DESCRIPTION

CYTOTOXICITY-INDUCING THERAPEUTIC AGENT

Technical Field

The present invention relates to multispecific antigen-binding molecules, uses thereof, and such.

Background Art

Antibodies are drawing attention as pharmaceuticals because of their high stability in plasma and few adverse reactions (Non-patent Documents 1 and 2). Antibodies are known to induce not only an antigen-binding action, an agonistic action, and an antagonistic action, but also effector-mediated cytotoxic activities (also called effector functions) such as antibody-dependent cellular cytotoxicity (ADCC), antibody dependent cell phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC), and exhibit antitumor effects against cancer cells (Non-Patent Document 3). ADCC is a cytotoxicity exhibited by effector cells against antibody-bound target cancer cells via binding of the antibody Fc region to an Fc receptor present on effector cells such as NK cells and macrophages. A complement complex binds to the complement-binding site present in an antibody structure. CDC is cell injury that results from cell destruction where an influx of water and ions into cells is promoted by pore formation on the cell membrane of the antibody-bound cells by complement components present in the complex. A number of therapeutic antibodies showing excellent anti-tumor effects have been developed as pharmaceuticals for cancer treatment (Non-patent Document 4); and while existing therapeutic antibodies have shown excellent actions, the therapeutic outcome achieved by administration of these antibodies is still not satisfactory.

For an antibody to express ADCC, ADCP, and CDC, it is necessary for the antibody Fc region, the antibody receptor (FcγR) present on effector cells such as NK cells and macrophages, and various complement components to bind. In humans, isoforms of FcγRIa, FcγRIIa, FcγRIIb, FcγRIIIa, and FcγRIIIb have been reported as the FcγR protein family, and the respective allotypes have been reported as well (Non-patent Document 5). Among these isoforms, FcγRIa, FcγRIIa, and FcγRIIIa carry a domain called the Immunoreceptor Tyrosine-based Activation Motif (ITAM) in the intracellular domain, and transmit activation signals. On the other hand, only FcγRIIb carries a domain called the Immunoreceptor Tyrosine-based Inhibitory Motif (ITIM) in the intracellular domain, and transmits inhibitory signals. Every one of the FcγRs is known to transmit signals via crosslinking by immune complexes and such (Non-patent Document 6). When antibodies actually exert an effector function on cancer cells, FcγRs on the

effector cell membrane form clusters at the Fc regions of several antibodies bound on the cancer cell membrane, and activation signals are transmitted by effector cells. A cytocidal effect is exerted as a result, but since FcγRs are crosslinked only in effector cells present near cancer cells this time, activation of immunity is shown to occur locally in cancer cells (Non-patent Document 7).

Naturally-occurring immunoglobulins bind to antigens at their variable regions, and bind to receptors such as FcγR, FcRn, FcαR, and FcεR, and complements at their constant regions. FcRn is one of the binding molecules that interact at the IgG Fc region, and since each of the antibody heavy chains binds one molecule of FcRn, two molecules of FcRn have been reported to bind one IgG-type antibody molecule. However, unlike FcRn and such, FcγR interacts at the antibody hinge region and CH2 domain, and only one molecule of FcγR binds to one molecule of IgG-type antibody (Non-patent Document 8). Furthermore, a common naturally-occurring IgG-type antibody recognizes and binds a single epitope via its variable region (Fab); therefore, it can bind to only one antigen. On the other hand, many types of proteins are known to be involved in cancer and inflammation, and there may be crosstalk among the proteins. For example, several inflammatory cytokines (TNF, IL1, and IL6) are known to be involved in immunological diseases (Non-patent Document 9). Furthermore, activation of other receptors is known as one of the mechanisms of cancer in acquiring drug resistance (Non-patent Document 10). In such cases, common antibodies that recognize a single epitope would be unable to inhibit multiple proteins.

Antibodies (bispecific antibodies) that bind to two or more types of antigens with one molecule are being studied as molecules that inhibit multiple targets. It is possible to confer binding activities to two different antigens (a first antigen and a second antigen) by modifying naturally-occurring IgG-type antibodies (Non-patent Document 11). Accordingly, there will not only be neutralization of two or more types of antigens by a single molecule, but also enhancement of antitumor activity due to crosslinks between cells having cytotoxic activity and cancer cells. As molecular forms of a bispecific antibody, a molecule comprising an antigen-binding site added to the N or C terminus of an antibody (DVD-Ig and scFv-IgG), a molecule having different sequences for the two Fab regions of an antibody (common L-chain bispecific antibody and hybrid hybridoma), a molecule in which one Fab region recognizes two antigens (two-in-one IgG), and a molecule having a CH3 region loop site as a new antigen-binding site (Fcab) have been reported so far (Non-patent Documents 12 and 13). Since all bispecific antibodies interact at their Fc regions with FcγR, antibody effector functions are preserved. Thus, the bispecific antibody binds to any antigen that it recognizes and at the same time binds to FcγR, and exhibits ADCC activity against cells expressing the antigen.

If all the antigens recognized by the bispecific antibody are antigens specifically expressed in cancer, the bispecific antibody exhibits cytotoxic activity to cancer cells when it binds to any of the antigens. Therefore, in comparison to a conventional antibody pharmaceutical that recognizes one antigen, a more efficient antitumor effect can be expected from such an antibody. However, in the case where any one of the antigens recognized by the bispecific antibody is expressed in normal tissues or cells expressed on immunocytes, damage on normal tissues or release of cytokines occurs due to crosslinking with FcγR (Non-patent Document 14). As a result, strong adverse reactions are induced.

A T-cell redirecting antibody that employs cytotoxicity mobilizing T cells as effector cells as the mechanism for its antitumor effect has been known from the 1980s as a bispecific antibody (Non-patent Documents 15, 16, and 17). Unlike antibodies that employ ADCC mobilizing NK cells or macrophages as effector cells as the mechanism for their antitumor effects, a T-cell redirecting antibody is an antibody against any one of the subunits constituting the T-cell receptor (TCR) complex on T cells, and is specifically a bi-specific antibody comprising an antibody that binds to the CD3 epsilon chain and an antibody that binds to an antigen on the target cancer cell. T cells come close to cancer cells via simultaneous binding of the CD3 epsilon chain and a cancer antigen by a T-cell redirecting antibody. As a result, antitumor effects against cancer cells are considered to be exerted through the cytotoxic activity possessed by T cells.

Catumaxomab, which is known as a T-cell redirecting antibody, binds at two Fabs each to a cancer antigen (EpCAM) and to a CD3ε (CD3 epsilon) chain expressed on T cells. Catumaxomab induces T cell-mediated cytotoxic activity by binding to the cancer antigen and the CD3ε at the same time, and induces cytotoxic activity mediated by antigen-presenting cells such as NK cells and macrophages, by binding to the cancer antigen and FcγR at the same time. By use of these two cytotoxic activities, catumaxomab exhibits a high therapeutic effect on malignant ascites by intraperitoneal administration and has thus been approved in Europe (Non-patent Document 18). In addition, there are cases where the administration of catumaxomab reportedly yields cancer cell-reactive antibodies, which clearly shows that acquired immunity is induced (Non-patent Document 19). From this result, antibodies having both T cell-mediated cytotoxic activity and the FcγR-mediated actions by cells such as NK cells or macrophages (these antibodies are particularly referred to as trifunctional antibodies) have received attention because a strong antitumor effect and induction of acquired immunity can be expected.

The trifunctional antibodies, however, bind to CD3ε and FcγR at the same time even in the absence of a cancer antigen and therefore crosslink CD3ε-expressing T cells with FcγR-expressing cells even in a cancer cell-absent environment, leading to production of various cytokines in large amounts. Such cancer antigen-independent induction of production of various

cytokines restricts the current administration of the trifunctional antibodies to an intraperitoneal route (Non-patent Document 20). The trifunctional antibodies are very difficult to administer systemically due to severe cytokine storm-like adverse reactions. In fact, in the Phase I clinical trial of administering catumaxomab systemically to non-small-cell lung cancer patients, a very low dose of 5 μg/body is the maximum permissible dose, and administration of a larger dose has been reported to cause various serious adverse reactions (Non-patent Document 21).

As such, bispecific antibodies by conventional techniques may bind to both antigens, the first antigen being the cancer antigen (EpCAM) and the second antigen being CD3ε, at the same time when they bind to FcγR; and therefore, in view of their molecular structure it is impossible to avoid adverse reactions caused by the simultaneous binding to FcγR and the second antigen CD3ε.

Meanwhile, unlike catumaxomab, BiTE has no Fcγ receptor-binding site, and therefore it does not cross-link the receptors expressed on T cells and cells such as NK cells and macrophages in a cancer antigen-dependent manner. Thus, it has been demonstrated that BiTE does not cause cancer antigen-independent cytokine induction which is observed when catumaxomab is administered. However, since BiTE is a modified low-molecular-weight antibody molecule without an Fc region, the problem is that its blood half-life after administration to a patient is significantly shorter than IgG-type antibodies conventionally used as therapeutic antibodies. In fact, the blood half-life of BiTE administered *in vivo* has been reported to be about several hours (Non-patent Documents 22 and 23). In the clinical trials of blinatumomab, it is administered by continuous intravenous infusion using a minipump. This administration method is not only extremely inconvenient for patients but also has the potential risk of medical accidents due to device malfunction or the like. Thus, it cannot be said that such an administration method is desirable.

In recent years, use of an Fc region with reduced FcγR-binding activity has enabled maintenance of the strong antitumor activity possessed by BiTE and the excellent safety property of not inducing a cytokine storm in a cancer antigen-dependent manner, and has provided novel polypeptide assemblies that have long half-lives in blood (Patent Document 1).

On the other hand, when expressing a bispecific antibody by conventional techniques, since two types of H chains and two types of L chains are expressed, ten combinations are conceivable. Among them, only one of the produced combinations has the binding specificity of interest. Therefore, to obtain the bispecific antibody of interest, the single antibody of interest must be purified from the ten types of antibodies, which is very inefficient and difficult.

A method of preferentially secreting IgGs with a heterodimeric combination of H chains, for example, a combination of an H chain against antigen A and an H chain against antigen B, by introducing amino acid substitutions into the IgG H-chain CH3 region has been reported as a

method for solving this problem (Patent Documents 2, 3, 4, 5, 6, 7, and Non-patent Documents 24 and 25). A method that utilizes physical disturbance, i.e., "knob" and "hole", and a method that utilizes electric charge repulsion have been reported as such methods.

To obtain the molecule of interest with better efficiency, methods using L chains that can bind to two different antigens even though the L chains have the same amino acid sequence have been reported (Patent Documents 8 and 9). However, the antigen affinity may decrease greatly with the use of common L chains, and it is difficult to find common L chains that maintain antigen affinity.

Citation List

[Patent Documents]
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[Patent Document 2] WO96/27011
[Patent Document 3] WO2006/106905
[Patent Document 4] WO2007/147901
[Patent Document 5] WO2009/089004
[Patent Document 6] WO2010/129304
[Patent Document 7] WO2013/065708
[Patent Document 8] WO98/050431
[Patent Document 9] WO2006/109592

[Non-patent Documents]
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[Non-patent Document 2] Eur J Pharm Biopharm. (2005) 59 (3), 389-396
[Non-patent Document 3] Drug Des Devel Ther (2009) 3, 7-16
[Non-patent Document 4] Clin Cancer Res. (2010) 16 (1), 11-20
[Non-patent Document 5] Immunol. Lett. (2002) 82, 57-65
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[Non-patent Document 8] J. Bio. Chem., (20001) 276, 16469-16477
[Non-patent Document 9] Nat. Biotech., (2011) 28, 502-10
[Non-patent Document 10] Endocr Relat Cancer (2006) 13, 45-51
[Non-patent Document 11] MAbs. (2012) Mar 1, 4(2)
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[Non-patent Document 13] Peds (2010), 23(4), 289-297
[Non-patent Document 14] J. Immunol. (1999) Aug 1, 163(3), 1246-52

[Non-patent Document 15] Nature (1985) 314 (6012), 628-31
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[Non-patent Document 18] Cancer Treat Rev. (2010) Oct 36(6), 458-67
[Non-patent Document 19] Future Oncol. (2012) Jan 8(1), 73-85
[Non-patent Document 20] Cancer Immunol Immunother. (2007) 56(9), 1397-406
[Non-patent Document 21] Cancer Immunol Immunother. (2007) 56 (10), 1637-44
[Non-patent Document 22] Cancer Immunol Immunother. (2006) 55(5), 503-14
[Non-patent Document 23] Cancer Immunol Immunother. (2009) 58(1), 95-109
[Non-patent Document 24] Protein Engineering. (1996) vol.9, p.617-621
[Non-patent Document 25] Nature Biotechnology. (1998) vol.16, p.677-681

Summary of the Invention

[Problems to be Solved by the Invention]

The present invention was achieved in view of the above circumstances. An objective of the present invention is to provide multispecific antigen-binding molecules that bring T cells close to the target cancer cells, and can treat cancer through the cytotoxic activity of T cells against target cancer tissues containing glypican 3-expressing cells, and are molecular forms that can be produced with high efficiency; methods for producing the antigen-binding molecules; and pharmaceutical compositions comprising the antigen-binding molecules as active ingredient.

[Means for Solving the Problems]

The present inventors discovered an L chain common to a domain comprising a glypican 3-binding antibody variable region, and a domain comprising a T-cell receptor complex-binding antibody variable region, where the common L chain is capable of improving affinity to both antigens. This allows preparation of molecular forms that can be produced with high efficiency, and further discovery of novel multispecific antigen-binding molecules that maintain the strong antitumor activity possessed by T-cell redirecting antibodies such as BiTE and the excellent safety property of not inducing a cytokine storm in a cancer antigen-dependent manner, and also have long half-lives in blood. Furthermore, the present inventors discovered that the multispecific antigen-binding molecules comprising common L chains target glypican 3-expressing cancer cells and cause cell injury. Based on this discovery, the present inventors elucidated that the multispecific antigen-binding molecules of the present invention cause injury to cancer tissues containing glypican 3-expressing cancer cells.

More specifically, the present invention provides the following:

[1] A multispecific antigen-binding molecule that comprises:

(1) a domain comprising an antibody variable region having glypican 3-binding activity,
(2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity, and
(3) a domain comprising an Fc region with reduced binding activity towards an Fcγ receptor,
wherein the L chain variable regions comprised in the variable region of (1) and the variable region of (2) have a common amino acid sequence; wherein the multispecific antigen-binding molecule has a cytotoxic activity equivalent to or greater than that of the bispecific antibody GPC3_ERY22_rCE115 comprising a glypican 3-binding domain comprising SEQ ID NOs: 47 and 48, and a T-cell receptor complex-binding domain comprising SEQ ID NOs: 49 and 50.

[2] The multispecific antigen-binding molecule of [1], wherein the cytotoxic activity is T-cell-dependent cytotoxic activity.

[3] The multispecific antigen-binding molecule of [1] or [2], wherein the T-cell receptor complex-binding activity is binding activity towards a T-cell receptor.

[4] The multispecific antigen-binding molecule of any one of [1] to [3], wherein the T-cell receptor complex-binding activity is binding activity towards a CD3ε chain.

[5] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable region of (1) in [1] is an antibody variable region that comprises any one of the combinations of H-chain CDR1, CDR2, and CDR3 selected from (a1) to (a5) below, or an antibody variable region functionally equivalent thereto:

(a1) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40;
(a2) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197;
(a3) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206;
(a4) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and
(a5) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215.

[6] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable region of (2) in [1] is an antibody variable region that comprises any one of the combinations of H-chain CDR1, CDR2, and CDR3 amino acid sequences selected from (b1) to (b15) below, or an antibody variable region functionally equivalent thereto:

(b1) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 52;

(b2) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103;

(b3) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 122;

(b4) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128;

(b5) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 129;

(b6) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 132;

(b7) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142;

(b8) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144;

(b9) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164;

(b10) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168;

(b11) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 421;

(b12) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 424;

(b13) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 426;

(b14) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 429; and

(b15) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 430.

[7] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable regions of (1) and (2) in [1] are antibody variable regions comprising any one of the combinations of H-chain CDR1, CDR2, and CDR3 selected from the following (c1) to (c19), or antibody variable regions functionally equivalent thereto:

(c1) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1]

and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 52;

(c2) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 421;

(c3) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 426;

(c4) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 429;

(c5) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 430;

(c6) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128;

(c7) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142;

(c8) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in

[1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144;

(c9) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164;

(c10) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168;

(c11) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142;

(c12) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144;

(c13) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164;

(c14) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168;

(c15) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in

[1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103;

(c16) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 122;

(c17) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 129;

(c18) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 132; and

(c19) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 424.

[8] The multispecific antigen-binding molecule of any one of [5] to [7], wherein CDR1, CDR2, and CDR3 are CDR1, CDR2, and CDR3 regions based on Kabat numbering.

[9] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable region of (1) in [1] is an antibody variable region comprising any one of the H-chain variable regions selected from (a1) to (a5) below, or an antibody variable region functionally equivalent thereto:

(a1) an H-chain variable region having the amino acid sequence of SEQ ID NO: 40;

(a2) an H-chain variable region having the amino acid sequence of SEQ ID NO: 197;

(a3) an H-chain variable region having the amino acid sequence of SEQ ID NO: 206;

(a4) an H-chain variable region having the amino acid sequence of SEQ ID NO: 211; and

(a5) an H-chain variable region having the amino acid sequence of SEQ ID NO: 215.

[10] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable region of (2) in [1] is an antibody variable region comprising any one of the H-chain

variable regions selected from (b1) to (b15) below, or an antibody variable region functionally equivalent thereto:

(b1) an H-chain variable region having the amino acid sequence of SEQ ID NO: 52;

(b2) an H-chain variable region having the amino acid sequence of SEQ ID NO: 103;

(b3) an H-chain variable region having the amino acid sequence of SEQ ID NO: 122;

(b4) an H-chain variable region having the amino acid sequence of SEQ ID NO: 128;

(b5) an H-chain variable region having the amino acid sequence of SEQ ID NO: 129;

(b6) an H-chain variable region having the amino acid sequence of SEQ ID NO: 132;

(b7) an H-chain variable region having the amino acid sequence of SEQ ID NO: 142;

(b8) an H-chain variable region having the amino acid sequence of SEQ ID NO: 144;

(b9) an H-chain variable region having the amino acid sequence of SEQ ID NO: 164;

(b10) an H-chain variable region having the amino acid sequence of SEQ ID NO: 168;

(b11) an H-chain variable region having the amino acid sequence of SEQ ID NO: 421;

(b12) an H-chain variable region having the amino acid sequence of SEQ ID NO: 424;

(b13) an H-chain variable region having the amino acid sequence of SEQ ID NO: 426;

(b14) an H-chain variable region having the amino acid sequence of SEQ ID NO: 429; and

(b15) an H-chain variable region having the amino acid sequence of SEQ ID NO: 430.

[11] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable regions of (1) and (2) in [1] are antibody variable regions comprising any one of the combinations of H-chain variable regions selected from (c1) to (c19) below, or antibody variable regions functionally equivalent thereto:

(c1) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 52;

(c2) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 421;

(c3) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 426;

(c4) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 429;

(c5) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 430;

(c6) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 197; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 128;

(c7) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 142;

(c8) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 144;

(c9) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 164;

(c10) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 168;

(c11) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 142;

(c12) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 144;

(c13) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 164;

(c14) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 168;

(c15) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 103;

(c16) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 122;

(c17) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 129;

(c18) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 132; and

(c19) an H-chain variable region comprised in the antibody variable region of (1) in [1] which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in [1] which has the amino acid sequence of SEQ ID NO: 424.

[12] The multispecific antigen-binding molecule of any one of [1] to [11], wherein the common L chain of [1] is a common L chain comprising any one of the combinations of CDR1, CDR2, and CDR3 selected from (d1) to (d11) below, or a common L chain functionally equivalent thereto:

(d1) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(d2) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(d3) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(d4) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 301;

(d5) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 302;

(d6) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 304;

(d7) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 306;

(d8) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 307;

(d9) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 309;

(d10) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 310; and

(d11) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 319.

