
675 680 685

Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp
690 695 700

Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr
705 710 715 720

Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
725 730 735

Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr
740 745 750

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
755 760

<210> 1008
<211> 228
<212> PRT
<213> Artificial Sequence

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

<400> 1008
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Asp
1 5 10 15

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
20 25 30

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
35 40 45

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
50 55 60

```
Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
65                  70                  75                  80


Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
                85                  90                  95


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe
            100                 105                 110


Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser
        115                 120                 125


Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala
    130                 135                 140


Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
145                 150                 155                 160


Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
                165                 170                 175


Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
            180                 185                 190


Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
        195                 200                 205


Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
    210                 215                 220


Arg Gly Glu Cys
225


<210> 1009
<211> 722
<212> PRT
<213> Artificial Sequence

<220>
```

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 1009

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                  10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser
        35                  40                  45


Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60


Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110


Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
        115                 120                 125


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


Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160


Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175


Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190
```

```
Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser
    370                 375                 380
```

```
Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
465                 470                 475                 480

Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn
            500                 505                 510

Ile Ser Ser Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Ser Ile Tyr Ser Ser Tyr Gly Tyr Thr Ser Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Thr Val Arg Gly Ser Lys Lys Pro Tyr Phe
            580                 585                 590
```

```
Ser Gly Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
        595                 600                 605


Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
    610                 615                 620


Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
625                 630                 635                 640


Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
                645                 650                 655


Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly
            660                 665                 670


Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
        675                 680                 685


Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    690                 695                 700


Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu
705                 710                 715                 720


Ile Lys
```

<210> 1010
<211> 716
<212> PRT
<213> Artificial Sequence

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

<400> 1010

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15
```

```
Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser
        35                  40                  45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205
```

```
Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Met Val Phe Asp
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
    370                 375                 380

Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415
```

```
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
465                 470                 475                 480

Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn
            500                 505                 510

Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp Ala Gly Ala Met
            580                 585                 590

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
        595                 600                 605
```

Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
610 615 620

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
625 630 635 640

Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
645 650 655

Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe
660 665 670

Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
675 680 685

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro
690 695 700

Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710 715

<210> 1011
<211> 717
<212> PRT
<213> Artificial Sequence

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

<400> 1011
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser
35 40 45

```
Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60

Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255
```

```
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
    370                 375                 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445
```

```
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
465                 470                 475                 480

Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
                485                 490                 495

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn
            500                 505                 510

Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly
        515                 520                 525

Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr
    530                 535                 540

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
545                 550                 555                 560

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
                565                 570                 575

Val Tyr Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp Ala Gly Ala Met
            580                 585                 590

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
        595                 600                 605

Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
    610                 615                 620

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser
625                 630                 635                 640

Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
                645                 650                 655
```

Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe
660 665 670

Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
675 680 685

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly
690 695 700

Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
705 710 715

<210> 1012
<211> 728
<212> PRT
<213> Artificial Sequence

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

<400> 1012
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110

Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285
```

```
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
    370                 375                 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
465                 470                 475                 480

Ser Gly Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
                485                 490                 495
```

```
Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
            500                 505                 510

Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
        515                 520                 525

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
    530                 535                 540

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
545                 550                 555                 560

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser
                565                 570                 575

Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly
            580                 585                 590

Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu
        595                 600                 605

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    610                 615                 620

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser
625                 630                 635                 640

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
                645                 650                 655

Tyr Ile Ser Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
            660                 665                 670

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
        675                 680                 685
```

```
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    690                 695                 700


Arg Ala His Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln
705                 710                 715                 720


Gly Thr Leu Val Thr Val Ser Ser
                725
```

<210> 1013
<211> 732
<212> PRT
<213> Artificial Sequence

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

<400> 1013

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
            20                  25                  30


Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser
        35                  40                  45


Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
    50                  55                  60


Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys
65                  70                  75                  80


Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
                85                  90                  95


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            100                 105                 110
```

```
Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
        115                 120                 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145                 150                 155                 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
                245                 250                 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            260                 265                 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
        275                 280                 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
    290                 295                 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305                 310                 315                 320
```

```
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
                325                 330                 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
            340                 345                 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
        355                 360                 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
    370                 375                 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385                 390                 395                 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
                405                 410                 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
            420                 425                 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
        435                 440                 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    450                 455                 460

Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
465                 470                 475                 480

Ser Gly Gly Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
                485                 490                 495

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
            500                 505                 510
```

```
Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
        515                 520                 525

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
    530                 535                 540

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
545                 550                 555                 560

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr
                565                 570                 575

Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Gly Thr
            580                 585                 590

Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu Val
        595                 600                 605

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
    610                 615                 620

Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile
625                 630                 635                 640

His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser
                645                 650                 655

Ile Tyr Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly
            660                 665                 670

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
        675                 680                 685

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
    690                 695                 700

Thr Val Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp
705                 710                 715                 720
```