[13] The multispecific antigen-binding molecule of any one of [1] to [11], wherein the L chain variable region of [1] is a variable region of any one of the L chain amino acid sequences selected from(d1) to (d11) below:

(d1) an L chain comprising the amino acid sequence of SEQ ID NO: 53;

(d2) an L chain comprising the amino acid sequence of SEQ ID NO: 223;

(d3) an L chain comprising the amino acid sequence of SEQ ID NO: 299;

(d4) an L chain comprising the amino acid sequence of SEQ ID NO: 301;

(d5) an L chain comprising the amino acid sequence of SEQ ID NO: 302;

(d6) an L chain comprising the amino acid sequence of SEQ ID NO: 304;

(d7) an L chain comprising the amino acid sequence of SEQ ID NO: 306;

(d8) an L chain comprising the amino acid sequence of SEQ ID NO: 307;

(d9) an L chain comprising the amino acid sequence of SEQ ID NO: 309;

(d10) an L chain comprising the amino acid sequence of SEQ ID NO: 310; and

(d11) an L chain comprising the amino acid sequence of SEQ ID NO: 319.

[14] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable regions of (1) and (2) of [1] and the common L chain variable region are antibody variable regions comprising any one of the combinations of H-chain CDR1, CDR2, and CDR3 and L-chain CDR1, CDR2, and CDR3 selected from (e1) to (e25) below, or antibody variable regions functionally equivalent thereto:

(e1) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e2) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(e3) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 310;

(e4) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 319;

(e5) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e6) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e7) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e8) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e9) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e10) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(e11) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e12) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e13) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e14) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e15) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(e16) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 301;

(e17) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 302;

(e18) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 304;

(e19) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 306;

(e20) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 307;

(e21) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 309;

(e22) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 122; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e23) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 129; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e24) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 132; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53; and

(e25) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 424; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53.

[15] The multispecific antigen-binding molecule of any one of [1] to [4], wherein the antibody variable regions of (1) and (2) of [1] and the common L chain variable region are antibody variable regions comprising any one of the combinations of variable regions selected from (f1) to (f26) below, or antibody variable regions functionally equivalent thereto:

(f1) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID

NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f2) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 299;

(f3) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 310;

(f4) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 319;

(f5) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 142; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f6) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 144; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f7) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 164; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f8) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID

NO: 168; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f9) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 142; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f10) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 142; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 299;

(f11) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 144; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f12) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 164; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f13) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 168; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f14) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f15) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID

NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 299;

(f16) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 301;

(f17) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 302;

(f18) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 304;

(f19) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 306;

(f20) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 307;

(f21) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 309;

(f22) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID

NO: 122; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f23) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 129; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f24) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 132; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f25) an H-chain variable region comprised in the antibody variable region of (1) in [1] and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in [1] and identical to the amino acid sequence of SEQ ID NO: 424; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53; and

(f26) multispecific antigen-binding molecule that binds to an epitope overlapping with each of the epitopes on glypican 3 and T-cell receptor complex bound by the multispecific antigen-binding molecule of any one of (f1) to (f25), and which has a common L chain.

[16] The multispecific antigen-binding molecule of any one of [1] to [15], wherein the Fc region of (3) in [1] is an Fc region with an amino acid mutation at any of the Fc region-constituting amino acids of SEQ ID NOs: 23 to 26 (IgG1 to IgG4).

[17] The multispecific antigen-binding molecule of [16], wherein the Fc region of (3) in [1] is an Fc region with mutation of at least one amino acid selected from the following amino acid positions specified by EU numbering:

position 220, position 226, position 229, position 231, position 232, position 233, position 234, position 235, position 236, position 237, position 238, position 239, position 240, position 264, position 265, position 266, position 267, position 269, position 270, position 295, position 296, position 297, position 298, position 299, position 300, position 325, position 327, position 328, position 329, position 330, position 331, and position 332.

[18] The multispecific antigen-binding molecule of [16], wherein the Fc region of (3) in [1] is an Fc region comprising at least one amino acid selected from the following amino acids specified by EU numbering:

Arg at amino acid position 234, Ala or Arg at amino acid position 235, Lys at amino acid position 239, and Ala at amino acid position 297.

[19] The multispecific antigen-binding molecule of any one of [16] to [18], wherein the Fc region of (3) in [1] further comprises an amino acid mutation for promoting formation of a heterodimeric Fc region.

[20] The multispecific antigen-binding molecule of [19], wherein the heterodimeric Fc region is the amino acid sequence combination of (g1) or (g2) below:

(g1) a combination of an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 57, and an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 58; and

(g2) a combination of an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 60 or 62, and an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 61.

[21] The multispecific antigen-binding molecule of any one of [1] to [20], wherein the multispecific antigen-binding molecule is a bispecific antibody.

[22] A bispecific antibody of any one of (h1) to (h25) below:

(h1) a bispecific antibody having an antibody H chain having glypican 3-binding activitythat comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 424 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h2) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h3) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 299;

(h4) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 301;

(h5) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 302;

(h6) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 304;

(h7) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 306;

(h8) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 307;

(h9) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 309;

(h10) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 122 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h11) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 129 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h12) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 132 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h13) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 299;

(h14) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 310;

(h15) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 319;

(h16) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h17) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 142 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 299;

(h18) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 142 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h19) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 144 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h20) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 144 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h21) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 142 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h22) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 164 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h23) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 168 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h24) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 164 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223; and

(h25) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 168 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223.

[23] A nucleic acid that encodes the multispecific antigen-binding molecule of any one of [1] to [20] or the bispecific antibody of [21] or [22].

[24] A vector into which the nucleic acid of [23] is introduced.

[25] A cell comprising the nucleic acid of [23] or the vector of [24].

[26] A method for producing the multispecific antigen-binding molecule of any one of [1] to [20] or the bispecific antibody of [21] or [22] by culturing the cell of [25].

[27] A multispecific antigen-binding molecule or a bispecific antibody produced by the method of [26].

[28] A pharmaceutical composition comprising the multispecific antigen-binding molecule of any one of [1] to [20] or the bispecific antibody of [21] or [22], and a pharmaceutically acceptable carrier.

[29] The pharmaceutical composition of [28], which induces cytotoxicity.

[30] The pharmaceutical composition of [29], wherein the cytotoxicity is T-cell-dependent cytotoxicity.

[31] The pharmaceutical composition of [28], which is for administration to a patient in need of the multispecific antigen-binding molecule of any one of [1] to [20] or the bispecific antibody of [21] or [22].

Furthermore, the present invention relates to a kit to be used in a method of the present invention, wherein the kit comprises a multispecific antigen-binding molecule of the present invention, or a multispecific antigen-binding molecule produced by the production method of the present invention. The present invention also relates to use of a multispecific antigen-binding

molecule of the present invention, or use of a multispecific antigen-binding molecule produced by the production method of the present invention in the manufacture of a pharmaceutical composition for activating cytotoxic activity. The present invention additionally relates to a multispecific antigen-binding molecule of the present invention, or a multispecific antigen-binding molecule produced by the production method of the present invention to be used in a method of the present invention. Herein, multispecific antigen-binding molecules include bispecific antibodies of the present invention.

Furthermore, the present invention relates to a multispecific antigen-binding molecule comprising the following domains:

(1) a domain comprising an antibody variable region having glypican 3-binding activity;

(2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity;

wherein the L-chain variable regions contained in the variable regions of (1) and (2) have a commonly shared amino acid sequence. The present invention also relates to the domain of (1), which is more specifically a domain that comprises antibody heavy-chain and/or light-chain variable regions having glypican 3-binding activity, and which is comprised in the multispecific antigen-binding molecule. The present invention additionally relates to the domain of (2), which is more specifically a domain that comprises an antibody variable region having T-cell receptor complex-binding activity, and which is comprised in the multispecific antigen-binding molecule. Details of the domains of (1) and (2) may include those described in [1] to [22] mentioned above. The multispecific antigen-binding molecule may be a bispecific antibody. Furthermore, the multispecific antigen-binding molecule may further comprise a domain comprising an Fc region, and the Fc region may have a reduced Fcγ receptor-binding activity. Details of the domain comprising an Fc region may include those described in [1] to [22] mentioned above. The present invention relates to a nucleic acid encoding the multispecific antigen-binding molecule or the domains, a vector introduced with the nucleic acid, a cell comprising the nucleic acid or the vector, a method for producing the multispecific antigen-binding molecule by culturing the cells, and a multispecific antigen-binding molecule or domains comprising an antibody variable region having glypican 3-binding activity or T-cell receptor complex-binding activity produced by the method. Furthermore, the present invention relates to a pharmaceutical composition comprising the multispecific antigen-binding molecule and a pharmaceutically acceptable carrier. The pharmaceutical composition may induce cell injury, the cell injury may be T-cell-dependent cellular cytotoxicity, and the composition may be for administration to a patient in need of the multispecific antigen-binding molecule.

The present invention also provides a multispecific antigen-binding molecule that binds to epitopes overlapping and/or competing with epitopes on each of glypican 3 and T-cell

receptor complex bound by the multispecific antigen-binding molecule of any one of (e1) to (e25) of [14] mentioned above, and a multispecific antigen-binding molecule that binds to epitopes overlapping and/or competing with epitopes on each of glypican 3 and T-cell receptor complex bound by the multispecific antigen-binding molecule of any one of (f1) to (f25) of [15].

Regarding (g1) and (g2) of [20] mentioned above, of the two Fc regions, the former Fc region may be included in the antibody H chain having glypican 3-binding activity and the latter Fc region may be included in the antibody H chain having T-cell receptor complex-binding activity; or the former Fc region may be included in the antibody H chain having T-cell receptor complex-binding activity and the latter Fc region may be included in the antibody H chain having glypican 3-binding activity.

[Effects of the Invention]

The present invention provides novel multispecific antigen-binding molecules with molecular forms that can be produced with high efficiency, which maintain the strong antitumor activity possessed by BiTE and the excellent safety property of not causing cancer antigen-independent induction of a cytokine storm and such, and have long half-lives in blood. Pharmaceutical compositions that activate cytotoxic activity, which comprise a multispecific antigen-binding molecule of the present invention as active ingredient, target cancer tissues containing glypican 3-expressing cancer cells to cause cell injury, and can treat or prevent various cancers. The invention enables desirable treatment which has not only a high level of safety but also reduced physical burden, and is highly convenient for patients.

Brief Description of the Drawings

Fig. 1 shows schematic diagrams of a: ERY22 and b: ERY27.

Fig. 2 is a graph showing the cytotoxic activities of GPC3_ERY22_rCE115 and GPC3_ERY27_hCE115 when NCI-H446 is used as the target cell. The filled diamond (♦) and the filled triangle (▲) indicate the cytotoxic activity of GPC3_ERY22_rCE115 and GPC3_ERY27_hCE115, respectively.

Fig. 3 is a graph showing the cytotoxic activities of GPC3_ERY22_rCE115 and GPC3_ERY27_hCE115 when PC-10 is used as the target cell. The filled diamond (♦) and the filled triangle (▲) indicate the cytotoxic activity of GPC3_ERY22_rCE115 and GPC3_ERY27_hCE115, respectively.

Fig. 4 is a graph showing the cytotoxic activities of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 5 is a graph showing the cytotoxic activities of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 6 is a graph showing the cytotoxic activities of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 7 is a graph showing the cytotoxic activities of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 8 is a graph showing the cytotoxic activities of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 9 is a graph showing the cytotoxic activities of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 10 shows the *in vivo* antitumor effects of the optimized antibodies when PC-10 is used as the target cell.

Fig. 11 shows the *in vivo* antitumor effects of the optimized antibodies when NCI-H446 is used as the target cell.

Fig. 12 shows the relationship between the amino acid residues constituting the Fc regions of IgG1, IgG2, IgG3, and IgG4, and the Kabat EU numbering system (herein, also referred to as EU INDEX).

Fig. 13-1 shows the heavy-chain variable region sequences and their numbering according to Kabat *et al.*

Fig. 13-2 shows the heavy-chain variable region sequences and their numbering according to Kabat *et al.*

Fig. 14 shows the light-chain variable region sequences and their numbering according to Kabat *et al.*

Mode for Carrying Out the Invention

The definitions below are provided to help understanding of the present invention illustrated herein.

Antibody

Herein, "antibody" refers to a natural immunoglobulin or an immunoglobulin produced by partial or complete synthesis. Antibodies can be isolated from natural sources such as naturally-occurring plasma and serum, or culture supernatants of antibody-producing hybridomas. Alternatively, antibodies can be partially or completely synthesized using techniques such as genetic recombination. Preferred antibodies include, for example, antibodies of an immunoglobulin isotype or subclass belonging thereto. Known human immunoglobulins include antibodies of the following nine classes (isotypes): IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD, IgE, and IgM. Of these isotypes, antibodies of the present invention include IgG1, IgG2, IgG3, and IgG4.

Methods for producing an antibody with desired binding activity are known to those skilled in the art. Below is an example that describes a method for producing an antibody (anti-GPC3 antibody) that binds to Glypican-3 (hereinafter, also referred to as GPC3), which belongs to the GPI-anchored receptor family (Int J Cancer. (2003) 103(4), 455-65). Antibodies that bind to a T-cell receptor complex can also be produced according to the example described below.

Anti-GPC3 antibodies can be obtained as polyclonal or monoclonal antibodies using known methods. The anti-GPC3 antibodies preferably produced are monoclonal antibodies derived from mammals. Such mammal-derived monoclonal antibodies include antibodies produced by hybridomas or host cells transformed with an expression vector carrying an antibody gene by genetic engineering techniques.

Monoclonal antibody-producing hybridomas can be produced using known techniques, for example, as described below. Specifically, mammals are immunized by conventional immunization methods using a GPC3 protein as a sensitizing antigen. Resulting immune cells are fused with known parental cells by conventional cell fusion methods. Then, hybridomas producing an anti-GPC3 antibody can be selected by screening for monoclonal antibody-producing cells using conventional screening methods.

Specifically, monoclonal antibodies are prepared as mentioned below. First, the GPC3 gene whose nucleotide sequence is disclosed in RefSeq accession number NM_001164617.1 (SEQ ID NO: 1) can be expressed to produce a GPC3 protein shown in RefSeq accession number NP_001158089.1 (SEQ ID NO: 2), which will be used as a sensitizing antigen for antibody preparation. That is, a gene sequence encoding GPC3 is inserted into a known expression vector, and appropriate host cells are transformed with this vector. The desired human GPC3 protein is purified from the host cells or their culture supernatants by known methods. For example, to prepare soluble GPC3 from culture supernatants, amino acids at positions 564 to 580 that form the hydrophobic region corresponding to the GPI-anchor sequence used to anchor GPC3 on the cell membrane are deleted from the GPC3 polypeptide sequence of SEQ ID NO: 2, and then the resulting protein is expressed instead of the GPC3 protein of SEQ ID NO: 2. Alternatively, it is possible to use a purified natural GPC3 protein as a sensitizing antigen.

The purified GPC3 protein can be used as a sensitizing antigen for use in immunization of mammals. Partial peptides of GPC3 can also be used as sensitizing antigens. In this case, the partial peptides may also be obtained by chemical synthesis from the human GPC3 amino acid sequence. Furthermore, they may also be obtained by incorporating a portion of the GPC3 gene into an expression vector and expressing it. Moreover, they may also be obtained by degrading the GPC3 protein using proteases, but the region and size of the GPC3 peptide used as the partial peptide are not particularly limited to a special embodiment. As the preferred region, any

sequence from the amino acid sequence corresponding to the amino acids at positions 524 to 563, or more preferably any sequence from the amino acid sequence corresponding to the amino acids at positions 537 to 563 in the amino acid sequence of SEQ ID NO: 2 may be selected. Preferably, any sequence may be selected from the amino acid sequence of the region not containing the amino acid sequence corresponding to amino acids at positions 550 to 663 in the amino acid sequence of SEQ ID NO: 2. Preferably, any sequence may be selected from the amino acid sequence corresponding to positions 544 to 553, and more preferably, any sequence may be selected from the amino acid sequence corresponding to positions 546 to 551 in the amino acid sequence of SEQ ID NO: 2. The number of amino acids constituting a peptide to be used as the sensitizing antigen is at least five or more, or preferably for example, six or more, or seven or more. More specifically, peptides consisting of 8 to 50 residues or preferably 10 to 30 residues may be used as the sensitizing antigen.

For sensitizing antigen, alternatively it is possible to use a fusion protein prepared by fusing a desired partial polypeptide or peptide of the GPC3 protein with a different polypeptide. For example, antibody Fc fragments and peptide tags are preferably used to produce fusion proteins to be used as sensitizing antigens. Vectors for expression of such fusion proteins can be constructed by fusing in frame genes encoding two or more desired polypeptide fragments and inserting the fusion gene into an expression vector as described above. Methods for producing fusion proteins are described in Molecular Cloning 2nd ed. (Sambrook, J *et al*., Molecular Cloning 2nd ed., 9.47-9.58 (1989) Cold Spring Harbor Lab. Press). Methods for preparing GPC3 to be used as a sensitizing antigen, and immunization methods using GPC3 are specifically described in WO 2003/000883, WO 2004/022754, and WO 2006/006693.

There is no particular limitation on the mammals to be immunized with the sensitizing antigen. However, it is preferable to select the mammals by considering their compatibility with the parent cells to be used for cell fusion. In general, rodents such as mice, rats, and hamsters, rabbits, and monkeys are preferably used.

The above animals are immunized with a sensitizing antigen by known methods. Generally performed immunization methods include, for example, intraperitoneal or subcutaneous injection of a sensitizing antigen into mammals. Specifically, a sensitizing antigen is appropriately diluted with PBS (Phosphate-Buffered Saline), physiological saline, or the like. If desired, a conventional adjuvant such as Freund's complete adjuvant is mixed with the antigen, and the mixture is emulsified. Then, the sensitizing antigen is administered to a mammal several times at 4- to 21-day intervals. Appropriate carriers may be used in immunization with the sensitizing antigen. In particular, when a low-molecular-weight partial peptide is used as the sensitizing antigen, it is sometimes desirable to couple the sensitizing antigen peptide to a carrier protein such as albumin or keyhole limpet hemocyanin for immunization.

Alternatively, hybridomas producing a desired antibody can be prepared using DNA immunization as mentioned below. DNA immunization is an immunization method that confers immunostimulation by expressing a sensitizing antigen in an animal immunized as a result of administering a vector DNA constructed to allow expression of an antigen protein-encoding gene in the animal. As compared to conventional immunization methods in which a protein antigen is administered to animals to be immunized, DNA immunization is expected to be superior in that:

- immunostimulation can be provided while retaining the structure of a membrane protein such as GPC3; and
- there is no need to purify the antigen for immunization.

In order to prepare a monoclonal antibody of the present invention using DNA immunization, first, a DNA expressing a GPC3 protein is administered to an animal to be immunized. The GPC3-encoding DNA can be synthesized by known methods such as PCR. The obtained DNA is inserted into an appropriate expression vector, and then this is administered to an animal to be immunized. Preferably used expression vectors include, for example, commercially-available expression vectors such as pcDNA3.1. Vectors can be administered to an organism using conventional methods. For example, DNA immunization is performed by using a gene gun to introduce expression vector-coated gold particles into cells in the body of an animal to be immunized. Antibodies that recognized GPC3 can also be produced by the methods described in WO 2003/104453.

After immunizing a mammal as described above, an increase in the titer of a GPC3-binding antibody is confirmed in the serum. Then, immune cells are collected from the mammal, and then subjected to cell fusion. In particular, splenocytes are preferably used as immune cells.

A mammalian myeloma cell is used as a cell to be fused with the above-mentioned immunocyte. The myeloma cells preferably comprise a suitable selection marker for screening. A selection marker confers characteristics to cells for their survival (or death) under a specific culture condition. Hypoxanthine-guanine phosphoribosyltransferase deficiency (hereinafter abbreviated as HGPRT deficiency) and thymidine kinase deficiency (hereinafter abbreviated as TK deficiency) are known as selection markers. Cells with HGPRT or TK deficiency have hypoxanthine-aminopterin-thymidine sensitivity (hereinafter abbreviated as HAT sensitivity). HAT-sensitive cells cannot synthesize DNA in a HAT selection medium, and are thus killed. However, when the cells are fused with normal cells, they can continue DNA synthesis using the salvage pathway of the normal cells, and therefore they can grow even in the HAT selection medium.

HGPRT-deficient and TK-deficient cells can be selected in a medium containing 6-thioguanine, 8-azaguanine (hereinafter abbreviated as 8AG), or 5'-bromodeoxyuridine, respectively. Normal cells are killed because they incorporate these pyrimidine analogs into

their DNA. Meanwhile, cells that are deficient in these enzymes can survive in the selection medium, since they cannot incorporate these pyrimidine analogs. In addition, a selection marker referred to as G418 resistance provided by the neomycin-resistant gene confers resistance to 2-deoxystreptamine antibiotics (gentamycin analogs). Various types of myeloma cells that are suitable for cell fusion are known.

For example, myeloma cells including the following cells can be preferably used:
P3(P3x63Ag8.653) (J. Immunol. (1979) 123 (4), 1548-1550);
P3x63Ag8U.1 (Current Topics in Microbiology and Immunology (1978)81, 1-7);
NS-1 (C. Eur. J. Immunol. (1976)6 (7), 511-519);
MPC-11 (Cell (1976) 8 (3), 405-415);
SP2/0 (Nature (1978) 276 (5685), 269-270);
FO (J. Immunol. Methods (1980) 35 (1-2), 1-21);
S194/5.XX0.BU.1 (J. Exp. Med. (1978) 148 (1), 313-323);
R210 (Nature (1979) 277 (5692), 131-133), etc.

Cell fusions between the immunocytes and myeloma cells are essentially carried out using known methods, for example, a method by Kohler and Milstein *et al.* (Methods Enzymol. (1981) 73: 3-46).

More specifically, cell fusion can be carried out, for example, in a conventional culture medium in the presence of a cell fusion-promoting agent. The fusion-promoting agents include, for example, polyethylene glycol (PEG) and Sendai virus (HVJ). If required, an auxiliary substance such as dimethyl sulfoxide is also added to improve fusion efficiency.

The ratio of immunocytes to myeloma cells may be determined at one's own discretion, preferably, for example, one myeloma cell for every one to ten immunocytes. Culture media to be used for cell fusions include, for example, media that are suitable for the growth of myeloma cell lines, such as RPMI1640 medium and MEM medium, and other conventional culture medium used for this type of cell culture. In addition, serum supplements such as fetal calf serum (FCS) may be preferably added to the culture medium.

For cell fusion, predetermined amounts of the above immune cells and myeloma cells are mixed well in the above culture medium. Then, a PEG solution (for example, the average molecular weight is about 1,000 to 6,000) prewarmed to about 37°C is added thereto at a concentration of generally 30% to 60% (w/v). This is gently mixed to produce desired fusion cells (hybridomas). Then, an appropriate culture medium mentioned above is gradually added to the cells, and this is repeatedly centrifuged to remove the supernatant. Thus, cell fusion agents and such which are unfavorable to hybridoma growth can be removed.

The hybridomas thus obtained can be selected by culture using a conventional selective medium, for example, HAT medium (a culture medium containing hypoxanthine, aminopterin,

and thymidine). Cells other than the desired hybridomas (non-fused cells) can be killed by continuing culture in the above HAT medium for a sufficient period of time. Typically, the period is several days to several weeks. Then, hybridomas producing the desired antibody are screened and singly cloned by conventional limiting dilution methods.

The hybridomas thus obtained can be selected using a selection medium based on the selection marker possessed by the myeloma used for cell fusion. For example, HGPRT- or TK-deficient cells can be selected by culture using the HAT medium (a culture medium containing hypoxanthine, aminopterin, and thymidine). Specifically, when HAT-sensitive myeloma cells are used for cell fusion, cells successfully fused with normal cells can selectively proliferate in the HAT medium. Cells other than the desired hybridomas (non-fused cells) can be killed by continuing culture in the above HAT medium for a sufficient period of time. Specifically, desired hybridomas can be selected by culture for generally several days to several weeks. Then, hybridomas producing the desired antibody are screened and singly cloned by conventional limiting dilution methods.

Desired antibodies can be preferably selected and singly cloned by screening methods based on known antigen/antibody reaction. For example, a GPC3-binding monoclonal antibody can bind to GPC3 expressed on the cell surface. Such a monoclonal antibody can be screened by fluorescence activated cell sorting (FACS). FACS is a system that assesses the binding of an antibody to cell surface by analyzing cells contacted with a fluorescent antibody using laser beam, and measuring the fluorescence emitted from individual cells.

To screen for hybridomas that produce a monoclonal antibody of the present invention by FACS, GPC3-expressing cells are first prepared. Cells preferably used for screening are mammalian cells in which GPC3 is forcedly expressed. As control, the activity of an antibody to bind to cell-surface GPC3 can be selectively detected using non-transformed mammalian cells as host cells. Specifically, hybridomas producing an anti-GPC3 monoclonal antibody can be isolated by selecting hybridomas that produce an antibody which binds to cells forced to express GPC3, but not to host cells.

Alternatively, the activity of an antibody to bind to immobilized GPC3-expressing cells can be assessed based on the principle of ELISA. For example, GPC3-expressing cells are immobilized to the wells of an ELISA plate. Culture supernatants of hybridomas are contacted with the immobilized cells in the wells, and antibodies that bind to the immobilized cells are detected. When the monoclonal antibodies are derived from mouse, antibodies bound to the cells can be detected using an anti-mouse immunoglobulin antibody. Hybridomas producing a desired antibody having the antigen-binding ability are selected by the above screening, and they can be cloned by a limiting dilution method or the like.

Monoclonal antibody-producing hybridomas thus prepared can be passaged in a

conventional culture medium, and stored in liquid nitrogen for a long period.

The above hybridomas are cultured by a conventional method, and desired monoclonal antibodies can be prepared from the culture supernatants. Alternatively, the hybridomas are administered to and grown in compatible mammals, and monoclonal antibodies are prepared from the ascites. The former method is suitable for preparing antibodies with high purity.

Antibodies encoded by antibody genes that are cloned from antibody-producing cells such as the above hybridomas can also be preferably used. A cloned antibody gene is inserted into an appropriate vector, and this is introduced into a host to express the antibody encoded by the gene. Methods for isolating antibody genes, inserting the genes into vectors, and transforming host cells have already been established, for example, by Vandamme *et al*. (Eur. J. Biochem. (1990) 192(3), 767-775). Methods for producing recombinant antibodies are also known as described below.

For example, a cDNA encoding the variable region (V region) of an anti-GPC3 antibody is prepared from hybridoma cells expressing the anti-GPC3 antibody. For this purpose, total RNA is first extracted from hybridomas. Methods used for extracting mRNAs from cells include, for example:

- the guanidine ultracentrifugation method (Biochemistry (1979) 18(24), 5294-5299), and
- the AGPC method (Anal. Biochem. (1987) 162(1), 156-159)

Extracted mRNAs can be purified using the mRNA Purification Kit (GE Healthcare Bioscience) or such. Alternatively, kits for extracting total mRNA directly from cells, such as the QuickPrep mRNA Purification Kit (GE Healthcare Bioscience), are also commercially available. mRNAs can be prepared from hybridomas using such kits. cDNAs encoding the antibody V region can be synthesized from the prepared mRNAs using a reverse transcriptase. cDNAs can be synthesized using the AMV Reverse Transcriptase First-strand cDNA Synthesis Kit (Seikagaku Co.) or such. Furthermore, the SMART RACE cDNA amplification kit (Clontech) and the PCR-based 5'-RACE method (Proc. Natl. Acad. Sci. USA (1988) 85(23), 8998-9002; Nucleic Acids Res. (1989) 17(8), 2919-2932) can be appropriately used to synthesize and amplify cDNAs. In such a cDNA synthesis process, appropriate restriction enzyme sites described below may be introduced into both ends of a cDNA.

The cDNA fragment of interest is purified from the resulting PCR product, and then this is ligated to a vector DNA. A recombinant vector is thus constructed, and introduced into *E. coli* or such. After colony selection, the desired recombinant vector can be prepared from the colony-forming *E. coli*. Then, whether the recombinant vector has the cDNA nucleotide sequence of interest is tested by a known method such as the dideoxy nucleotide chain termination method.

The 5'-RACE method which uses primers to amplify the variable region gene is conveniently used for isolating the gene encoding the variable region. First, a 5'-RACE cDNA

library is constructed by cDNA synthesis using RNAs extracted from hybridoma cells as a template. A commercially available kit such as the SMART RACE cDNA amplification kit is appropriately used to synthesize the 5'-RACE cDNA library.

The antibody gene is amplified by PCR using the prepared 5'-RACE cDNA library as a template. Primers for amplifying the mouse antibody gene can be designed based on known antibody gene sequences. The nucleotide sequences of the primers vary depending on the immunoglobulin subclass. Therefore, it is preferable that the subclass is determined in advance using a commercially available kit such as the Iso Strip mouse monoclonal antibody isotyping kit (Roche Diagnostics).

Specifically, for example, primers that allow amplification of genes encoding γ1, γ2a, γ2b, and γ3 heavy chains and κ and λ light chains are used to isolate mouse IgG-encoding genes. In general, a primer that anneals to a constant region site close to the variable region is used as a 3'-side primer to amplify an IgG variable region gene. Meanwhile, a primer attached to a 5' RACE cDNA library construction kit is used as a 5'-side primer.

PCR products thus amplified are used to reshape immunoglobulins composed of a combination of heavy and light chains. A desired antibody can be selected using the GPC3-binding activity of a reshaped immunoglobulin as an indicator. For example, when the objective is to isolate an antibody against GPC3, it is more preferred that the binding of the antibody to GPC3 is specific. A GPC3-binding antibody can be screened, for example, by the following steps:

(1) contacting a GPC3-expressing cell with an antibody comprising the V region encoded by a cDNA isolated from a hybridoma;

(2) detecting the binding of the antibody to the GPC3-expressing cell; and

(3) selecting an antibody that binds to the GPC3-expressing cell.

Methods for detecting the binding of an antibody to GPC3-expressing cells are known. Specifically, the binding of an antibody to GPC3-expressing cells can be detected by the above-described techniques such as FACS. Immobilized samples of GPC3-expressing cells are appropriately used to assess the binding activity of an antibody.

Preferred antibody screening methods that use the binding activity as an indicator also include panning methods using phage vectors. Screening methods using phage vectors are advantageous when the antibody genes are isolated from heavy-chain and light-chain subclass libraries from a polyclonal antibody-expressing cell population. Genes encoding the heavy-chain and light-chain variable regions can be linked by an appropriate linker sequence to form a single-chain Fv (scFv). Phages presenting scFv on their surface can be produced by inserting a gene encoding scFv into a phage vector. The phages are contacted with an antigen of interest. Then, a DNA encoding scFv having the binding activity of interest can be isolated by collecting

phages bound to the antigen. This process can be repeated as necessary to enrich scFv having a desired binding activity.

After isolation of the cDNA encoding the V region of the anti-GPC3 antibody of interest, the cDNA is digested with restriction enzymes that recognize the restriction sites introduced into both ends of the cDNA. Preferred restriction enzymes recognize and cleave a nucleotide sequence that occurs in the nucleotide sequence of the antibody gene at a low frequency. Furthermore, a restriction site for an enzyme that produces a sticky end is preferably introduced into a vector to insert a single-copy digested fragment in the correct orientation. The cDNA encoding the V region of the anti-GPC3 antibody is digested as described above, and this is inserted into an appropriate expression vector to construct an antibody expression vector. In this case, if a gene encoding the antibody constant region (C region) and a gene encoding the above V region are fused in-frame, a chimeric antibody is obtained. Herein, "chimeric antibody" means that the origin of the constant region is different from that of the variable region. Thus, in addition to mouse/human heterochimeric antibodies, human/human allochimeric antibodies are included in the chimeric antibodies of the present invention. A chimeric antibody expression vector can be constructed by inserting the above V region gene into an expression vector that already has the constant region. Specifically, for example, a recognition sequence for a restriction enzyme that excises the above V region gene can be appropriately placed on the 5' side of an expression vector carrying a DNA encoding a desired antibody constant region (C region). A chimeric antibody expression vector is constructed by fusing in frame the two genes digested with the same combination of restriction enzymes.

To produce an anti-GPC3 monoclonal antibody, antibody genes are inserted into an expression vector so that the genes are expressed under the control of an expression regulatory region. The expression regulatory region for antibody expression includes, for example, enhancers and promoters. Furthermore, an appropriate signal sequence may be attached to the amino terminus so that the expressed antibody is secreted to the outside of cells. In the Examples described below, a peptide having the amino acid sequence MGWSCIILFLVATATGVHS (SEQ ID NO: 3) is used as a signal sequence. Meanwhile, other appropriate signal sequences may be attached. The expressed polypeptide is cleaved at the carboxyl terminus of the above sequence, and the resulting polypeptide is secreted to the outside of cells as a mature polypeptide. Then, appropriate host cells are transformed with the expression vector, and recombinant cells expressing the anti-GPC3 antibody-encoding DNA are obtained.

DNAs encoding the antibody heavy chain (H chain) and light chain (L chain) are separately inserted into different expression vectors to express the antibody gene. An antibody molecule having the H and L chains can be expressed by co-transfecting the same host cell with

vectors into which the H-chain and L-chain genes are respectively inserted. Alternatively, host cells can be transformed with a single expression vector into which DNAs encoding the H and L chains are inserted (see WO 94/11523).

There are various known host cell/expression vector combinations for antibody preparation by introducing isolated antibody genes into appropriate hosts. All of these expression systems are applicable to isolation of domains including antibody variable regions of the present invention. Appropriate eukaryotic cells used as host cells include animal cells, plant cells, and fungal cells. Specifically, the animal cells include, for example, the following cells.
(1) mammalian cells: CHO, COS, myeloma, baby hamster kidney (BHK), HeLa, Vero, or such;
(2) amphibian cells: Xenopus oocytes, or such; and
(3) insect cells: sf9, sf21, Tn5, or such.

In addition, as a plant cell, an antibody gene expression system using cells derived from the *Nicotiana* genus such as *Nicotiana tabacum* is known. Callus cultured cells can be appropriately used to transform plant cells.

Furthermore, the following cells can be used as fungal cells:
yeasts: the *Saccharomyces* genus such as *Saccharomyces cerevisiae*, and the *Pichia* genus such as *Pichia pastoris*; and
filamentous fungi: the *Aspergillus* genus such as *Aspergillus niger*.

Furthermore, antibody gene expression systems that utilize prokaryotic cells are also known. For example, when using bacterial cells, *E. coli* cells, *Bacillus subtilis* cells, and such can suitably be utilized in the present invention. Expression vectors carrying the antibody genes of interest are introduced into these cells by transfection. The transfected cells are cultured *in vitro*, and the desired antibody can be prepared from the culture of transformed cells.

In addition to the above-described host cells, transgenic animals can also be used to produce a recombinant antibody. That is, the antibody can be obtained from an animal into which the gene encoding the antibody of interest is introduced. For example, the antibody gene can be constructed as a fusion gene by inserting in frame into a gene that encodes a protein produced specifically in milk. Goat β-casein or such can be used, for example, as the protein secreted in milk. DNA fragments containing the fused gene inserted with the antibody gene is injected into a goat embryo, and then this embryo is introduced into a female goat. Desired antibodies can be obtained as a protein fused with the milk protein from milk produced by the transgenic goat born from the embryo-recipient goat (or progeny thereof). In addition, to increase the volume of milk containing the desired antibody produced by the transgenic goat, hormones can be administered to the transgenic goat as necessary (Ebert, K. M. *et al.*, Bio/Technology (1994) 12 (7), 699-702).

When an antigen-binding molecule described herein is administered to human, a domain

derived from a genetically recombinant antibody that has been artificially modified to reduce the heterologous antigenicity against human and such, can be appropriately used as the domain of the antigen-binding molecule including an antibody variable region. Such genetically recombinant antibodies include, for example, humanized antibodies. These modified antibodies are appropriately produced by known methods.

An antibody variable region used to produce a domain of an antigen-binding molecule including an antibody variable region described herein is generally formed by three complementarity-determining regions (CDRs) that are separated by four framework regions (FRs). CDR is a region that substantially determines the binding specificity of an antibody. The amino acid sequences of CDRs are highly diverse. On the other hand, the FR-forming amino acid sequences often have high identity even among antibodies with different binding specificities. Therefore, generally, the binding specificity of a certain antibody can be introduced to another antibody by CDR grafting.

A humanized antibody is also called a reshaped human antibody. Specifically, humanized antibodies prepared by grafting the CDR of a non-human animal antibody such as a mouse antibody to a human antibody and such are known. Common genetic engineering techniques for obtaining humanized antibodies are also known. Specifically, for example, overlap extension PCR is known as a method for grafting a mouse antibody CDR to a human FR. In overlap extension PCR, a nucleotide sequence encoding a mouse antibody CDR to be grafted is added to primers for synthesizing a human antibody FR. Primers are prepared for each of the four FRs. It is generally considered that when grafting a mouse CDR to a human FR, selecting a human FR that has high identity to a mouse FR is advantageous for maintaining the CDR function. That is, it is generally preferable to use a human FR comprising an amino acid sequence which has high identity to the amino acid sequence of the FR adjacent to the mouse CDR to be grafted.

Nucleotide sequences to be ligated are designed so that they will be connected to each other in frame. Human FRs are individually synthesized using the respective primers. As a result, products in which the mouse CDR-encoding DNA is attached to the individual FR-encoding DNAs are obtained. Nucleotide sequences encoding the mouse CDR of each product are designed so that they overlap with each other. Then, complementary strand synthesis reaction is conducted to anneal the overlapping CDR regions of the products synthesized using a human antibody gene as template. Human FRs are ligated *via* the mouse CDR sequences by this reaction.

The full length V region gene, in which three CDRs and four FRs are ultimately ligated, is amplified using primers that anneal to its 5'- or 3'-end, which are added with suitable restriction enzyme recognition sequences. An expression vector for humanized antibody can be

produced by inserting the DNA obtained as described above and a DNA that encodes a human antibody C region into an expression vector so that they will ligate in frame. After the recombinant vector is transfected into a host to establish recombinant cells, the recombinant cells are cultured, and the DNA encoding the humanized antibody is expressed to produce the humanized antibody in the cell culture (see, European Patent Publication No. EP 239400 and International Patent Publication No. WO 1996/002576).

By qualitatively or quantitatively measuring and evaluating the antigen-binding activity of the humanized antibody produced as described above, one can suitably select human antibody FRs that allow CDRs to form a favorable antigen-binding site when ligated through the CDRs. Amino acid residues in FRs may be substituted as necessary, so that the CDRs of a reshaped human antibody form an appropriate antigen-binding site. For example, amino acid sequence mutations can be introduced into FRs by applying the PCR method used for grafting a mouse CDR into a human FR. More specifically, partial nucleotide sequence mutations can be introduced into primers that anneal to the FR. Nucleotide sequence mutations are introduced into the FRs synthesized by using such primers. Mutant FR sequences having the desired characteristics can be selected by measuring and evaluating the activity of the amino acid-substituted mutant antibody to bind to the antigen by the above-mentioned method (Sato, K. *et al.*, Cancer Res. (1993) 53: 851-856).

Alternatively, desired human antibodies can be obtained by immunizing transgenic animals having the entire repertoire of human antibody genes (see WO 1993/012227; WO 1992/003918; WO 1994/002602; WO 1994/025585; WO 1996/034096; WO 1996/033735) by DNA immunization.

Furthermore, techniques for preparing human antibodies by panning using human antibody libraries are also known. For example, the V region of a human antibody is expressed as a single-chain antibody (scFv) on phage surface by the phage display method. Phages expressing an scFv that binds to the antigen can be selected. The DNA sequence encoding the human antibody V region that binds to the antigen can be determined by analyzing the genes of selected phages. The DNA sequence of the scFv that binds to the antigen is determined. An expression vector is prepared by fusing the V region sequence in frame with the C region sequence of a desired human antibody, and inserting this into an appropriate expression vector. The expression vector is introduced into cells appropriate for expression such as those described above. The human antibody can be produced by expressing the human antibody-encoding gene in the cells. These methods are already known (see WO 1992/001047; WO 1992/020791; WO 1993/006213; WO 1993/011236; WO 1993/019172; WO 1995/001438; WO 1995/015388).