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
725 730

<210> 1014
<211> 742
<212> PRT
<213> Artificial Sequence

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

<400> 1014
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser
35 40 45

Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

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

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
100 105 110

Cys Ala Arg Thr Val Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp
115 120 125

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

```
Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
145                 150                 155                 160

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
                165                 170                 175

Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
            180                 185                 190

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
        195                 200                 205

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
    210                 215                 220

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr
225                 230                 235                 240

Phe Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Leu Glu
                245                 250                 255

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

Asn Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
        275                 280                 285

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
    290                 295                 300

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
305                 310                 315                 320

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
                325                 330                 335
```

```
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
            340                 345                 350

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
        355                 360                 365

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
    370                 375                 380

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
385                 390                 395                 400

Pro Ile Arg Glu Leu Met Thr Ser Asn Gln Val Ser Leu Ser Cys Ala
                405                 410                 415

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
            420                 425                 430

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
        435                 440                 445

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
    450                 455                 460

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
465                 470                 475                 480

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser
                485                 490                 495

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
            500                 505                 510

Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
        515                 520                 525

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His
    530                 535                 540
```

```
Ser Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
545                 550                 555                 560

Trp Val Ala Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp
                565                 570                 575

Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr
            580                 585                 590

Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
        595                 600                 605

Tyr Cys Ala Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp
    610                 615                 620

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
625                 630                 635                 640

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
                645                 650                 655

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
            660                 665                 670

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
        675                 680                 685

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
    690                 695                 700

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
705                 710                 715                 720

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
                725                 730                 735
```

Cys Asp Lys Thr His Thr
            740

<210> 1015
<211> 737
<212> PRT
<213> Artificial Sequence

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

<400> 1015
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1   5   10   15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20   25   30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr
        35   40   45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50   55   60

Val Ala Ser Ile Ser Pro Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser
65   70   75   80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85   90   95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100   105   110

Cys Ala Arg Ser Ser Tyr Phe Pro Trp Phe Ser Ala Met Asp Tyr Trp
        115   120   125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
    130   135   140

```
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
                165                 170                 175


Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190


Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205


Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe
225                 230                 235                 240


Gly Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr
                245                 250                 255


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


Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        275                 280                 285


Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    290                 295                 300


Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
305                 310                 315                 320


Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                325                 330                 335


Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            340                 345                 350
```

```
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        355                 360                 365

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    370                 375                 380

Gln Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu
385                 390                 395                 400

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr
                405                 410                 415

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            420                 425                 430

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        435                 440                 445

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    450                 455                 460

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
465                 470                 475                 480

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro
                485                 490                 495

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln
            500                 505                 510

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
        515                 520                 525

Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser Ile His
    530                 535                 540
```

```
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Thr
545                 550                 555                 560

Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys Gly Arg
                565                 570                 575

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
            580                 585                 590

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr
        595                 600                 605

His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
625                 630                 635                 640

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
                645                 650                 655

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
            660                 665                 670

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
        675                 680                 685

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
    690                 695                 700

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
705                 710                 715                 720

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
                725                 730                 735

Thr
```

<210> 1016
<211> 480
<212> PRT
<213> Artificial Sequence

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

<400> 1016
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
20 25 30

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile His Ser Ser Ser
35 40 45

Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
50 55 60

Ala Thr Tyr Ser Ser Phe Gly Ser Ile Thr Tyr Ala Asp Ser Val Lys
65 70 75 80

Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu
85 90 95

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
100 105 110

Arg Tyr His His Pro Phe Gly Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
115 120 125