A domain comprising an antibody variable region having glypican 3 (GPC3)-binding activity

Herein, the phrase "a domain comprising an antibody variable region having glypican 3 (GPC3)-binding activity" refers to an antibody portion that comprises a region that specifically binds to the above-mentioned GPC3 protein, or to all or a portion of a partial peptide of the GPC3 protein, and is also complementary thereto. Domains comprising an antibody variable region may be provided from variable domains of one or a plurality of antibodies. Preferably, domains comprising an antibody variable region comprise antibody light-chain and heavy-chain variable regions (VL and VH). Suitable examples of such domains comprising antibody variable regions include "single chain Fv (scFv)", "single chain antibody", "Fv", "single chain Fv 2 (scFv2)", "Fab", "F(ab')2", etc.

A domain comprising an antibody variable region having T-cell receptor complex-binding activity

Herein, the phrase "a domain comprising an antibody variable region having T-cell receptor complex-binding activity" refers to a T-cell receptor complex-binding antibody portion that comprises a region that specifically binds to all or a portion of a T-cell receptor complex and is also complementary thereto. The T-cell receptor complex may be a T-cell receptor itself, or an adaptor molecule constituting a T-cell receptor complex along with a T-cell receptor. CD3 is suitable as an adaptor molecule.

A domain comprising an antibody variable region that has T-cell receptor-binding activity

Herein, the phrase "a domain comprising an antibody variable region having T-cell receptor-binding activity" refers to a T-cell receptor-binding antibody portion produced by including a region that specifically binds to all or a portion of a T-cell receptor and is also complementary thereto.

The portion of a T cell receptor to which the domain of the present invention binds may be a variable region or a constant region, but an epitope present in the constant region is preferred. Examples of the constant region sequence include the T cell receptor α chain of RefSeq Accession No. CAA26636.1 (SEQ ID NO: 4), the T cell receptor β chain of RefSeq Accession No. C25777 (SEQ ID NO: 5), the T cell receptor γ1 chain of RefSeq Accession No. A26659 (SEQ ID NO: 6), the T cell receptor γ2 chain of RefSeq Accession No. AAB63312.1 (SEQ ID NO: 7), and the T cell receptor δ chain of RefSeq Accession No. AAA61033.1 (SEQ ID NO: 8).

A domain comprising an antibody variable region that has CD3-binding activity

Herein, the phrase "a domain comprising an antibody variable region that has CD3-binding activity" refers to a CD3-binding antibody portion produced by including a region that

specifically binds to all or a portion of CD3 and is also complementary thereto. Preferably, the domain comprises the light-chain and heavy-chain variable regions (VL and VH) of an anti-CD3 antibody. Suitable examples of such a domain include "single chain Fv (scFv)", "single chain antibody", "Fv", "single chain Fv 2 (scFv2)", "Fab", "F(ab')2", etc.

The domain comprising an antibody variable region that has CD3-binding activity of the present invention may be any epitope-binding domain as long as the epitope exists in the γ-chain, δ-chain, or ε-chain sequence that constitutes human CD3. In the present invention, preferably, a domain comprising an anti-CD3 antibody light-chain variable region (VL) and an anti-CD3 antibody heavy-chain variable region (VH) that bind to an epitope present in the extracellular region of the ε chain of the human CD3 complex is suitably used. Besides the anti-CD3 antibody light chain variable region (VL) and anti-CD3 antibody heavy chain variable region (VH) described in the Examples, various known CD3-binding domains containing a CD3-binding antibody light chain variable region (VL) and a CD3-binding antibody heavy chain variable region (VH), and those of the OKT3 antibody (Proc. Natl. Acad. Sci. USA (1980) 77, 4914-4917) are suitably used as such domains. One may appropriately use an antibody variable region-containing domain derived from the anti-CD3 antibody having desired properties, which is obtained by immunizing a desired animal by the above-mentioned method using the γ-chain, δ-chain, or ε-chain constituting the human CD3. Human antibodies and properly humanized antibodies as described above may be appropriately used as the anti-CD3 antibody to give rise to the domain containing the antibody variable region having CD3-binding activity. Regarding the structure of the γ-chain, δ-chain, or ε-chain constituting CD3, their polynucleotide sequences are shown in SEQ ID NOs: 9 (NM_000073.2), 10 (NM_000732.4), and 11 (NM_000733.3), and their polypeptide sequences are shown in SEQ ID NOs: 12 (NP_000064.1), 13 (NP_000723.1), and 14 (NP_000724.1) (the RefSeq accession number is shown in parentheses).

Antibody variable region-containing domains in antigen binding molecules of the present invention may bind to the same epitope. Herein, the same epitope may be present in a protein comprising the amino acid sequence of SEQ ID NO: 2 or 14. Alternatively, antibody variable region-containing domains in antigen binding molecules of the present invention may bind to different epitopes, respectively. Herein, the different epitopes may be present in a protein comprising the amino acid sequence of SEQ ID NO: 2 or 14.

Specific

The term "specific" means that one of molecules involved in specific binding does not show any significant binding to molecules other than a single or a number of binding partner molecules. Furthermore, the term is also used when a domain containing an antibody variable region is specific to a particular epitope among multiple epitopes in an antigen. When an epitope

bound by a domain containing an antibody variable region is included in a number of different antigens, antigen-binding molecules comprising the antibody variable region-containing domain can bind to various antigens that have the epitope.

Epitope

"Epitope" means an antigenic determinant in an antigen, and refers to an antigen site to which a domain of an antigen-binding molecule including an antibody variable region disclosed herein binds. Thus, for example, the epitope can be defined according to its structure. Alternatively, the epitope may be defined according to the antigen-binding activity of an antigen-binding molecule that recognizes the epitope. When the antigen is a peptide or polypeptide, the epitope can be specified by the amino acid residues forming the epitope. Alternatively, when the epitope is a sugar chain, the epitope can be specified by its specific sugar chain structure.

A linear epitope is an epitope that contains an epitope whose primary amino acid sequence is recognized. Such a linear epitope typically contains at least three and most commonly at least five, for example, about 8 to 10 or 6 to 20 amino acids in its specific sequence.

In contrast to the linear epitope, "conformational epitope" is an epitope in which the primary amino acid sequence containing the epitope is not the only determinant of the recognized epitope (for example, the primary amino acid sequence of a conformational epitope is not necessarily recognized by an epitope-defining antibody). Conformational epitopes may contain a greater number of amino acids compared to linear epitopes. A conformational epitope-recognizing antibody recognizes the three-dimensional structure of a peptide or protein. For example, when a protein molecule folds and forms a three-dimensional structure, amino acids and/or polypeptide main chains that form a conformational epitope become aligned, and the epitope is made recognizable by the antibody. Methods for determining epitope conformations include, for example, X ray crystallography, two-dimensional nuclear magnetic resonance, site-specific spin labeling, and electron paramagnetic resonance, but are not limited thereto. See, for example, Epitope Mapping Protocols in Methods in Molecular Biology (1996), Vol. 66, Morris (ed.).

A method for confirming binding to an epitope by a test antigen-binding molecule comprising a domain that contains an antibody variable region having GPC3-binding activity is exemplified below, and a method for confirming binding to an epitope by a test antigen-binding molecule comprising a domain that contains an antibody variable region having T-cell receptor complex-binding activity may also be performed suitably according to the examples below.

For example, recognition of a linear epitope present in the GPC3 molecule by a test antigen-binding molecule comprising a domain that contains an antibody variable region having GPC3-binding activity can be confirmed below. A linear peptide comprising the amino acid

sequence constituting the extracellular domain of GPC3 is synthesized for the above-mentioned objective. The peptide may be synthesized chemically. Alternatively, it can be obtained by genetic engineering methods using a region in the cDNA of GPC3 that encodes an amino acid sequence corresponding to the extracellular domain. Next, the binding activity between a linear peptide comprising the amino acid sequence constituting the extracellular domain and the test antigen-binding molecule comprising a domain that contains an antibody variable region having GPC3-binding activity is evaluated. For example, ELISA which uses an immobilized linear peptide as the antigen may enable evaluation of the binding activity of the antigen-binding molecule towards the peptide. Alternatively, binding activity towards the linear peptide may be elucidated based on the level of inhibition caused by the linear peptide in the binding of the antigen-binding molecule to GPC3-expressing cells. These tests may elucidate the binding activity of the antigen-binding molecules toward the linear peptide.

Furthermore, recognition of the three-dimensional structure of the epitope by a test antigen-binding molecule comprising a domain that contains an antibody variable region having GPC3-binding activity can be confirmed below. GPC3-expressing cells are prepared for the above-mentioned objective. For example, when the test antigen-binding molecule comprising a domain that contains an antibody variable region having GPC3-binding activity contacts GPC3-expressing cells, it binds strongly to the cells, but on the other hand, there are cases when the antigen-binding molecule does not substantially bind to the immobilized linear peptide comprising the amino acid sequence constituting the extracellular domain of GPC3. In these cases, “does not substantially bind” refers to a binding activity of 80% or less, generally 50% or less, preferably 30% or less, and particularly preferably 15% or less relative to the binding activity towards human GPC3-expressing cells.

Methods for assaying the binding activity of a test antigen-binding molecule containing a GPC3 antigen-binding domain towards GPC3-expressing cells include, for example, the methods described in Antibodies: A Laboratory Manual (Ed Harlow, David Lane, Cold Spring Harbor Laboratory (1988) 359-420). Specifically, the assessment can be performed based on the principle of ELISA or fluorescence activated cell sorting (FACS) using GPC3-expressing cells as antigen.

In the ELISA format, the binding activity of a test antigen-binding molecule containing a GPC3 antigen-binding domain towards GPC3-expressing cells can be assessed quantitatively by comparing the levels of signal generated by enzymatic reaction. Specifically, a test antigen-binding molecule is added to an ELISA plate onto which GPC3-expressing cells are immobilized. Then, the test antigen-binding molecule bound to the cells is detected using an enzyme-labeled antibody that recognizes the test antigen-binding molecule. Alternatively, when FACS is used, a dilution series of a test antigen-binding molecule is prepared, and the antibody binding titer for

GPC3-expressing cells can be determined to compare the binding activity of the test antigen-binding molecule towards GPC3-expressing cells.

The binding of a test antigen-binding molecule towards an antigen expressed on the surface of cells suspended in buffer or the like can be detected using a flow cytometer. Known flow cytometers include, for example, the following devices:

FACSCanto™ II
FACSAria™
FACSArray™
FACSVantage™ SE
FACSCalibur™ (all are trade names of BD Biosciences)
EPICS ALTRA HyPerSort
Cytomics FC 500
EPICS XL-MCL ADC EPICS XL ADC
Cell Lab Quanta/Cell Lab Quanta SC (all are trade names of Beckman Coulter)

Preferable methods for assaying the binding activity of a test antigen-binding molecule containing a GPC3 antigen-binding domain towards an antigen include, for example, the following method. First, GPC3-expressing cells are reacted with a test antigen-binding molecule, and then this is stained with an FITC-labeled secondary antibody that recognizes the polypeptide complex. The test antigen-binding molecule is appropriately diluted with a suitable buffer to prepare the complex at a desired concentration. For example, the complex can be used at a concentration within the range of 10 μg/ml to 10 ng/ml. Then, the fluorescence intensity and cell count are determined using FACSCalibur (BD). The fluorescence intensity obtained by analysis using the CELL QUEST Software (BD), i.e., the Geometric Mean value, reflects the quantity of antibody bound to cells. That is, the binding activity of a test antigen-binding molecule, which is represented by the quantity of the test antigen-binding molecule bound, can be determined by measuring the Geometric Mean value.

Whether a test antigen-binding molecule containing a GPC3 antigen-binding domain shares a common epitope with another antigen-binding molecule can be assessed based on the competition between the two complexes for the same epitope. The competition between antigen-binding molecules can be detected by cross-blocking assay or the like. For example, the competitive ELISA assay is a preferred cross-blocking assay.

Specifically, in cross-blocking assay, the GPC3 protein immobilized to the wells of a microtiter plate is pre-incubated in the presence or absence of a candidate competitor antigen-binding molecule, and then a test antigen-binding molecule is added thereto. The quantity of test antigen-binding molecule bound to the GPC3 protein in the wells is indirectly correlated with the binding ability of a candidate competitor antigen-binding molecule that competes for the binding

to the same epitope. That is, the greater the affinity of the competitor antigen-binding molecule for the same epitope, the lower the binding activity of the test antigen-binding molecule towards the GPC3 protein-coated wells.

The quantity of the test antigen-binding molecule bound to the wells via the GPC3 protein can be readily determined by labeling the antigen-binding molecule in advance. For example, a biotin-labeled antigen-binding molecule is measured using an avidin/peroxidase conjugate and appropriate substrate. In particular, cross-blocking assay that uses enzyme labels such as peroxidase is called "competitive ELISA assay". The antigen-binding molecule can also be labeled with other labeling substances that enable detection or measurement. Specifically, radiolabels, fluorescent labels, and such are known.

When the candidate competitor antigen-binding molecule can block the binding by a test antigen-binding molecule containing a GPC3 antigen-binding domain by at least 20%, preferably at least 20 to 50%, and more preferably at least 50% compared to the binding activity in a control experiment conducted in the absence of the competitor antigen-binding molecule, the test antigen-binding molecule is determined to substantially bind to the same epitope bound by the competitor antigen-binding molecule, or compete for the binding to the same epitope.

When the structure of an epitope bound by a test antigen-binding molecule containing a GPC3 antigen-binding domain has already been identified, whether the test and control antigen-binding molecules share a common epitope can be assessed by comparing the binding activities of the two antigen-binding molecules towards a peptide prepared by introducing amino acid mutations into the peptide forming the epitope.

To measure the above binding activities, for example, the binding activities of test and control antigen-binding molecules towards a linear peptide into which a mutation is introduced are compared in the above ELISA format. Besides the ELISA methods, the binding activity towards the mutant peptide bound to a column can be determined by flowing test and control antigen-binding molecules in the column, and then quantifying the antigen-binding molecule eluted in the elution solution. Methods for adsorbing a mutant peptide to a column, for example, in the form of a GST fusion peptide, are known.

Alternatively, when the identified epitope is a conformational epitope, whether test and control antigen-binding molecules share a common epitope can be assessed by the following method. First, GPC3-expressing cells and cells expressing GPC3 with a mutation introduced into the epitope are prepared. The test and control antigen-binding molecules are added to a cell suspension prepared by suspending these cells in an appropriate buffer such as PBS. Then, the cell suspensions are appropriately washed with a buffer, and an FITC-labeled antibody that recognizes the test and control antigen-binding molecules is added thereto. The fluorescence intensity and number of cells stained with the labeled antibody are determined using

FACSCalibur (BD). The test and control polypeptide complexes are appropriately diluted using a suitable buffer, and used at desired concentrations. For example, they may be used at a concentration within the range of 10 μg/ml to 10 ng/ml. The fluorescence intensity determined by analysis using the CELL QUEST Software (BD), i.e., the Geometric Mean value, reflects the quantity of labeled antibody bound to cells. That is, the binding activities of the test and control antigen-binding molecules, which are represented by the quantity of labeled antibody bound, can be determined by measuring the Geometric Mean value.

In the above method, whether an antigen-binding molecule does "not substantially bind to cells expressing mutant GPC3" can be assessed, for example, by the following method. First, the test and control antigen-binding molecules bound to cells expressing mutant GPC3 are stained with a labeled antibody. Then, the fluorescence intensity of the cells is determined. When FACSCalibur is used for fluorescence detection by flow cytometry, the determined fluorescence intensity can be analyzed using the CELL QUEST Software. From the Geometric Mean values in the presence and absence of the antigen-binding molecule, the comparison value (ΔGeo-Mean) can be calculated according to the following formula to determine the ratio of increase in fluorescence intensity as a result of the binding by the antigen-binding molecule.

ΔGeo-Mean = Geo-Mean (in the presence of the antigen-binding molecule)/Geo-Mean (in the absence of the antigen-binding molecule)

The Geometric Mean comparison value (ΔGeo-Mean value for the mutant GPC3 molecule) determined by the above analysis, which reflects the quantity of a test antigen-binding molecule bound to cells expressing mutant GPC3, is compared to the ΔGeo-Mean comparison value that reflects the quantity of the test antigen-binding molecule bound to GPC3-expressing cells. In this case, the concentrations of the test antigen-binding molecule used to determine the ΔGeo-Mean comparison values for GPC3-expressing cells and cells expressing mutant GPC3 are particularly preferably adjusted to be equal or substantially equal. An antigen-binding molecule that has been confirmed to recognize an epitope in GPC3 is used as a control antigen-binding molecule.

If the ΔGeo-Mean comparison value of a test antigen-binding molecule for cells expressing mutant GPC3 is smaller than the ΔGeo-Mean comparison value of the test antigen-binding molecule for GPC3-expressing cells by at least 80%, preferably 50%, more preferably 30%, and particularly preferably 15%, then the test polypeptide complex "does not substantially bind to cells expressing mutant GPC3". The formula for determining the Geo-Mean (Geometric Mean) value is described in the CELL QUEST Software User's Guide (BD biosciences). When the comparison shows that the comparison values are substantially equivalent, the epitope for the

test and control antigen-binding molecules can be determined to be the same.

Variable fragment (Fv)

Herein, the term "variable fragment (Fv)" refers to the minimum unit of an antibody-derived antigen-binding domain that is composed of a pair of the antibody light chain variable region (VL) and antibody heavy chain variable region (VH). In 1988, Skerra and Pluckthun found that homogeneous and active antibodies can be prepared from the *E. coli* periplasm fraction by inserting an antibody gene downstream of a bacterial signal sequence and inducing expression of the gene in *E. coli* (Science (1988) 240(4855), 1038-1041). In the Fv prepared from the periplasm fraction, VH associates with VL in a manner so as to bind to an antigen.

Herein, Fv preferably includes, for example, a pair of Fv which is an antigen-binding molecule or such comprising:

(1) a bivalent antigen-binding domain which is a bivalent scFv, wherein one monovalent scFv of the bivalent scFv is linked to one polypeptide forming an Fc domain by a heavy-chain Fv fragment forming a CD3-binding domain, and the other monovalent scFv is linked to the other polypeptide forming an Fc domain by a light-chain Fv fragment forming a CD3-binding domain;

(2) a domain comprising an Fc domain that has no Fcγ receptor-binding activity, and which is derived from amino acids forming the Fc domain of IgG1, IgG2a, IgG3, or IgG4; and

(3) at least a monovalent CD3-binding domain,

wherein the light-chain and heavy-chain Fv fragments associate to form a CD3-binding domain such that it can bind to the CD3 antigen.

scFv, single-chain antibody, and sc(Fv)2

Herein, the terms "scFv", "single-chain antibody", and "sc(Fv)2" all refer to an antibody fragment of a single polypeptide chain that contains variable regions derived from the heavy and light chains, but not the constant region. In general, a single-chain antibody also contains a polypeptide linker between the VH and VL domains, which enables formation of a desired structure that is thought to allow antigen binding. The single-chain antibody is discussed in detail by Pluckthun in "The Pharmacology of Monoclonal Antibodies, Vol. 113, Rosenburg and Moore, eds., Springer-Verlag, New York, 269-315 (1994)". See also International Patent Publication WO 1988/001649; US Patent Nos. 4,946,778 and 5,260,203. In a particular embodiment, the single-chain antibody can be bispecific and/or humanized.

scFv is an antigen-binding domain in which VH and VL forming Fv are linked together by a peptide linker (Proc. Natl. Acad. Sci. U.S.A. (1988) 85(16), 5879-5883). VH and VL can be retained in close proximity by the peptide linker.

sc(Fv)2 is a single-chain antibody in which four variable regions of two VL and two VH

are linked by linkers such as peptide linkers to form a single chain (J Immunol. Methods (1999) 231(1-2), 177-189). The two VH and two VL may be derived from different monoclonal antibodies. Such sc(Fv)2 preferably includes, for example, a bispecific sc(Fv)2 that recognizes two epitopes present in a single antigen as disclosed in the Journal of Immunology (1994) 152(11), 5368-5374. sc(Fv)2 can be produced by methods known to those skilled in the art. For example, sc(Fv)2 can be produced by linking scFv by a linker such as a peptide linker.

Herein, the form of an antigen-binding domain forming an sc(Fv)2 include an antibody in which the two VH units and two VL units are arranged in the order of VH, VL, VH, and VL ([VH]-linker-[VL]-linker-[VH]-linker-[VL]) beginning from the N terminus of a single-chain polypeptide. The order of the two VH units and two VL units is not limited to the above form, and they may be arranged in any order. Example order of the form is listed below.

[VL]-linker-[VH]-linker-[VH]-linker-[VL]
[VH]-linker-[VL]-linker-[VL]-linker-[VH]
[VH]-linker-[VH]-linker-[VL]-linker-[VL]
[VL]-linker-[VL]-linker-[VH]-linker-[VH]
[VL]-linker-[VH]-linker-[VL]-linker-[VH]

The molecular form of sc(Fv)2 is also described in detail in WO 2006/132352. According to these descriptions, those skilled in the art can appropriately prepare desired sc(Fv)2 to produce the antigen-binding molecules disclosed herein.

Furthermore, the antigen-binding molecules of the present invention may be conjugated with a carrier polymer such as PEG or an organic compound such as an anticancer agent. Alternatively, a sugar chain addition sequence is preferably inserted into the polypeptide complexes such that the sugar chain produces a desired effect.

The linkers to be used for linking the variable regions of an antibody comprise arbitrary peptide linkers that can be introduced by genetic engineering, synthetic linkers, and linkers disclosed in, for example, Protein Engineering, 9(3), 299-305, 1996. However, peptide linkers are preferred in the present invention. The length of the peptide linkers is not particularly limited, and can be suitably selected by those skilled in the art according to the purpose. The length is preferably five amino acids or more (without particular limitation, the upper limit is generally 30 amino acids or less, preferably 20 amino acids or less), and particularly preferably 15 amino acids. When sc(Fv)2 contains three peptide linkers, their length may be all the same or different.

For example, such peptide linkers include:

Ser
Gly·Ser
Gly·Gly·Ser
Ser·Gly·Gly

Gly·Gly·Gly·Ser (SEQ ID NO: 15)
Ser·Gly·Gly·Gly (SEQ ID NO: 16)
Gly·Gly·Gly·Gly·Ser (SEQ ID NO: 17)
Ser·Gly·Gly·Gly·Gly (SEQ ID NO: 18)
Gly·Gly·Gly·Gly·Gly·Ser (SEQ ID NO: 19)
Ser·Gly·Gly·Gly·Gly·Gly (SEQ ID NO: 20)
Gly·Gly·Gly·Gly·Gly·Gly·Ser (SEQ ID NO: 21)
Ser·Gly·Gly·Gly·Gly·Gly·Gly (SEQ ID NO: 22)
(Gly·Gly·Gly·Gly·Ser (SEQ ID NO: 17))n
(Ser·Gly·Gly·Gly·Gly (SEQ ID NO: 18))n

where n is an integer of 1 or larger. The length or sequences of peptide linkers can be selected accordingly by those skilled in the art depending on the purpose.

Synthetic linkers (chemical crosslinking agents) is routinely used to crosslink peptides, and for example:

N-hydroxy succinimide (NHS),
disuccinimidyl suberate (DSS),
bis(sulfosuccinimidyl) suberate (BS^3),
dithiobis(succinimidyl propionate) (DSP),
dithiobis(sulfosuccinimidyl propionate) (DTSSP),
ethylene glycol bis(succinimidyl succinate) (EGS),
ethylene glycol bis(sulfosuccinimidyl succinate) (sulfo-EGS),
disuccinimidyl tartrate (DST), disulfosuccinimidyl tartrate (sulfo-DST),
bis[2-(succinimidoxycarbonyloxy)ethyl] sulfone (BSOCOES),
and bis[2-(sulfosuccinimidoxycarbonyloxy)ethyl] sulfone (sulfo-BSOCOES). These crosslinking agents are commercially available.

In general, three linkers are required to link four antibody variable regions together. The linkers to be used may be of the same type or different types.

Fab, F(ab')2, and Fab'

"Fab" consists of a single light chain, and a CH1 domain and variable region from a single heavy chain. The heavy chain of Fab molecule cannot form disulfide bonds with another heavy chain molecule.

"F(ab')2" or "Fab" is produced by treating an immunoglobulin (monoclonal antibody) with a protease such as pepsin and papain, and refers to an antibody fragment generated by digesting an immunoglobulin (monoclonal antibody) at near the disulfide bonds present between the hinge regions in each of the two H chains. For example, papain cleaves IgG upstream of the

disulfide bonds present between the hinge regions in each of the two H chains to generate two homologous antibody fragments, in which an L chain comprising VL (L-chain variable region) and CL (L-chain constant region) is linked to an H-chain fragment comprising VH (H-chain variable region) and CHγ1 (γ1 region in an H-chain constant region) *via* a disulfide bond at their C-terminal regions. Each of these two homologous antibody fragments is called Fab'.

"F(ab')2" consists of two light chains and two heavy chains comprising the constant region of a CH1 domain and a portion of CH2 domains so that disulfide bonds are formed between the two heavy chains. The F(ab')2 forming an antigen-binding molecule disclosed herein can be preferably produced as follows. A whole monoclonal antibody or such comprising a desired antigen-binding domain is partially digested with a protease such as pepsin; and Fc fragments are removed by adsorption onto a Protein A column. The protease is not particularly limited, as long as it can cleave the whole antibody in a selective manner to produce F(ab')2 under an appropriate setup enzyme reaction condition such as pH. Such proteases include, for example, pepsin and ficin.

Fc domain

An Fc domain that forms an antigen-binding molecule disclosed herein can be preferably produced in the following manner. An antibody such as a monoclonal antibody is partially digested with a protease such as pepsin. Then, the resulting fragment is adsorbed onto a Protein A or Protein G column, and eluted with an appropriate elution buffer. The protease is not particularly limited, as long as it can cleave antibodies such as monoclonal antibodies under an appropriate setup enzyme reaction condition such as pH. Such proteases include, for example, pepsin and ficin.

The antigen-binding molecules described herein comprise an Fc domain with reduced Fcγ receptor-binding activity, which includes amino acids forming the Fc domain of IgG1, IgG2, IgG3, or IgG4.

Antibody isotype is determined according to the structure of the constant region. Constant regions of the isotypes IgG1, IgG2, IgG3, and IgG4 are called Cγ1, Cγ2, Cγ3, and Cγ4, respectively. The amino acid sequences of Fc domain polypeptides forming human Cγ1, Cγ2, Cγ3, and Cγ4 are exemplified in SEQ ID NO: 23, 24, 25, and 26, respectively. The relationship between amino acid residues forming each amino acid sequence and Kabat's EU numbering (herein also referred to as EU INDEX) are shown in Fig. 18.

The Fc domain refers to the region besides F(ab')2 which comprises two light chains and two heavy chains comprising a portion of the constant region that comprises a CH1 domain and a region between the CH1 and CH2 domains so that disulfide bonds are formed between the two heavy chains. The Fc domain forming an antigen-binding molecule disclosed herein can be

preferably produced as follows. A monoclonal IgG1, IgG2, IgG3, or IgG4 antibody or the like is partially digested with a protease such as pepsin, followed by elution of the fraction adsorbed onto a Protein A column. The protease is not particularly limited, as long as it can cleave the whole antibody in a selective manner to produce F(ab')2 in an appropriate setup enzyme reaction condition such as pH. Such proteases include, for example, pepsin and ficin.

Fcγ receptor

Fcγ receptor refers to a receptor capable of binding to the Fc domain of monoclonal IgG1, IgG2, IgG3, or IgG4 antibodies, and includes all members belonging to the family of proteins substantially encoded by an Fcγ receptor gene. In human, the family includes FcγRI (CD64) including isoforms FcγRIa, FcγRIb and FcγRIc; FcγRII (CD32) including isoforms FcγRIIa (including allotype H131 and R131), FcγRIIb (including FcγRIIb-1 and FcγRIIb-2), and FcγRIIc; and FcγRIII (CD16) including isoform FcγRIIIa (including allotype V158 and F158) and FcγRIIIb (including allotype FcγRIIIb-NA1 and FcγRIIIb-NA2); as well as all unidentified human FcγRs, FcγR isoforms, and allotypes thereof. However, Fcγ receptor is not limited to these examples. Without being limited thereto, FcγR includes those derived from humans, mice, rats, rabbits, and monkeys. FcγR may be derived from any organisms. Mouse FcγR includes, without being limited to, FcγRI (CD64), FcγRII (CD32), FcγRIII (CD16), and FcγRIII-2 (CD16-2), as well as all unidentified mouse FcγRs, FcγR isoforms, and allotypes thereof. Such preferred Fcγ receptors include, for example, human FcγRI (CD64), FcγRIIA (CD32), FcγRIIB (CD32), FcγRIIIA (CD16), and/or FcγRIIIB (CD16). The polynucleotide sequence and amino acid sequence of FcγRI are shown in SEQ ID NOs: 27 (NM_000566.3) and 28 (NP_000557.1), respectively; the polynucleotide sequence and amino acid sequence of FcγRIIA are shown in SEQ ID NOs: 29 (BC020823.1) and 30 (AAH20823.1), respectively; the polynucleotide sequence and amino acid sequence of FcγRIIB are shown in SEQ ID NOs: 31 (BC146678.1) and 32 (AAI46679.1), respectively; the polynucleotide sequence and amino acid sequence of FcγRIIIA are shown in SEQ ID NOs: 33 (BC033678.1) and 34 (AAH33678.1), respectively; and the polynucleotide sequence and amino acid sequence of FcγRIIIB are shown in SEQ ID NOs: 35 (BC128562.1) and 36 (AAI28563.1), respectively (RefSeq accession number is shown in each parentheses). Whether an Fcγ receptor has binding activity to the Fc domain of a monoclonal IgG1, IgG2, IgG3, or IgG4 antibody can be assessed by ALPHA screen (Amplified Luminescent Proximity Homogeneous Assay), surface plasmon resonance (SPR)-based BIACORE method, and others (Proc. Natl. Acad. Sci. USA (2006) 103(11), 4005-4010), in addition to the above-described FACS and ELISA formats.

Meanwhile, "Fc ligand" or "effector ligand" refers to a molecule and preferably a polypeptide that binds to an antibody Fc domain, forming an Fc/Fc ligand complex. The

molecule may be derived from any organisms. The binding of an Fc ligand to Fc preferably induces one or more effector functions. Such Fc ligands include, but are not limited to, Fc receptors, FcγR, FcαR, FcεR, FcRn, C1q, and C3, mannan-binding lectin, mannose receptor, *Staphylococcus* Protein A, *Staphylococcus* Protein G, and viral FcγRs. The Fc ligands also include Fc receptor homologs (FcRH) (Davis *et al*., (2002) Immunological Reviews 190, 123-136), which are a family of Fc receptors homologous to FcγR. The Fc ligands also include unidentified molecules that bind to Fc.

Fcγ receptor-binding activity

The impaired binding activity of Fc domain to any of the Fcγ receptors FcγI, FcγIIA, FcγIIB, FcγIIIA, and/or FcγIIIB can be assessed by using the above-described FACS and ELISA formats as well as ALPHA screen (Amplified Luminescent Proximity Homogeneous Assay) and surface plasmon resonance (SPR)-based BIACORE method (Proc. Natl. Acad. Sci. USA (2006) 103(11), 4005-4010).

ALPHA screen is performed by the ALPHA technology based on the principle described below using two types of beads: donor and acceptor beads. A luminescent signal is detected only when molecules linked to the donor beads interact biologically with molecules linked to the acceptor beads and when the two beads are located in close proximity. Excited by laser beam, the photosensitizer in a donor bead converts oxygen around the bead into excited singlet oxygen. When the singlet oxygen diffuses around the donor beads and reaches the acceptor beads located in close proximity, a chemiluminescent reaction within the acceptor beads is induced. This reaction ultimately results in light emission. If molecules linked to the donor beads do not interact with molecules linked to the acceptor beads, the singlet oxygen produced by donor beads do not reach the acceptor beads and chemiluminescent reaction does not occur.

For example, a biotin-labeled antigen-binding molecule is immobilized to the donor beads and glutathione S-transferase (GST)-tagged Fcγ receptor is immobilized to the acceptor beads. In the absence of an antigen-binding molecule comprising a competitive mutant Fc domain, Fcγ receptor interacts with an antigen-binding molecule comprising a wild-type Fc domain, inducing a signal of 520 to 620 nm as a result. The antigen-binding molecule having a non-tagged mutant Fc domain competes with the antigen-binding molecule comprising a wild-type Fc domain for the interaction with Fcγ receptor. The relative binding affinity can be determined by quantifying the reduction of fluorescence as a result of competition. Methods for biotinylating antigen-binding molecules such as antibodies using Sulfo-NHS-biotin or the like are known. Appropriate methods for adding the GST tag to an Fcγ receptor include methods that involve fusing polypeptides encoding Fcγ and GST in-frame, expressing the fused gene using cells introduced with a vector carrying the gene, and then purifying using a glutathione column.

The induced signal can be preferably analyzed, for example, by fitting to a one-site competition model based on nonlinear regression analysis using software such as GRAPHPAD PRISM (GraphPad; San Diego).

One of the substances for observing their interaction is immobilized as a ligand onto the gold thin layer of a sensor chip. When light is shed on the rear surface of the sensor chip so that total reflection occurs at the interface between the gold thin layer and glass, the intensity of reflected light is partially reduced at a certain site (SPR signal). The other substance for observing their interaction is injected as an analyte onto the surface of the sensor chip. The mass of immobilized ligand molecule increases when the analyte binds to the ligand. This alters the refraction index of solvent on the surface of the sensor chip. The change in refraction index causes a positional shift of SPR signal (conversely, the dissociation shifts the signal back to the original position). In the Biacore system, the amount of shift described above (*i.e.*, the change of mass on the sensor chip surface) is plotted on the vertical axis, and thus the change of mass over time is shown as measured data (sensorgram). Kinetic parameters (association rate constant (ka) and dissociation rate constant (kd)) are determined from the curve of sensorgram, and affinity (KD) is determined from the ratio between these two constants. Inhibition assay is preferably used in the BIACORE methods. Examples of such inhibition assay are described in Proc. Natl. Acad. Sci. USA (2006) 103(11), 4005-4010.

Herein, "Fcγ receptor-binding activity is reduced" means, for example, that based on the above-described analysis method the competitive activity of a test antigen-binding molecule is 50% or less, preferably 45% or less, 40% or less, 35% or less, 30% or less, 20% or less, or 15% or less, and particularly preferably 10% or less, 9% or less, 8% or less, 7% or less, 6% or less, 5% or less, 4% or less, 3% or less, 2% or less, or 1% or less than the competitive activity of a control antigen-binding molecule.

Antigen-binding molecules comprising the Fc domain of a monoclonal IgG1, IgG2, IgG3, or IgG4 antibody can be appropriately used as control antigen-binding molecules. The Fc domain structures are shown in SEQ ID NOs: 37 (A is added to the N terminus of RefSeq accession number AAC82527.1), 38 (A is added to the N terminus of RefSeq accession number AAB59393.1), 25 (A is added to the N terminus of RefSeq accession number CAA27268.1), and 39 (A is added to the N terminus of RefSeq accession number AAB59394.1). Furthermore, when an antigen-binding molecule comprising an Fc domain mutant of an antibody of a particular isotype is used as a test substance, the effect of the mutation of the mutant on the Fcγ receptor-binding activity is assessed using as a control an antigen-binding molecule comprising an Fc domain of the same isotype. As described above, antigen-binding molecules comprising an Fc domain mutant whose Fcγ receptor-binding activity has been judged to be reduced are appropriately prepared.

Such known mutants include, for example, mutants having a deletion of amino acids 231A-238S (EU numbering) (WO 2009/011941), as well as mutants C226S, C229S, P238S, (C220S) (J. Rheumatol (2007) 34, 11); C226S and C229S (Hum. Antibod. Hybridomas (1990) 1(1), 47-54); C226S, C229S, E233P, L234V, and L235A (Blood (2007) 109, 1185-1192).

Specifically, the preferred antigen-binding molecules include those comprising an Fc domain with a substitution of the amino acid at position 220, 226, 229, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 264, 265, 266, 267, 269, 270, 295, 296, 297, 298, 299, 300, 325, 327, 328, 329, 330, 331, or 332 (EU numbering) in the amino acids forming the Fc domain of an antibody of a particular isotype. The isotype of antibody from which the Fc domain originates is not particularly limited, and it is possible to use an appropriate Fc domain derived from a monoclonal IgG1, IgG2, IgG3, or IgG4 antibody. It is preferable to use Fc domains derived from IgG1 antibodies.

The preferred antigen-binding molecules include, for example, those comprising an Fc domain which has any one of the substitutions shown below, whose positions are specified according to EU numbering (each number represents the position of an amino acid residue in the EU numbering; and the one-letter amino acid symbol before the number represents the amino acid residue before substitution, while the one-letter amino acid symbol after the number represents the amino acid residue before the substitution) in the amino acids forming the Fc domain of IgG1 antibody:

(a) L234F, L235E, P331S;
(b) C226S, C229S, P238S;
(c) C226S, C229S;
(d) C226S, C229S, E233P, L234V, L235A;
(e) L234A, L235A or L235R, N297A;
(f) L235A or L235R, S239K, N297A

as well as those having an Fc domain which has a deletion of the amino acid sequence at positions 231 to 238.

Furthermore, the preferred antigen-binding molecules also include those comprising an Fc domain that has any one of the substitutions shown below, whose positions are specified according to EU numbering in the amino acids forming the Fc domain of an IgG2 antibody:

(g) H268Q, V309L, A330S, and P331S;
(h) V234A;
(i) G237A;
(j) V234A and G237A;
(k) A235E and G237A;
(l) V234A, A235E, and G237A. Each number represents the position of an amino acid residue

in EU numbering; and the one-letter amino acid symbol before the number represents the amino acid residue before substitution, while the one-letter amino acid symbol after the number represents the amino acid residue before the substitution.

Furthermore, the preferred antigen-binding molecules also include those comprising an Fc domain that has any one of the substitutions shown below, whose positions are specified according to EU numbering in the amino acids forming the Fc domain of an IgG3 antibody:

(m) F241A;

(n) D265A;

(o) V264A. Each number represents the position of an amino acid residue in EU numbering; and the one-letter amino acid symbol before the number represents the amino acid residue before substitution, while the one-letter amino acid symbol after the number represents the amino acid residue before the substitution.

Furthermore, the preferred antigen-binding molecules also include those comprising an Fc domain that has any one of the substitutions shown below, whose positions are specified according to EU numbering in the amino acids forming the Fc domain of an IgG4 antibody:

(p) L235A, G237A, and E318A;

(q) L235E;

(r) F234A and L235A. Each number represents the position of an amino acid residue in EU numbering; and the one-letter amino acid symbol before the number represents the amino acid residue before substitution, while the one-letter amino acid symbol after the number represents the amino acid residue before the substitution.

The other preferred antigen-binding molecules include, for example, those comprising an Fc domain in which any amino acid at position 233, 234, 235, 236, 237, 327, 330, or 331 (EU numbering) in the amino acids forming the Fc domain of an IgG1 antibody is substituted with an amino acid of the corresponding position in EU numbering in the corresponding IgG2 or IgG4.

The preferred antigen-binding molecules also include, for example, those comprising an Fc domain in which any one or more of the amino acids at positions 234, 235, and 297 (EU numbering) in the amino acids forming the Fc domain of an IgG1 antibody is substituted with other amino acids. The type of amino acid after substitution is not particularly limited; however, the antigen-binding molecules comprising an Fc domain in which any one or more of the amino acids at positions 234, 235, and 297 are substituted with alanine are particularly preferred.

The preferred antigen-binding molecules also include, for example, those comprising an Fc domain in which an amino acid at position 265 (EU numbering) in the amino acids forming the Fc domain of an IgG1 antibody is substituted with another amino acid. The type of amino acid after substitution is not particularly limited; however, antigen-binding molecules comprising an Fc domain in which an amino acid at position 265 is substituted with alanine are particularly

preferred.