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

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145 150 155 160

```
Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                165                 170                 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            180                 185                 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        195                 200                 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    210                 215                 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225                 230                 235                 240

Thr His Thr Gly Gly Ser Gly Gly Glu Val Gln Leu Val Glu Ser Gly
                245                 250                 255

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
            260                 265                 270

Ser Gly Phe Thr Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala
        275                 280                 285

Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Pro Tyr Tyr Gly
    290                 295                 300

Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala
305                 310                 315                 320

Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala
                325                 330                 335

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Ser Tyr Phe Pro Trp
            340                 345                 350
```

```
Phe Ser Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        355                 360                 365


Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    370                 375                 380


Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
385                 390                 395                 400


Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys
                405                 410                 415


Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val
            420                 425                 430


Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr
        435                 440                 445


Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    450                 455                 460


Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
465                 470                 475                 480


<210> 1017
<211> 470
<212> PRT
<213> Artificial Sequence

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

<400> 1017
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Asp
1               5                   10                  15


Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
            20                  25                  30
```

```
Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
        35                  40                  45

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
    50                  55                  60

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
65                  70                  75                  80

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
                85                  90                  95

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe
            100                 105                 110

Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser
        115                 120                 125

Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala
    130                 135                 140

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
145                 150                 155                 160

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
                165                 170                 175

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
            180                 185                 190

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
        195                 200                 205

Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
    210                 215                 220

Arg Gly Glu Cys Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
225                 230                 235                 240
```

```
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
               245                 250                 255

Ala Ser Gly Phe Thr Ile Ser Ser Tyr Tyr Ile His Trp Val Arg Gln
            260                 265                 270

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser Ser Tyr
        275                 280                 285

Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
    290                 295                 300

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
305                 310                 315                 320

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val Arg Gly Ser
               325                 330                 335

Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp Gly Gln Gly
            340                 345                 350

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
        355                 360                 365

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
    370                 375                 380

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
385                 390                 395                 400

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
               405                 410                 415

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
            420                 425                 430
```

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
435 440 445

Thr Tyr Tyr Cys Gln Gln Tyr Tyr Phe Leu Ile Thr Phe Gly Gln Gly
450 455 460

Thr Lys Val Glu Ile Lys
465 470

<210> 1018
<211> 629
<212> PRT
<213> Artificial Sequence

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

<400> 1018
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65 70 75 80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
100 105 110

```
Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Asp Lys Thr His Thr Lys Val Glu
                245                 250                 255

Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Gly Gln
            260                 265                 270

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
        275                 280                 285

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    290                 295                 300

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
305                 310                 315                 320
```

```
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                325                 330                 335

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            340                 345                 350

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        355                 360                 365

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Thr Thr Ala Ala Ser Gly
    370                 375                 380

Ser Ser Gly Gly Ser Ser Ser Gly Ala Gly Arg Thr Glu Val Gln Leu
385                 390                 395                 400

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
                405                 410                 415

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
            420                 425                 430

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
        435                 440                 445

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
    450                 455                 460

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
465                 470                 475                 480

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
                485                 490                 495

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
            500                 505                 510
```

```
Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
        515                 520                 525


Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
    530                 535                 540


Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
545                 550                 555                 560


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
                565                 570                 575


Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
            580                 585                 590


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
        595                 600                 605


Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln Gly Thr
    610                 615                 620


Lys Val Glu Ile Lys
625
```

<210> 1019
<211> 738
<212> PRT
<213> Artificial Sequence

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

<400> 1019

```
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 Asn Ile Ser Tyr Ser
            20                  25                  30
```

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

Ala Ser Ile Ser Pro Tyr Tyr Ser Tyr Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60

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

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

Ala Arg Pro Ser Ala Trp Ser His Tyr Tyr Pro Ser Ser Ser Ser Ser
            100                 105                 110

Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser
    210                 215                 220

Tyr Ser Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Leu
225                 230                 235                 240
```

```
Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys Ser Ser Asp Lys Thr
                245                 250                 255

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
            260                 265                 270

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
        275                 280                 285

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
    290                 295                 300

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
305                 310                 315                 320

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
                325                 330                 335

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
            340                 345                 350

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
        355                 360                 365

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
    370                 375                 380