Multispecific antigen-binding molecule

Examples of a preferred embodiment of the "multispecific antigen-binding molecule" of the present invention include multispecific antibodies. When an Fc region with reduced Fcγ receptor-binding activity is used as the multispecific antibody Fc region, an Fc region derived from the multispecific antibody may be used appropriately. Bispecific antibodies are particularly preferred as the multispecific antibodies of the present invention. In this case, a bispecific antibody is an antibody having two different specificities. IgG-type bispecific antibodies can be secreted from a hybrid hybridoma (quadroma) produced by fusing two types of hybridomas that produce IgG antibodies (Milstein *et al.*, Nature (1983) 305, 537-540).

Furthermore, IgG-type bispecific antibodies are secreted by introducing the genes of L chains and H chains constituting the two types of IgGs of interest, i.e. a total of four genes, into cells, and co-expressing them. However, the number of combinations of H and L chains of IgG that can be produced by these methods is theoretically ten combinations. Accordingly, it is difficult to purify an IgG comprising the desired combination of H and L chains from ten types of IgGs. Furthermore, theoretically the amount of secretion of the IgG having the desired combination will decrease remarkably, and therefore large-scale culturing will be necessary, and production costs will increase further.

Therefore, techniques for promoting the association among H chains and between L and H chains having the desired combinations can be applied to the multispecific antigen-binding molecules of the present invention.

For example, techniques for suppressing undesired H-chain association by introducing electrostatic repulsion at the interface of the second constant region or the third constant region of the antibody H chain (CH2 or CH3) can be applied to multispecific antibody association (WO2006/106905).

In the technique of suppressing unintended H-chain association by introducing electrostatic repulsion at the interface of CH2 or CH3, examples of amino acid residues in contact at the interface of the other constant region of the H chain include regions corresponding to the residues at EU numbering positions 356, 439, 357, 370, 399, and 409 in the CH3 region.

More specifically, examples include an antibody comprising two types of H-chain CH3 regions, in which one to three pairs of amino acid residues in the first H-chain CH3 region, selected from the pairs of amino acid residues indicated in (1) to (3) below, carry the same type of charge: (1) amino acid residues comprised in the H chain CH3 region at EU numbering positions 356 and 439; (2) amino acid residues comprised in the H-chain CH3 region at EU

numbering positions 357 and 370; and (3) amino acid residues comprised in the H-chain CH3 region at EU numbering positions 399 and 409.

Furthermore, the antibody may be an antibody in which pairs of the amino acid residues in the second H-chain CH3 region which is different from the first H-chain CH3 region mentioned above, are selected from the aforementioned pairs of amino acid residues of (1) to (3), wherein the one to three pairs of amino acid residues that correspond to the aforementioned pairs of amino acid residues of (1) to (3) carrying the same type of charges in the first H-chain CH3 region mentioned above carry opposite charges from the corresponding amino acid residues in the first H-chain CH3 region mentioned above.

Each of the amino acid residues indicated in (1) to (3) above come close to each other during association. Those skilled in the art can find out positions that correspond to the above-mentioned amino acid residues of (1) to (3) in a desired H-chain CH3 region or H-chain constant region by homology modeling and such using commercially available software, and amino acid residues of these positions can be appropriately subjected to modification.

In the antibodies mentioned above, “charged amino acid residues” are preferably selected, for example, from amino acid residues included in either one of the following groups:
(a) glutamic acid (E) and aspartic acid (D); and
(b) lysine (K), arginine (R), and histidine (H).

In the above-mentioned antibodies, the phrase “carrying the same charge” means, for example, that all of the two or more amino acid residues are selected fromthe amino acid residues included in either one of groups (a) and (b) mentioned above. The phrase “carrying opposite charges” means, for example, that when at least one of the amino acid residues among two or more amino acid residues is selected from the amino acid residues included in either one of groups (a) and (b) mentioned above, the remaining amino acid residues are selected fromthe amino acid residues included in the other group.

In a preferred embodiment, the antibodies mentioned above may have their first H-chain CH3 region and second H-chain CH3 region crosslinked by disulfide bonds.

In the present invention, amino acid residues subjected to modification are not limited to the above-mentioned amino acid residues of the antibody variable regions or the antibody constant regions. Those skilled in the art can identify the amino acid residues that form an interface in mutant polypeptides or heteromultimers by homology modeling and such using commercially available software; and amino acid residues of these positions can then be subjected to modification so as to regulate the association.

Other known techniques can also be used for the association of multispecific antibodies of the present invention. Fc region-containing polypeptides comprising different amino acids can be efficiently associated with each other by substituting an amino acid side chain present in

one of the H-chain Fc regions of the antibody with a larger side chain (knob), and substituting an amino acid side chain present in the corresponding Fc region of the other H chain with a smaller side chain (hole) to allow placement of the knob within the hole (WO1996/027011; Ridgway JB *et al.*, Protein Engineering (1996) 9, 617-621; Merchant A. M. *et al.* Nature Biotechnology (1998) 16, 677-681; and US20130336973).

In addition, other known techniques can also be used for formation of multispecific antibodies of the present invention. Association of polypeptides having different sequences can be induced efficiently by complementary association of CH3 using a strand-exchange engineered domain CH3 produced by changing part of one of the H-chain CH3s of an antibody to a corresponding IgA-derived sequence and introducing a corresponding IgA-derived sequence into the complementary portion of the other H-chain CH3 (Protein Engineering Design & Selection, 23; 195-202, 2010). This known technique can also be used to efficiently form multispecific antibodies of interest.

In addition, technologies for antibody production using association of antibody CH1 and CL and association of VH and VL as described in WO 2011/028952, WO2014/018572, and Nat Biotechnol. 2014 Feb; 32(2):191-8; technologies for producing bispecific antibodies using separately prepared monoclonal antibodies in combination (Fab Arm Exchange) as described in WO2008/119353 and WO2011/131746; technologies for regulating association between antibody heavy-chain CH3s as described in WO2012/058768 and WO2013/063702; technologies for producing bispecific antibodies composed of two types of light chains and one type of heavy chain as described in WO2012/023053; technologies for producing bispecific antibodies using two bacterial cell strains that individually express one of the chains of an antibody comprising a single H chain and a single L chain as described by Christoph *et al.* (Nature Biotechnology Vol. 31, p 753-758 (2013)); and such may be used for the formation of multispecific antibodies.

Alternatively, even when a multispecific antibody of interest cannot be formed efficiently, a multispecific antibody of the present invention can be obtained by separating and purifying the multispecific antibody of interest from the produced antibodies. For example, a method for enabling purification of two types of homomeric forms and the heteromeric antibody of interest by ion-exchange chromatography by imparting a difference in isoelectric points by introducing amino acid substitutions into the variable regions of the two types of H chains has been reported (WO2007114325). To date, as a method for purifying heteromeric antibodies, methods using Protein A to purify a heterodimeric antibody comprising a mouse IgG2a H chain that binds to Protein A and a rat IgG2b H chain that does not bind to Protein A have been reported (WO98050431 and WO95033844). Furthermore, a heterodimeric antibody can be purified efficiently on its own by using H chains comprising substitution of amino acid residues

at EU numbering positions 435 and 436, which is the IgG-Protein A binding site, with Tyr, His, or such which are amino acids that yield a different Protein A affinity, or using H chains with a different protein A affinity obtained according to the method of Reference Example 5, to change the interaction of each of the H chains with Protein A, and then using a Protein A column.

Alternatively, a common L chain that can provide binding ability to a plurality of different H chains can be obtained and used as the common L chain of a multispecific antibody. Efficient expression of a multispecific IgG can be achieved by introducing the genes of such a common L chain and a plurality of different H chains into cells to express the IgG (Nature Biotechnology (1998) 16, 677-681). A method for selecting a common L chain that shows a strong binding ability to any of the different H chains can also be used when selecting the common H chain (WO 2004/065611).

Furthermore, an Fc region whose Fc region C-terminal heterogeneity has been improved can be appropriately used as an Fc region of the present invention. More specifically, the present invention provides Fc regions produced by deleting glycine at position 446 and lysine at position 447 as specified by EU numbering from the amino acid sequences of two polypeptides constituting an Fc region derived from IgG1, IgG2, IgG3, or IgG4.

A plurality, such as two or more, of these technologies can be used in combination. Furthermore, these technologies can be appropriately and separately applied to the two H chains to be associated. Furthermore, these techniques can be used in combination with the above-mentioned Fc region which has reduced binding activity to an Fcγ receptor. Furthermore, an antigen-binding molecule of the present invention may be a molecule produced separately so that it has the same amino acid sequence, based on the antigen-binding molecule subjected to the above-described modifications.

An appropriate multispecific antigen-binding molecule of the present invention comprises

(1) a domain comprising an antibody variable region having glypican 3-binding activity;

(2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity; and

(3) a domain comprising an Fc region with reduced Fcγ receptor-binding activity mentioned above, without limitation to its structure.

In the present invention, each of the above-mentioned domains can be linked directly by peptide bonds. For example, when using $F(ab')_2$ as the domain comprising an antibody variable region of (1) and (2), and these Fc regions as the domain comprising an Fc region with reduced Fcγ receptor-binding activity of (3), the polypeptides formed by linking the antibody variable region-containing domains of (1) and (2) and the Fc region-containing domain of (3) by peptide bonds will form an antibody structure. Such antibodies can be produced by purification from the

above-mentioned hybridoma culture medium, and also by purifying antibodies from the culture medium of desired host cells that stably carry polynucleotides encoding the polypeptides constituting the antibody.

Examples of a preferred antibody H-chain variable region of the present invention contained in the antibody variable region having glypican 3-binding activity comprises the antibody H-chain variable regions of Table 1, or antibody H-chain variable regions having CDR sequences whose CDR1, CDR2, and CDR3 amino acid sequences are the same as the CDR1, CDR2, and CDR3 amino acid sequences contained in the H-chain variable regions of Table 1, or antibody H-chain variable regions which are functionally equivalent to the above-mentioned variable regions.

Table 1

Sequence Name	SEQ ID NO:
H0000	40
GCH003	170
GCH005	171
GCH006	172
GCH007	173
GCH008	174
GCH010	175
GCH012	176
GCH013	177
GCH014	178
GCH015	179
GCH016	180
GCH019	181
GCH022	182
GCH023	183
GCH025	184
GCH026	185
GCH027	186
GCH029	187
GCH032	188
GCH034	189
GCH035	190
GCH039	191
GCH040	192

Sequence Name	SEQ ID NO:
GCH042	193
GCH043	194
GCH045	195
GCH053	196
GCH054	197
GCH055	198
GCH056	199
GCH057	200
GCH059	201
GCH060	202
GCH061	203
GCH062	204
GCH064	205
GCH065	206
GCH066	207
GCH067	208
GCH068	209
GCH073	210
GCH094	211
GCH098	212
GCH099	213
GCH100	214
H0610	215

Examples of a preferred antibody variable region having T-cell receptor complex-binding activity of the present invention include antibody variable regions having T-cell receptor-binding activity. Of the T-cell receptors, CD3 is preferred, and CD3ε is particularly preferred. Examples of an antibody H-chain variable region contained in such antibody variable regions include the antibody H-chain variable regions of Table 2, antibody H-chain variable regions having CDR sequences whose CDR1, CDR2, and CDR3 amino acid sequences are the same as the CDR1, CDR2, and CDR3 amino acid sequences contained in the antibody H-chain variable regions of Table 2, and antibody H-chain variable regions that are functionally equivalent to the above-mentioned variable regions.

Table 2

Sequence Name	SEQ ID NO:
hCE115HA	52
CE115HA177	64
CE115HA178	65
CE115HA179	66
CE115HA180	67
hCE115HAa	68
TR01H006	69
TR01H007	70
TR01H008	71
TR01H009	72
TR01H010	73
TR01H011	74
TR01H012	75
TR01H013	76
TR01H014	77
TR01H015	78
TR01H016	79
TR01H017	80
TR01H018	81
TR01H019	82
TR01H020	83
TR01H021	84
TR01H022	85
TR01H023	86
TR01H024	87
TR01H025	88
TR01H026	89
TR01H027	90
TR01H028	91
TR01H029	92
TR01H030	93
TR01H031	94
TR01H032	95
TR01H033	96
TR01H034	97
TR01H035	98

Sequence Name	SEQ ID NO:
TR01H036	99
TR01H037	100
TR01H038	101
TR01H039	102
TR01H040	103
TR01H041	104
TR01H042	105
TR01H043	106
TR01H044	107
TR01H045	108
TR01H046	109
TR01H047	110
TR01H048	111
TR01H049	112
TR01H050	113
TR01H051	114
TR01H052	115
TR01H053	116
TR01H054	117
TR01H055	118
TR01H056	119
TR01H057	120
TR01H058	121
TR01H061	122
TR01H062	123
TR01H063	124
TR01H064	125
TR01H065	126
TR01H066	127
TR01H067	128
TR01H068	129
TR01H069	130
TR01H070	131
TR01H071	132
TR01H072	133
TR01H073	134

Sequence Name	SEQ ID NO:
TR01H074	135
TR01H075	136
TR01H076	137
TR01H077	138
TR01H079	139
TR01H080	140
TR01H081	141
TR01H082	142
TR01H083	143
TR01H084	144
TR01H090	145
TR01H091	146
TR01H092	147
TR01H093	148
TR01H094	149
TR01H095	150
TR01H096	151
TR01H097	152
TR01H098	153
TR01H099	154
TR01H100	155
TR01H101	156
TR01H102	157
TR01H103	158
TR01H104	159
TR01H105	160
TR01H106	161
TR01H107	162
TR01H108	163
TR01H109	164
TR01H110	165
TR01H111	166
TR01H112	167
TR01H113	168
TR01H114	169
TR01H001	420
TR01H002	421
TR01H003	422
TR01H004	423
rCE115H	424
CE115HA121	425
CE115HA122	426
CE115HA124	427
CE115HA192	428
CE115HA236	429
CE115HA251	430
CE115HA252	431

The relationship between the CDR regions of the amino acid residues constituting the antibody H chain amino acid sequence and Kabat numbering is as shown in Fig. 13.

For the antibody L-chain variable regions contained in the antibody variable region having glypican 3-binding activity and the antibody variable region having T-cell receptor complex-binding activity of the present invention, it is preferable to obtain a common L chain that may provide a binding activity to the H chain having glypican3-binding activity and a binding activity to the H chain having T-cell receptor complex, and to use this as the common L-chain variable region of the multispecific antigen-binding molecule.

Examples of the common L-chain variable region to be used in the present invention include the L-chain variable regions of Table 3, antibody L-chain variable regions having CDR sequences whose CDR1, CDR2, and CDR3 amino acid sequences are the same as the CDR1, CDR2, and CDR3 amino acid sequences contained in the antibody L-chain variable regions of Table 3, and antibody L-chain variable regions that are functionally equivalent to the above-mentioned variable regions.

Table 3

Sequence Name	SEQ ID NO:
L0000	53
L0002	217
L0003	218
L0006	219
L0007	220
L0008	221
L0009	222
L0011	223
L0012	224
L0013	225
L0014	226
L0015	227
L0016	228
L0032	229
L0038	230
L0039	231
L0041	232
L0042	233
L0043	234
L0044	235
L0045	236
L0046	237
L0047	238
L0062	239
L0063	240
L0064	241
L0065	242
L0066	243
L0069	244
L0075	245
L0079	246
L0082	247
L0085	248
L0089	249
L0090	250
L0091	251
L0093	252
L0104	253
L0106	254
L0107	255
L0109	256
L0113	257
L0115	258
L0117	259
L0120	260
L0122	261
L0123	262
L0124	263

Sequence Name	SEQ ID NO:
L0125	264
L0126	265
L0127	266
L0129	267
L0132	268
L0134	269
L0136	270
L0137	271
L0138	272
L0139	273
L0140	274
L0141	275
L0143	276
L0144	277
L0145	278
L0147	279
L0148	280
L0149	281
L0151	282
L0152	283
L0154	284
L0155	285
L0157	286
L0160	287
L0161	288
L0163	289
L0167	290
L0168	291
L0173	292
L0175	293
L0180	294
L0181	295
L0186	296
L0187	297
L0200	298
L0201	299
L0202	300
L0203	301
L0204	302
L0205	303
L0206	304
L0207	305
L0208	306
L0209	307
L0210	308
L0211	309
L0212	310
L0213	311

Sequence Name	SEQ ID NO:
L0214	312
L0215	313
L0216	314
L0217	315
L0218	316
L0219	317
L0220	318
L0222	319
L0223	320
L0224	321
L0226	322
L0227	323
L0228	324
L0229	325
L0230	326
L0231	327
L0232	328
L0233	329
L0234	330
L0235	331
L0236	332
L0237	333
L0238	334
L0239	335
L0240	336
L0241	337
L0242	338
L0243	339
L0246	340
L0247	341
L0248	342
L0249	343
L0250	344
L0258	345
L0259	346
L0260	347
L0261	348
L0262	349
L0263	350
L0264	351
L0265	352
L0266	353
L0267	354
L0268	355
L0269	356
L0270	357
L0271	358
L0272	359

The relationship between the CDR regions of the amino acid residues constituting the antibody L-chain amino acid sequence and Kabat numbering is as shown in Fig. 14.

In the present invention, the phrase “functionally equivalent” means that the binding affinities for an antigen are equivalent, or alternatively, it means that the cytotoxic activities against glypican 3-expressing cells or tissues containing these cells are equivalent when it is used as a multispecific antigen-binding molecule. The binding affinity and cytotoxic activity can be measured based on the description herein. The cells used for measurement of cytotoxic activity may be the desired GPC3-expressing cells or a desired tissue containing these cells, and for example, PC-10 or NCI-H446 which are GPC3-expressing human cancer cell lines can be used. Regarding the antibody constant regions, the phrase may mean that the decreases in Fcγ receptor-binding activity are equivalent.

For example, an antibody H-chain variable region functionally equivalent to the antibody H chain variable region described herein (i.e., the original H chain variable region) means that this region has the same binding affinity when it is combined with the antibody L-chain variable region described herein which forms a pair with the original H chain, or alternatively that the region has the same cytotoxic activity towards glypican 3-expressing cells or a tissue containing these cells when used for a multispecific antigen-binding molecule. Furthermore, an antibody L-chain variable region functionally equivalent to the antibody L-chain variable region described herein (i.e., the original L-chain variable region) means that this region has the same binding affinity when it is combined with the antibody H-chain variable region described herein which forms a pair with the original L chain, or alternatively that the region has the same cytotoxic activity towards glypican 3-expressing cells or a tissue containing these cells when used for a multispecific antigen-binding molecule.

The term “equivalent” does not necessarily have to mean the same degree of activity, and the activity may be enhanced. Specifically, for antigen-binding affinity, examples include the case where the value (KD value / parent KD value) obtained by comparison to the binding affinity of the antibody variable region serving as the control (parent KD value) is 1.5 or less. The value of KD value / parent KD value is preferably 1.3 or less, more preferably 1.2 or less, 1.1 or less, 1.0 or less, 0.9 or less, 0.8 or less, 0.7 or less, 0.6 or less, or 0.5 or less. While there is no lower limit, examples include 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}, or 10^{-6}. More specifically, in the present invention, the value of KD value / parent KD value is preferably 10^{-6} to 1.5×10^{-0}, more preferably 10^{-6} to 10^{-1}, even more preferably 10^{-6} to 10^{-2}, and yet even more preferably 10^{-6} to 10^{-3}. For cytotoxic activity, examples include the case where the value (cell growth inhibition rate / parent cell growth inhibition rate) obtained by comparison to the cell growth inhibition rate of the multispecific antigen-binding molecule serving as the control (parent cell growth inhibition rate) is 0.7 or more. The concentration of the added multispecific antigen-binding molecule can

be determined appropriately, but is preferably, for example, 0.01 nM, 0.05 nM, 0.1 nM, 0.5 nM, or 1 nM; and preferably, measurements are taken at 0.05 nM or 0.1 nM. The value for cell growth inhibition rate / parent cell growth inhibition rate is preferably 0.8 or higher, more preferably 0.9 or higher, 1.0 or higher, 1.2 or higher, 1.5 or higher, 2 or higher, 3 or higher, 5 or higher, 10 or higher, or 20 or higher. While there is no upper limit, the value may be 10, 10^2, 10^3, 10^4, 10^5, or 10^6.