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
385                 390                 395                 400

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
                405                 410                 415

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
            420                 425                 430
```

```
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
        435                 440                 445

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
    450                 455                 460

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465                 470                 475                 480

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                485                 490                 495

Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
            500                 505                 510

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile
        515                 520                 525

Ser Tyr Ser Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    530                 535                 540

Glu Trp Val Ala Ser Ile Ser Pro Tyr Tyr Ser Tyr Thr Ser Tyr Ala
545                 550                 555                 560

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
                565                 570                 575

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
            580                 585                 590

Tyr Tyr Cys Ala Arg Pro Ser Ala Trp Ser His Tyr Tyr Pro Ser Ser
        595                 600                 605

Ser Ser Ser Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
    610                 615                 620

Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
625                 630                 635                 640
```

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
645 650 655

Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
660 665 670

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly
675 680 685

Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu
690 695 700

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
705 710 715 720

Gln Ser Ser Tyr Ser Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Glu
725 730 735

Ile Lys

<210> 1020
<211> 740
<212> PRT
<213> Artificial Sequence

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

<400> 1020

Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Tyr Tyr
35 40 45

```
Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Pro Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr Tyr His Tyr Gly Leu Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
            180                 185                 190

Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Trp His Ser Tyr Leu Ile Thr Phe Gly
225                 230                 235                 240
```

```
Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445
```

```
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
545                 550                 555                 560

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
        595                 600                 605

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
625                 630                 635                 640
```

```
Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
                645                 650                 655


Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
            660                 665                 670


Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
        675                 680                 685


Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
    690                 695                 700


Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
705                 710                 715                 720


Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys
                725                 730                 735


Val Glu Ile Lys
            740
```

<210> 1021
<211> 746
<212> PRT
<213> Artificial Sequence

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

<400> 1021

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30


Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Tyr Tyr
        35                  40                  45
```

```
Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Pro Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr Tyr His Tyr Gly Leu Asp Tyr Trp Gly Gln Gly Thr
        115                 120                 125

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
            180                 185                 190

Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Trp His Ser Tyr Leu Ile Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255
```

```
Val Glu Pro Lys Ser Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro
            260                 265                 270

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445
```

```
Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr
545                 550                 555                 560

Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val
        595                 600                 605

Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp
    610                 615                 620

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
625                 630                 635                 640

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                645                 650                 655
```

```
Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
            660                 665                 670


Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        675                 680                 685


Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    690                 695                 700


Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
705                 710                 715                 720


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr
                725                 730                 735


Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            740                 745


<210> 1022
<211> 736
<212> PRT
<213> Artificial Sequence

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

<400> 1022

Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15


Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30


Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr
        35                  40                  45


Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
```

```
    50                  55                  60

Val Ala Ser Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
        115                 120                 125

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ala Phe Tyr Tyr Pro Ile Thr Phe Gly Gln Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys
                245                 250                 255
```

```
Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
            260                 265                 270

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
385                 390                 395                 400

Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
```

```
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480

Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
                485                 490                 495

Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly
            500                 505                 510

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
        515                 520                 525

Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp Val Arg Gln Ala
    530                 535                 540

Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser Tyr Tyr Gly
545                 550                 555                 560

Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala
                565                 570                 575

Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala
            580                 585                 590

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His Tyr Phe Pro Trp
        595                 600                 605

Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    610                 615                 620

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
625                 630                 635                 640

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
                645                 650                 655
```

```
Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys
            660                 665                 670

Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr Ser Gly Val
        675                 680                 685

Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr
    690                 695                 700

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
705                 710                 715                 720

Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                725                 730                 735
```

<210> 1023
<211> 742
<212> PRT
<213> Artificial Sequence

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

<400> 1023

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr
        35                  40                  45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Pro Ser Tyr Ser Ser Thr Tyr Tyr Ala Asp Ser
65                  70                  75                  80
```

```
Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
        115                 120                 125

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Ala Phe Tyr Tyr Pro Ile Thr Phe Gly Gln Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys Val Glu Pro Lys
                245                 250                 255

Ser Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro Ala Pro Glu Leu
            260                 265                 270
```

```
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr Ser Asn Gln
385                 390                 395                 400

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
        435                 440                 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480
```

```
Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
                485                 490                 495

Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly
            500                 505                 510

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
        515                 520                 525

Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp Val Arg Gln Ala
    530                 535                 540

Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser Ser Tyr Gly
545                 550                 555                 560

Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala
                565                 570                 575

Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala
            580                 585                 590

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val Arg Gly Ser Lys
        595                 600                 605

Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp Gly Gln Gly Thr
    610                 615                 620

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
625                 630                 635                 640

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
                645                 650                 655

Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln
            660                 665                 670
```

```
Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser
        675                 680                 685

Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr
    690                 695                 700

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
705                 710                 715                 720

Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe Gly Gln Gly
                725                 730                 735

Thr Lys Val Glu Ile Lys
            740
```

<210> 1024
<211> 739
<212> PRT
<213> Artificial Sequence

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

<400> 1024

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser
        35                  40                  45

Ser Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Ser Tyr Tyr Gly Ser Thr Tyr Tyr Ala Asp Ser
65                  70                  75                  80
```

```
Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Trp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
        115                 120                 125

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Pro Gly Ser Trp Tyr Phe Pro Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys Val
                245                 250                 255

Glu Pro Lys Thr Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
            260                 265                 270

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
        275                 280                 285
```

```
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
    290                 295                 300

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
305                 310                 315                 320

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
                325                 330                 335

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
            340                 345                 350

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
        355                 360                 365

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
    370                 375                 380

Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met Thr
385                 390                 395                 400

Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro Ser
                405                 410                 415

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
            420                 425                 430

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
        435                 440                 445

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
    450                 455                 460

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
465                 470                 475                 480
```

```
Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr
                485                 490                 495

Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu Val
            500                 505                 510

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
        515                 520                 525

Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp Val
    530                 535                 540

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser Ser
545                 550                 555                 560

Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
                565                 570                 575

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
            580                 585                 590

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His Tyr
        595                 600                 605

Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
    610                 615                 620

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
625                 630                 635                 640

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                645                 650                 655

Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys
            660                 665                 670

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr
        675                 680                 685
```

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe
690 695 700

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
705 710 715 720

Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys Val
725 730 735

Glu Ile Lys

<210> 1025
<211> 745
<212> PRT
<213> Artificial Sequence

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

<400> 1025

Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser
35 40 45

Ser Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

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

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

```
Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Trp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
        115                 120                 125

Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu Tyr
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220

Cys Gln Gln Pro Gly Ser Trp Tyr Phe Pro Pro Ile Thr Phe Gly Gln
225                 230                 235                 240

Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys Val
                245                 250                 255

Glu Pro Lys Ser Ser Asp Lys Thr His Asn Cys Pro Pro Cys Pro Ala
            260                 265                 270

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
        275                 280                 285
```

```
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
    290                 295                 300

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
305                 310                 315                 320

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
                325                 330                 335

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
            340                 345                 350

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
        355                 360                 365

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
    370                 375                 380

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met Thr
385                 390                 395                 400

Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser
                405                 410                 415

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
            420                 425                 430

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val
        435                 440                 445

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
    450                 455                 460

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
465                 470                 475                 480

Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly Thr
                485                 490                 495
```

```
Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu Val
            500                 505                 510

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser
        515                 520                 525

Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp Val
    530                 535                 540

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Ser
545                 550                 555                 560

Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
                565                 570                 575

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser
            580                 585                 590

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val Arg
        595                 600                 605

Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp Gly
    610                 615                 620

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
625                 630                 635                 640

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                645                 650                 655

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
            660                 665                 670

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
        675                 680                 685
```

```
Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
    690                 695                 700

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
705                 710                 715                 720

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr Phe
                725                 730                 735

Gly Gln Gly Thr Lys Val Glu Ile Lys
            740                 745
```

<210> 1026
<211> 740
<212> PRT
<213> Artificial Sequence

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

<400> 1026

```
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1               5                   10                  15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
            20                  25                  30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
        35                  40                  45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
    50                  55                  60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65                  70                  75                  80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
                85                  90                  95
```

```
Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
```

```
    290                 295                 300

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495
```

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
545                 550                 555                 560

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
        595                 600                 605

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
625                 630                 635                 640

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
                645                 650                 655

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
            660                 665                 670