Furthermore, for cytotoxic activity, examples include the case where the value (concentration for 50% inhibition of cell growth / parent concentration for 50% inhibition of cell growth) obtained by comparison to the concentration of the original multispecific antigen-binding molecule for 50% inhibition of cell growth (parent concentration for 50% inhibition of cell growth) is 1.5 or less. Concentration for 50% growth inhibition refers to the concentration of the multispecific antigen-binding molecule necessary for reducing the cell proliferation rate to one half compared to when the multispecific antigen-binding molecule is not added. The value of "concentration for 50% inhibition of cell growth / parent concentration for 50% inhibition of cell growth" is preferably 1.3 or less, more preferably 1.2 or less, 1.1 or less, 1.0 or less, 0.9 or less, 0.8 or less, 0.7 or less, 0.6 or less, or 0.5 or less. While there is no lower limit, the value may be, for example, 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}, or 10^{-6}. Specifically, the value is preferably 10^{-6} to 1.5×10^{-0}, more preferably 10^{-6} to 10^{-1}, even more preferably 10^{-6} to 10^{-2}, and yet even more preferably 10^{-6} to 10^{-3}.

Regarding the domain comprising an antibody variable region having GPC3-binding activity, the KD value towards GPC3 (for example, human GPC3) may be, for example, 5×10^{-9} M or less, preferably 4×10^{-9} M or less, such as 3×10^{-9} M or less, 2×10^{-9} M or less, 1×10^{-9} M or less, 8×10^{-10} M or less, 5×10^{-10} M or less, 4×10^{-10} M or less, 3×10^{-10} M or less, 2×10^{-10} M or less, 1×10^{-10} M or less, 8×10^{-11} M or less, 5×10^{-11} M or less, 4×10^{-11} M or less, 3×10^{-11} M or less, 2×10^{-11} M or less, 1×10^{-11} M or less, 8×10^{-12} M or less, 5×10^{-12} M or less, 4×10^{-12} M or less, 3×10^{-12} M or less, 2×10^{-12} M or less, 1×10^{-12} M or less, 8×10^{-13} M or less, 5×10^{-13} M or less, 4×10^{-13} M or less, 3×10^{-13} M or less, 2×10^{-13} M or less, or 1×10^{-13} M or less.

Regarding the domain comprising an antibody variable region having T-cell receptor complex-binding activity, the KD value towards a human T-cell receptor complex such as a human T cell receptor, or more specifically for example human CD3ε may be, for example, 2×10^{-7} M or less, preferably 1.5×10^{-7} M or less, such as 1.4×10^{-7} M or less, 1.3×10^{-7} M or less, 1.2×10^{-7} M or less, 1×10^{-7} M or less, 3×10^{-8} M or less, 2×10^{-8} M or less, 1×10^{-8} M or less, 8×10^{-9} M or less, 5×10^{-9} M or less, 4×10^{-9} M or less, 3×10^{-9} M or less, 2×10^{-9} M or less, 1×10^{-9} M or less, 8×10^{-10} M or less, 5×10^{-10} M or less, 4×10^{-10} M or less, 3×10^{-10} M or less, 2×10^{-10} M or less, 1×10^{-10} M or less, 8×10^{-11} M or less, 5×10^{-11} M or less, 4×10^{-11} M or less, 3

x 10^{-11} M or less, 2 x 10^{-11} M or less, 1 x 10^{-11} M or less, 8 x 10^{-12} M or less, 5 x 10^{-12} M or less, 4 x 10^{-12} M or less, 3 x 10^{-12} M or less, 2 x 10^{-12} M or less, or 1 x 10^{-12} M or less.

The multispecific antigen-binding molecules of the present invention preferably have KD values toward human GPC3 and human T-cell receptor complex (for example, human CD3ε chain) that are 5 x 10^{-9} M or less and 2 x 10^{-7} M or less, respectively, and more preferably 1 x 10^{-9} M or less and 5 x 10^{-8} M or less, respectively.

In the present invention, antibody variable regions that are "functionally equivalent" are not particularly limited as long as they are antibody H-chain and/or antibody L-chain variable regions that satisfy the above-described conditions. Examples of such antibody variable regions include regions produced by introducing substitution, deletion, addition, and/or insertion of one or more amino acids (for example, 1, 2, 3, 4, 5, or 10 amino acids) into the amino acid sequences of the variable regions of Tables 1 to 3 mentioned above. A method well known to those skilled in the art for introducing one or more amino-acid substitutions, deletions, additions, and/or insertions into an amino acid sequence is a method of introducing mutations into proteins. For example, those skilled in the art can prepare variable regions that are functionally equivalent to the antibody variable regions having the above-mentioned functions by appropriately introducing mutations into amino acid sequences using methods such as site-directed mutagenesis (Hashimoto-Gotoh, T., Mizuno, T., Ogasahara, Y., and Nakagawa, M. (1995) An oligodeoxyribonucleotide-directed dual amber method for site-directed mutagenesis. Gene 152, 271-275; Zoller, M.J., and Smith, M. (1983) Oligonucleotide-directed mutagenesis of DNA fragments cloned into M13 vectors.Methods Enzymol. 100, 468-500; Kramer, W., Drutsa, V., Jansen, H.W., Kramer, B., Pflugfelder, M., and Fritz, H.J. (1984) The gapped duplex DNA approach to oligonucleotide-directed mutation construction. Nucleic Acids Res. 12, 9441-9456; Kramer, W., and Fritz, H.J. (1987) Oligonucleotide-directed construction of mutations *via* gapped duplex DNA Methods. Enzymol. 154, 350-367; and Kunkel, T.A. (1985) Rapid and efficient site-specific mutagenesis without phenotypic selection. Proc Natl Acad. Sci. U S A. 82, 488-492).

When an amino acid residue is altered, the amino acid is preferably mutated into a different amino acid(s) that conserves the properties of the amino acid side-chain. Examples of amino-acid side chain properties are: hydrophobic amino acids (A, I, L, M, F, P, W, Y, and V), hydrophilic amino acids (R, D, N, C, E, Q, G, H, K, S, and T), amino acids containing aliphatic side chains (G, A, V, L, I, and P), amino acids containing hydroxyl group-containing side chains (S, T, and Y), amino acids containing sulfur atom-containing side chains (C and M), amino acids containing carboxylic acid- and amide-containing side chains (D, N, E, and Q), amino acids containing basic side chains (R, K, and H), and amino acids containing aromatic side chains (H, F, Y, and W) (amino acids are represented by one-letter codes in parentheses). Amino acid

substitutions within each of these groups are called conservative substitutions. It is already known that a polypeptide containing a modified amino acid sequence in which one or more amino acid residues in a given amino acid sequence are deleted, added, and/or substituted with other amino acids can retain the original biological activity (Mark, D. F. *et al*., Proc. Natl. Acad. Sci. USA; (1984) 81: 5662-6; Zoller, M. J. and Smith, M., Nucleic Acids Res. (1982) 10: 6487-500; Wang, A. *et al*., Science (1984) 224: 1431-3; Dalbadie-McFarland, G. *et al*., Proc. Natl. Acad. Sci. USA (1982) 79: 6409-13). Variable regions of the present invention containing such amino acid modifications have an amino acid sequence identity of at least 70%, more preferably at least 75%, even more preferably at least 80%, still more preferably at least 85%, yet more preferably at least 90%, and most preferably at least 95%, with the amino acid sequence of the CDR sequences, FR sequences, or whole variable regions of the variable region prior to modification. Herein, sequence identity is defined as the percentage of residues identical to those in the original amino acid sequence of the H-chain variable region or L-chain variable region determined after the sequences are aligned, and gaps are appropriately introduced to maximize the sequence identity as necessary. The identity of amino acid sequences can be determined by the method described below.

Furthermore, a "functionally equivalent antibody variable region" can be obtained, for example, from nucleic acids that hybridize under stringent conditions with nucleic acids comprising a nucleotide sequence encoding the amino acid sequence of a variable region in Tables 1 to 3 mentioned above. Stringent hybridization conditions for isolating a nucleic acid that hybridizes under stringent conditions with a nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of a variable region include, for example, the conditions of 6 M urea, 0.4% SDS, 0.5x SSC, and 37°C, or hybridization conditions with a stringency equivalent thereto. Isolation of nucleic acids with a much higher homology can be expected with more stringent conditions, for example, the conditions of 6 M urea, 0.4% SDS, 0.1x SSC, and 42°C. The washing conditions following the hybridization are, for example, washing using 0.5x SSC (1x SSC is 0.15 M NaCl and 0.015 M sodium citrate at pH7.0) and 0.1% SDS at 60°C, more preferably washing using 0.2x SSC and 0.1% SDS at 60°C, even more preferably washing using 0.2x SSC and 0.1% SDS at 62°C, yet even more preferably washing using 0.2x SSC and 0.1% SDS at 65°C, and still more preferably washing using 0.1x SSC and 0.1% SDS at 65°C. The sequences of the isolated nucleic acids can be determined by the known methods described below. The overall nucleotide sequence homology of the isolated nucleic acid is at least 50% or higher, preferably 70% or higher, and more preferably 90% or higher (for example, 95%, 96%, 97%, 98%, 99%, or higher) sequence identity.

Nucleic acids that hybridize under stringent conditions to a nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of a variable region can also be isolated

by using, instead of the above-described methods using hybridization techniques, gene amplification methods such as polymerase chain reaction (PCR) that uses primers synthesized based on information of the nucleotide sequence encoding the variable-region amino acid sequence.

The identity of one nucleotide sequence or amino acid sequence to another can be determined using the algorithm BLAST, by Karlin and Altschul (Proc. Natl. Acad. Sci. USA (1993) 90: 5873-7). Programs called BLASTN and BLASTX were developed based on this algorithm (Altschul *et al.*, J. Mol. Biol. (1990) 215: 403-10). To analyze nucleotide sequences according to BLASTN based on BLAST, the parameters are set, for example, as score = 100 and wordlength = 12. On the other hand, parameters used for the analysis of amino acid sequences by BLASTX based on BLAST include, for example, score = 50 and wordlength = 3. Default parameters for each program are used when using the BLAST and Gapped BLAST programs. Specific techniques for such analyses are known in the art (see the website of the National Center for Biotechnology Information (NCBI), Basic Local Alignment Search Tool (BLAST); http://www.ncbi.nlm.nih.gov).

The combination of the antibody variable region having glypican 3-binding activity and the antibody variable region having T-cell receptor complex binding activity as comprised in the multispecific antigen-binding molecule of the present invention is not particularly limited as long as it has the above-described activities. However, in the present invention, the cytotoxic activity of the multispecific antigen-binding molecule is preferably equivalent to or greater than that of the bispecific antibody GPC3_ERY22_rCE115 described in Example 3. Here, the term "equivalent" does not necessarily have to mean the same degree of activity as described above, and the activity may be enhanced. Being equivalent to GPC3_ERY22_rCE115 is, for example, when the value of (cell growth inhibition rate / cell growth inhibition rate (GPC3_ERY22_rCE115)) relative to the cell growth inhibition rate of GPC3_ERY22_rCE115 (cell growth inhibition rate (GPC3_ERY22_rCE115)) is 0.7 or greater, preferably 0.8 or greater, 0.9 or greater, 1.0 or greater, 1.2 or greater, 1.5 or greater, 2 or greater, 3 or greater, 5 or greater, 10 or greater, or 20 or greater. While there is no upper limit, the value may be, for example, 10, 10^2, 10^3, 10^4, 10^5, or 10^6. The concentration of the multispecific antigen-binding molecule to be added can be determined appropriately, but is preferably, for example, 0.01 nM, 0.05 nM, 0.1 nM, 0.5 nM, or 1 nM; and preferably, measurements are taken at 0.05 nM or 0.1 nM.

Furthermore, examples include the case where the value (concentration for 50% inhibition of cell growth / concentration for 50% inhibition of cell growth (GPC3_ERY22_rCE115)) obtained by comparison to the concentration for 50% inhibition of growth of GPC3_ERY22_rCE115 cells (concentration for 50% inhibition of cell growth (GPC3_ERY22_rCE115)) is 1.5 or less. The value for "concentration for 50% inhibition of cell

growth / concentration for 50% inhibition of cell growth (GPC3_ERY22_rCE115)" is preferably 1.3 or less, more preferably 1.2 or less, 1.1 or less, 1.0 or less, 0.9 or less, 0.8 or less, 0.7 or less, 0.6 or less, or 0.5 or less. While there is no lower limit, the value may be for example, 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}, or 10^{-6}. Specifically, the value is preferably 10^{-6} to 1.5×10^{-0}, more preferably 10^{-6} to 10^{-1}, even more preferably 10^{-6} to 10^{-2}, and yet even more preferably 10^{-6} to 10^{-3}.

The preferred specific KD values for human GPC3 and human T cell receptor complex (for example, human CD3ε chain) are also as indicated above. Desired cells showing GPC3 expression or desired tissues containing these cells may be used for the cells, and for example, PC-10 or NCI-H446 which are GPC3-expressing human cancer cell lines can be used.

Examples of such a combination of the antibody variable region having glypican 3-binding activity and the antibody variable region having T-cell receptor complex binding activity, include the combinations of antibody H-chain variable regions shown in Table 4, combinations of antibody H-chain variable regions having CDR sequences whose CDR1, CDR2, and CDR3 amino acid sequences are the same as the CDR1, CDR2, and CDR3 amino acid sequences carried by the antibody H-chain variable regions of Table 4, and combinations of antibody H-chain variable regions functionally equivalent to these variable regions. Here, "functionally equivalent" has the same meaning described above.

Table 4

GPC3 side / T cell receptor complex side	SEQ ID NO:
H0000/hCE115HA	40/52
H0000/CE115HA251	40/500
H0000/CE115HA236	40/429
H0000/TR01H002	40/421
H0000/CE115HA122	40/426
H0610/rCE115H	215/424
H0610/TR01H040	215/103
H0610/TR01H061	215/122
H0610/TR01H068	215/129
H0610/TR01H071	215/132
GCH054/TR01H067	197/128
GCH094/TR01H082	211/142
GCH094/TR01H084	211/144
GCH065/TR01H084	206/144
GCH065/TR01H082	206/142
GCH094/TR01H109	211/164
GCH065/TR01H109	206/164
GCH094/TR01H113	211/168
GCH065/TR01H113	206/168

A preferred common L chain for such combinations of an antibody variable region having glypican 3-binding activity and an antibody variable region having T-cell receptor complex binding activity includes, for example, L0000, L0011, L0201, L0203, L0204, L0206, L0208, L0209, L0211, L0212, L0222, and a common L chain having CDR sequences (CDR1, CDR2, and CDR3 amino acid sequences) identical to the CDR1, CDR2, and CDR3 amino acid sequences as in the above common L chain. Specific combinations include, for example, the combinations of antibody H-chain variable regions and a common L chain shown in Table 5, combinations of antibody variable regions having CDR sequences (CDR1, CDR2, and CDR3 amino acid sequences) identical to the amino acid sequences of CDR1, CDR2, and CDR3 carried by the antibody variable regions and a common L chain of Table 5, and combinations of antibody H-chain variable regions and a common L chain functionally equivalent to these variable regions. Here, “functionally equivalent” has the same meaning as described above.

Table 5

GPC3 side / T cell receptor complex side / common L chain	SEQ ID NO:
H0610/rCE115H/L0000	215/424/53
H0610/TR01H040/L0000	215/103/53
H0610/TR01H040/L0201	215/103/299
H0610/TR01H040/L0203	215/103/301
H0610/TR01H040/L0204	215/103/302
H0610/TR01H040/L0206	215/103/304
H0610/TR01H040/L0208	215/103/306
H0610/TR01H040/L0209	215/103/307
H0610/TR01H040/L0211	215/103/309
H0610/TR01H061/L0000	215/122/53
H0610/TR01H068/L0000	215/129/53
H0610/TR01H071/L0000	215/132/53
GCH054/TR01H067/L0201	197/128/299
GCH054/TR01H067/L0212	197/128/310
GCH054/TR01H067/L0222	197/128/319
GCH054/TR01H067/L0000	197/128/53
GCH094/TR01H082/L0201	211/142/299
GCH094/TR01H082/L0011	211/142/223
GCH094/TR01H084/L0011	211/144/223
GCH065/TR01H084/L0011	206/144/223
GCH065/TR01H082/L0011	206/142/223
GCH094/TR01H109/L0011	211/164/223
GCH065/TR01H109/L0011	206/164/223
GCH094/TR01H113/L0011	211/168/223
GCH065/TR01H113/L0011	206/168/223

The Fc region comprised in the multispecific antigen-binding molecule of the present invention is not particularly limited as long as it is an Fc region having reduced Fcγ receptor-binding activity, but examples of a preferred Fc region of the present invention include a combination of the Fc-region portion of E22Hh and the Fc-region portion of E22Hk, a combination of the Fc-region portion of E2702GsKsc and the Fc-region portion of E2704sEpsc, and a combination of the Fc-region portion of E2702sKsc and the Fc-region portion of E2704sEpsc.

Examples of a preferred multispecific antigen-binding molecule of the present invention include bispecific antibodies comprising an antibody variable region having glypican 3-binding activity and an antibody variable region having CD3ε-binding activity. More preferably, the

cytotoxic activity is the same or greater than that of the GPC3_ERY22_rCE115 bispecific antibody. Examples of such bispecific antibodies include bispecific antibodies comprising H and L chains described in Table 13, and bispecific antibodies that bind to an epitope overlapping with an epitope bound by the above antibodies, and which contain an Fc region with reduced Fcγ receptor-binding activity.

Whether an antibody recognizes an epitope that overlaps with an epitope recognized by another antibody can be confirmed by the competition between the two antibodies against the epitope. Competition between the antibodies can be evaluated by competitive binding assays using means such as enzyme-linked immunosorbent assay (ELISA), fluorescence energy transfer method (FRET), and fluorometric microvolume assay technology (FMAT (Registered trademark)). The amount of an antibody bound to an antigen indirectly correlates with the binding ability of a candidate competitor antibody (a test antibody) that competitively binds to the overlapping epitope. In other words, as the amount or affinity of a test antibody against the overlapping epitope increases, the amount of the antibody bound to the antigen decreases, and the amount of the antigen-bound test antibody increases. Specifically, the appropriately labeled antibody and antibody to be evaluated are simultaneously added to the antigen, and the antibody bound as a result are detected using the label. The amount of the antigen-bound antibody can be easily determined by labeling the antibody beforehand. This label is not particularly limited, and the labeling method is selected according to the assay technique used. Specifically, the labeling method includes fluorescent labeling, radiolabeling, enzymatic labeling, and such.

For example, the fluorescently labeled antibody and the unlabeled antibody or test antibody are simultaneously added to beads immobilized with GPC3 or CD3ε, and the labeled antibody is detected by fluorometric microvolume assay technology.

Herein, the "antibody that binds to the overlapping epitope" refers to a test antibody that can reduce the amount of the bound labeled antibody by at least 50% at a concentration that is usually 100 times higher, preferably 80 times higher, more preferably 50 times higher, even more preferably 30 times higher, and still more preferably 10 times higher than the concentration at which the non-labeled antibody reduces 50% of the amount of the labeled antibody bound (IC_{50}).

Multispecific antigen-binding molecules, which have the antigen-binding sites of antibodies that bind to epitopes overlapping with epitopes bound by the above-mentioned antibodies, can yield excellent cytotoxic activity.

The multispecific antigen-binding molecules of the present invention are produced by the same technique as the method for producing recombinant antibodies mentioned above.

The present invention also relates to polynucleotides encoding the antigen-binding molecules of the present invention, and they can be inserted into discretionary expression vectors.

Suitable hosts can be transformed with the expression vectors to produce cells that express the antigen-binding molecules. Antigen-binding molecules encoded by the polynucleotides can be obtained by culturing the cells that express the antigen-binding molecules, and collecting the expression products from culture supernatants. That is, the present invention relates to vectors comprising a polynucleotide encoding an antigen-binding molecule of the present invention, cells carrying such a vector, and methods for producing antigen-binding molecules, which comprise culturing the cells and collecting antigen-binding molecules from culture supernatants. These can be obtained by techniques similar to those for recombinant antibodies mentioned above.