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
        675                 680                 685

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
```

690 695 700

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
705 710 715 720

Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys
725 730 735

Val Glu Ile Lys
740

<210> 1027
<211> 746
<212> PRT
<213> Artificial Sequence

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

<400> 1027

Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Gly Ser
35 40 45

Ser Ser Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Ser Ala Phe Ala Ser Thr Ser Tyr Ala Asp Ser
65 70 75 80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

```
Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
            100                 105                 110

Cys Ala Arg Tyr His Phe Pro Phe Gly Phe Ala Leu Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser
            180                 185                 190

Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Val Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300
```

```
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495
```

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr
545                 550                 555                 560

Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val
        595                 600                 605

Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp
    610                 615                 620

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
625                 630                 635                 640

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                645                 650                 655

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
            660                 665                 670

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        675                 680                 685

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    690                 695                 700
```

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
705 710 715 720

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr
725 730 735

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
740 745

<210> 1028
<211> 746
<212> PRT
<213> Artificial Sequence

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

<400> 1028

Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr
35 40 45

Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Pro Ser Ser Gly Tyr Thr Tyr Tyr Ala Asp Ser
65 70 75 80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr

```
            100                 105                 110

Cys Ala Arg Ser Ser Phe Tyr Trp Ala Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
            180                 185                 190

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ala Ala Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300
```

```
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ile Arg Glu Leu Met
385                 390                 395                 400

Thr Ser Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
```

```
            500                 505                 510

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr Tyr Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr
545                 550                 555                 560

Ser Ser Tyr Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Thr Val
        595                 600                 605

Arg Gly Ser Lys Lys Pro Tyr Phe Ser Gly Trp Ala Met Asp Tyr Trp
    610                 615                 620

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
625                 630                 635                 640

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                645                 650                 655

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val
            660                 665                 670

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        675                 680                 685

Ser Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    690                 695                 700
```

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
705 710 715 720

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Trp Gly Pro Phe Thr
725 730 735

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
740 745

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<211> 740
<212> PRT
<213> Artificial Sequence

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

<400> 1029

Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Val Ala Glu
1 5 10 15

Phe Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
20 25 30

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr
35 40 45

Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Val Ala Ser Ile Tyr Pro Ser Ser Gly Tyr Thr Tyr Tyr Ala Asp Ser
65 70 75 80

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
100 105 110

```
Cys Ala Arg Ser Ser Phe Tyr Trp Ala Met Asp Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser
            180                 185                 190

Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ala Ala Tyr Leu Phe Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Leu Glu Asp Lys Thr His Thr Lys
                245                 250                 255

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        275                 280                 285

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    290                 295                 300
```

```
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
305                 310                 315                 320

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                325                 330                 335

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            340                 345                 350

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        355                 360                 365

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    370                 375                 380

Pro Arg Glu Pro Met Val Phe Asp Leu Pro Pro Ser Arg Glu Glu Met
385                 390                 395                 400

Thr Lys Asn Gln Val Ser Leu Trp Cys Met Val Lys Gly Phe Tyr Pro
                405                 410                 415

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            420                 425                 430

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        435                 440                 445

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    450                 455                 460

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
465                 470                 475                 480

Lys Ser Leu Ser Leu Ser Pro Gly Lys Ser Gly Ser Glu Thr Pro Gly
                485                 490                 495

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Gly Gly Glu Val Gln Leu
            500                 505                 510
```

```
Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
        515                 520                 525

Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Tyr Ser Ser Ile His Trp
    530                 535                 540

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Tyr Ile Ser
545                 550                 555                 560

Ser Tyr Tyr Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe
                565                 570                 575

Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
            580                 585                 590

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala His
        595                 600                 605

Tyr Phe Pro Trp Ala Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
    610                 615                 620

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
625                 630                 635                 640

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
                645                 650                 655

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Val Ala Trp Tyr Gln Gln
            660                 665                 670

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Ser Leu
        675                 680                 685

Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp
    690                 695                 700
```

```
Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
705                 710                 715                 720


Tyr Cys Gln Gln Tyr Tyr Trp Pro Ile Thr Phe Gly Gln Gly Thr Lys
                725                 730                 735


Val Glu Ile Lys
            740
```