Pharmaceutical compositions

From another viewpoint, the present invention provides pharmaceutical compositions comprising as the active ingredient a multispecific antigen-binding molecule that comprises: (1) a domain comprising an antibody variable region having glypican 3-binding activity, (2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity, and (3) a domain comprising an Fc region with reduced binding activity towards an Fcγ receptor. Furthermore, the present invention relates to pharmaceutical compositions that induce cell injury, which comprise the antigen-binding molecule as an active ingredient. Pharmaceutical compositions of the present invention which induce the described cell injury, particularly T-cell-dependent cellular cytotoxicity, are preferably administered to a subject suffering from a disease for which the activities are needed for prevention or treatment, or a subject in which the disease is possible to relapse.

Furthermore, in the present invention, cytotoxicity-inducing agents and cell growth-inhibiting agents comprising as the active ingredient a multispecific antigen-binding molecule that comprises:

(1) a domain comprising an antibody variable region having glypican 3-binding activity,

(2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity, and

(3) a domain comprising an Fc region with reduced binding activity towards an Fcγ receptor

can be presented as a method for inducing cell injury which comprises the step of administering the antigen-binding molecule to a subject, or it can be presented as use of the antigen-binding molecule in the manufacture of a cytotoxicity-inducing agent and a cell growth-inhibiting agent.

In the present invention "comprising as the active ingredient a multispecific antigen-binding molecule that comprises (1) a domain comprising an antibody variable region having glypican 3-binding activity, (2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity, and (3) a domain comprising an Fc region with reduced

binding activity towards an Fcγ receptor" means comprising the antigen-binding molecule as a major active component, without limitation to the content ratio of the antigen-binding molecule.

If necessary, multispecific antigen-binding molecules of the present invention may be encapsulated in microcapsules (e.g., those made of hydroxymethylcellulose, gelatin, and poly(methylmetacrylate)), or incorporated as components of a colloidal drug delivery system (e.g., liposomes, albumin microspheres, microemulsion, nanoparticles, and nanocapsules) (see, for example, "Remington's Pharmaceutical Science 16th edition", Oslo Ed. (1980)). Methods for preparing the pharmaceutical agents as controlled-release pharmaceutical agents are also well known, and such methods may be applied to the multispecific antigen-binding molecules of the present invention (J. Biomed. Mater. Res. (1981) 15: 267-277; Chemtech. (1982) 12: 98-105; U.S. Patent No. 3,773,719; European Patent Application Publication Nos. EP 58,481 and EP 133,988; Biopolymers (1983) 22: 547-556).

The pharmaceutical compositions of the present invention or cytotoxicity-inducing agents and cell growth-inhibiting agents may be administered to patients by oral or parenteral administration, and parenteral administration is preferred. Specific examples of the administration method include administration by injection, transnasal administration, transpulmonary administration, and transdermal administration. Examples of administration by injection include intravenous injection, intramuscular injection, intraperitoneal injection, and subcutaneous injection. A pharmaceutical composition of the present invention or a cytotoxicity-inducing agent and a cell growth-inhibiting agent can be administered systemically or locally, for example, through administration by injection. The method of administration can be selected appropriately according to the age and symptoms of the patient. The dose can be selected from the range of 0.0001 mg to 1000 mg per kilogram body weight for a single administration. Alternatively, for example, the dose may be selected from the range of 0.001 mg/body to 100000 mg/body per patient. However, the pharmaceutical compositions of the present invention or a cytotoxicity-inducing agent and cell growth-inhibiting agent are not limited to these doses.

The pharmaceutical compositions of the present invention or cytotoxicity-inducing agents and cell growth-inhibiting agents can be formulated according to conventional methods (for example, Remington's Pharmaceutical Science, latest edition, Mark Publishing Company, Easton, U.S.A), and may also contain pharmaceutically acceptable carriers and additives. Examples include, but are not limited to surfactants, excipients, coloring agents, perfumes, preservatives, stabilizers, buffers, suspending agents, isotonization agents, binders, disintegrants, lubricants, fluidity promoting agents, and flavoring agents; and other commonly used carriers can be suitably used. Specific examples of the carriers include light anhydrous silicic acid, lactose, crystalline cellulose, mannitol, starch, carmellose calcium, carmellose sodium,

hydroxypropyl cellulose, hydroxypropyl methyl cellulose, polyvinylacetal diethylaminoacetate, polyvinylpyrrolidone, gelatin, medium chain fatty acid triglyceride, polyoxyethylene hardened castor oil 60, saccharose, carboxymethyl cellulose, corn starch, inorganic salt, and such.

The present invention also provides methods for damaging glypican 3 antigen-expressing cells or tumor tissues containing the antigen-expressing cells, or methods for suppressing growth of these cells or tumor tissues by contacting the glypican 3 antigen-expressing cells with a multispecific antigen-binding molecule of the present invention that binds to the antigen. The multispecific antigen-binding molecule that binds to the antigen is as described above for an antigen-binding molecule of the present invention that binds to the antigen, which is comprised in the cytotoxicity-inducing agents and cell growth-inhibiting agents of the present invention. The cells bound by a multispecific antigen-binding molecule of the present invention that binds to the antigen are not particularly limited as long as they are cells expressing the antigen.

In the present invention, "contact" is carried out, for example, by adding a multispecific antigen-binding molecule of the present invention which binds to the antigen to the culture medium of GPC3 antigen-expressing cells cultured *in vitro*. In this case, a liquid or a solid obtained by freeze-drying or such may be suitably used as the form of the added antigen-binding molecule. When added as an aqueous solution, it may be an aqueous solution that simply contains only the multispecific antigen-binding molecule of the present invention, or it may be a solution containing also, for example, the above-mentioned surfactants, excipients, coloring agents, perfumes, preservatives, stabilizers, buffers, suspending agents, isotonization agents, binders, disintegrants, lubricants, fluidity promoting agents, and flavoring agents. The concentration at which the addition is performed is not particularly limited, but a suitable final concentration in the culture solution is preferably in the range of 1 pg/ml to 1 g/ml, more preferably 1 ng/ml to 1 mg/ml, and even more preferably 1 μg/mL to 1 mg/mL.

Furthermore, in another embodiment, "contact" of the present invention is also carried out by administering an antigen-binding molecule of the present invention to non-human animals with cells expressing the GPC3 antigen transplanted into their bodies, and to animals carrying cells that intrinsically express the antigen. The method of administration may be oral or parenteral, and parenteral administration is particularly preferred. Specific examples of the administration method include administration by injection, transnasal administration, transpulmonary administration, and transdermal administration. Examples of administration by injection include intravenous injection, intramuscular injection, intraperitoneal injection, and subcutaneous injection. A pharmaceutical composition of the present invention or a cytotoxicity-inducing agent and a cell growth-inhibiting agent can be administered systemically or locally, for example, through administration by injection. The method of administration can

be selected appropriately according to the age and symptoms of the test animal. When administered as an aqueous solution, an aqueous solution containing simply only a multispecific antigen-binding molecule of the present invention may be used, or a solution containing also the above-mentioned surfactants, excipients, coloring agents, perfumes, preservatives, stabilizers, buffers, suspending agents, isotonization agents, binders, disintegrants, lubricants, fluidity promoting agents, flavoring agents, and such may be used. The dose can be selected from the range of 0.0001 mg to 1000 mg per kilogram body weight for a single administration. Alternatively, for example, the dose may be selected from the range of 0.001 mg/body to 100000 mg/body per patient. However, the amount of the multispecific antigen-binding molecule of the present invention administered is not limited to these doses.

The following method is suitably used as a method for evaluating or measuring cell injury induced in cells expressing the glypican 3 antigen which is bound by a domain carrying an antibody variable region having glypican 3-binding activity that constitutes the antigen-binding molecule as a result of contacting the cells with a multispecific antigen-binding molecule of the present invention. Examples of a method for evaluating or measuring the cytotoxic activity *in vitro* include methods for measuring cytotoxic T cell activity and such. Whether or not a multispecific antigen-binding molecule of the present invention has T cellular cytotoxicity can be measured by known methods (for example, Current protocols in Immunology, Chapter 7. Immunologic studies in humans, Editor, John E. Coligan *et al.*, John Wiley & Sons, Inc., (1993) and the like). For activity measurements, an antigen-binding molecule that binds to an antigen different from glypican 3, which is an antigen not expressed in the cells used for the examination, can be used as a control in the same manner as a multispecific antigen-binding molecule of the present invention, and the activity can be determined to be present when the multispecific antigen-binding molecule of the present invention shows a stronger cytotoxic activity than when the antigen-binding molecule is used as a control.

To evaluate or measure cytotoxic activity *in vivo*, for example, cells expressing a glypican 3 antigen are intradermally or subcutaneously transplanted to a non-human test animal, and then a test antigen-binding molecule is intravenously or intraperitoneally administered daily or with an interval of few days, starting from the day of transplantation or the following day. Cytotoxic activity can be determined by daily measurement of tumor size and by observing difference in the change of tumor size. In a similar manner to the *in vitro* evaluation, the cytotoxic activity of an antigen-binding molecule of the present invention can be determined to be present when administration of a control antigen-binding molecule shows that the tumor size in the group subjected to administration of an antigen-binding molecule of the present invention is significantly smaller than the tumor size in the group subjected to administration of the control antigen-binding molecule.

As a method for evaluating or measuring the suppressive effect on proliferation of cells expressing a glypican 3 antigen, a method of measuring the uptake of isotope-labeled thymidine into cells or the MTT method may be suitably used. As a method for evaluating or measuring the cell proliferation-suppressing activity *in vivo*, the same method described above for evaluating or measuring cytotoxic activity *in vivo* may be suitably used.

The present invention also provides kits for use in the methods of the present invention, which comprise a multispecific antigen-binding molecule of the present invention or a multispecific antigen-binding molecule produced by a production method of the present invention. Additionally, the kit may include in its package, a pharmaceutically acceptable carrier, solvent, and instructions describing the method of use.

The present invention also relates to a multispecific antigen-binding molecule of the present invention or a multispecific antigen-binding molecule produced by a production method of the present invention for use in a method of the present invention.

The present invention also relates to molecules having GPC3-binding activity, which contain a domain comprising an antibody variable region having GPC3-binding activity of the multispecific antigen-binding molecule of the present invention. Furthermore, the present invention relates to a molecule having GPC3-binding activity, which comprises the antibody variable regions of H and L chains respectively comprising the three CDRs of the H and L chains (total of six CDRs) contained in the molecule. The present invention also relates to molecules having T-cell receptor complex-binding activity, which contain a domain comprising an antibody variable region having T-cell receptor complex-binding activity of the multispecific antigen-binding molecule of the present invention. Furthermore, the present invention relates to a molecule having T-cell receptor complex-binding activity that comprises the antibody variable regions of the H and L chains respectively comprising the three CDRs of the H and L chains (total of six CDRs) contained in the molecule. Such molecules may be antibodies or polypeptides comprising antigen-binding fragments of an antibody. The present invention also relates to antibodies that bind to epitopes overlapping or competing with these molecules or polypeptides containing the antigen-binding fragments thereof. Suitable examples of such polypeptides comprising antigen-binding fragments of an antibody include scFv, single chain antibody, Fv, single chain Fv 2 (scFv2), Fab, and $F(ab')_2$. Furthermore, these molecules do not have to be multispecific (bispecific), and may bind only to either GPC3 or a T cell receptor complex (for example, the CD3ε chain).

These molecules include a molecule comprising a domain that comprises an antibody variable region having GPC-binding activity of the multispecific antigen-binding molecule exemplified in detail in the Examples herein (which comprises the H-chain variable regions having GPC3-binding activity and the common L-chain variable region), a molecule comprising

a domain that comprises an antibody variable region having T cell receptor complex-binding activity of the multispecific antigen-binding molecule exemplified in the Examples herein (which comprises the H-chain variable regions having T cell receptor complex-binding activity and the common L-chain variable region), and also a molecule having an activity to bind to the same antigenic protein (GPC3 or T-cell receptor complex), which comprises the three CDRs of each of the H and L chains (total of six CDRs) contained in the above molecule.

These molecules have CDRs that are in common with those of a multispecific antigen-binding molecule of the present invention; and therefore, they are expected to bind to an epitope overlapping with an epitope for the multispecific antigen-binding molecule of the present invention. Therefore, these molecules can compete with multispecific antigen-binding molecules of the present invention when they coexist with the multispecific antigen-binding molecules of the present invention. Accordingly, these molecules can be used, for example, as regulatory agents for suppressing activities (such as antigen-binding activity, cytotoxic activity, and antitumor activity) of the multispecific antigen-binding molecules of the present invention. Furthermore, such a molecule can be bound to a target protein (GPC3 or T cell receptor complex) in advance, and when a multispecific antigen-binding molecule of the present invention is added, the molecules that dissociate through competition can be detected. This way, the molecule is useful as an agent for detecting binding of a multispecific antigen-binding molecule of the present invention to a target protein. Here, such molecules may be labeled appropriately with fluorescent substances or such. Alternatively, these molecules are useful for screening novel antibodies that bind to epitopes overlapping with the epitopes bound by the multispecific antigen-binding molecules of the present invention. As described above, such a molecule can be bound to a target protein (GPC3 or T cell receptor complex) in advance, and when a test antibody is added, if the bound molecules dissociate, then the test antibody is a candidate for an antibody that binds to an epitope overlapping with the epitope bound by the multispecific antigen-binding molecule of the present invention. This will enable efficient screening of novel multispecific antigen-binding molecules.

The combinations presented as examples herein as combinations of each CDR of the multispecific antigen-binding molecules of the present invention can be directly used as specific combinations of CDRs of the H-chain and L-chain variable regions in these molecules. The antigen affinity of these molecules (KD values) is preferably a value exemplified herein as the KD value of a multispecific antigen-binding molecule of the present invention, but is not limited thereto.

The present invention also relates to nucleic acids encoding these molecules, vectors comprising the nucleic acids, cells comprising the nucleic acids or the vectors, methods for producing the molecules by culturing the cells, and molecules produced by these methods.

All prior art references cited herein are incorporated by reference into this description.

Examples

Herein below, the present invention will be specifically described with reference to the Examples, but it is not to be construed as being limited thereto.

[Example 1] Production of GPC3_ERY22_rCE115 and measurement of cytotoxic activity

(1-1) Production of GPC3_ERY22_rCE115

A molecule in which one of the Fabs has been replaced with a CD3 epsilon-binding domain was produced using IgG against a cancer antigen (GPC3) as the basic structure. In this case, the IgG Fc used as the basic structure was a silent Fc with attenuated affinity for FcgR (an Fcγ (Fc gamma) receptor). An anti-GPC3 antibody, H0000 (SEQ ID NO: 40) / GL4 (SEQ ID NO: 41), was used as the GPC3-binding domain. An anti-CD3 antibody, rCE115H/rCE115L (SEQ ID NO: 42 / SEQ ID NO: 43), was used as the CD3-binding domain.

G1d produced by removing Gly and Lys at the C terminus of IgG1 was used as the antibody H-chain constant region, and this was used in combination with H0000/GL4 and rCE115H/rCE115L. When the antibody H-chain constant region was named H1, the sequence corresponding to the H chain of the antibody carrying H0000 in the variable region was shown as H0000-H1. Here, an amino acid alteration was shown, for example, as D356K. The first alphabet (corresponding to D in D356K) is the one-letter code representation for the amino acid residue before modification, the number that follows (corresponding to 356 of D356K) is the position of modification indicated by EU numbering, and the final alphabet (corresponding to K of D356K) is the one-letter code representation for the amino acid residue after modification. G1dh (SEQ ID NO: 44) produced by removing Gly and Lys at the C terminus of IgG1, ERY22_Hk (SEQ ID NO: 45) produced by introducing the L234A/L235A/Y349C/T366W mutations into G1dh, and ERY22_Hh (SEQ ID NO: 46) produced by introducing the L234A/L235A/D356C/T366S/L368A/Y407V mutations into G1dh were prepared according to the method of Reference Example 1. The L234A and L235A mutations were introduced into the respective H chains to attenuate affinity for FcgR (an Fcγ receptor), and the Y349C/T366W and D356C/T366S/L368A/Y407V mutations were introduced to efficiently form heteromers of each H chain when producing heterodimeric antibodies comprising two types of H chains.

The heterodimeric antibody, GPC3_ERY22_rCE115, produced by substitution with the VH and VL domains of Fab against GPC3 was prepared according to Reference Example 1 (Fig. 1a).

A series of expression vectors inserted with a polynucleotide encoding each of GL4-ERY22_Hk (SEQ ID NO: 47), H0000-ERY22_L (SEQ ID NO: 48), rCE115H-ERY22_Hh (SEQ

ID NO: 49), and rCE115L-k0 (SEQ ID NO: 50) were produced by methods well-known to those skilled in the art, such as PCR methods using primers added with an appropriate sequence similar to those in the above-described method.

The following combination of expression vectors were introduced into FreeStyle 293-F cells for transient expression of each target molecule.

Target molecule: GPC3_ERY22_rCE115

Polypeptides encoded by the polynucleotides inserted into the expression vectors: GL4-ERY22_Hk, H0000-ERY22_L, rCE115H-ERY22_Hh, rCE115L-k0

(1-2) Purification of GPC3_ERY22_rCE115

The obtained culture supernatant was added to an anti-FLAG M2 column (Sigma), and then the column was washed, followed by elution using 0.1 mg/mL of a FLAG peptide (Sigma). The fractions containing the molecule of interest were added to a HisTrap HP column (GE Healthcare), and then the column was washed, followed by elution using an imidazole concentration gradient. Fractions containing the molecule of interest were concentrated using an ultrafiltration membrane, then the fractions were added to a Superdex 200 column (GE Healthcare), and each of the purified molecules of interest was obtained by collecting only the monomeric fractions from the eluted solution.

(1-3) Measurement of the cytotoxic activity of GPC3_ERY22_rCE115 using human peripheral blood mononuclear cells

The *in vitro* cytotoxic activity of GPC3_ERY22_rCE115 was assessed.

(1-3-1) Preparation of a human peripheral blood mononuclear cell (PBMC) solution

Using a syringe preloaded with 100 μL of 1,000 units/mL heparin solution (Novo Heparin for injection, 5000 units, Novo Nordisk), 50 mL of peripheral blood was collected from each healthy volunteer (adult individual). This peripheral blood was diluted two-fold in PBS(-), divided into four aliquots, and added into a Leucosep tube for lymphocyte separation (Cat. No. 227290, Greiner Bio-One) that had been loaded with 15 mL of Ficoll-Paque PLUS and subjected to centrifugation in advance. This separation tube was centrifuged (at 2150 rpm for ten minutes at room temperature), and then the mononuclear cell fraction was collected. The cells in the mononuclear cell fraction were washed once with the Dulbecco's Modified Eagle's Medium containing 10% FBS (manufactured by SIGMA, hereinafter referred to as 10% FBS/D-MEM), and then prepared to have a cell density of 4 x 10^6 cells/mL using 10% FBS/D-MEM. The cell suspension prepared this way was used as the human PBMC solution in the experiment below.

(1-3-2) Measurement of cytotoxic activity

Cytotoxic activity was assessed by the rate of cell growth inhibition using the xCELLigence Real-Time Cell Analyzer (Roche Diagnostics). The NCI-H446 human cancer cell line or the PC-10 human cancer cell line, which expresses human GPC3, was used as the target cell. NCI-H446 or PC-10 was detached from the dish, then the cells were plated into E-Plate 96 (Roche Diagnostics) in aliquots of 100 μL/well by adjusting the cells to 1 x 10^4 cells/well, and measurement of live cells was begun using the xCELLigence Real-Time Cell Analyzer. On the following day, the plate was removed from the xCELLigence Real-Time Cell Analyzer, and 50 μL of the respective antibodies prepared at each concentration (0.004, 0.04, 0.4, 4, or 40 nM) were added to the plate. After 15 minutes of reaction at room temperature, 50 μL of the human PBMC solution prepared in (1-2) was added (2 x 10^5 cells/well), and measurement of live cells was begun by setting the plate into the xCELLigence Real-Time Cell Analyzer again. The reaction was carried out under the conditions of 5% carbon dioxide gas at 37°C, and from the Cell Index value obtained 72 hours after addition of the human PBMC, the cell growth inhibition rate (%) was determined using the equation below. The Cell Index value used in the calculation was a normalized value where the Cell Index value immediately before antibody addition was defined as 1.

Cell growth inhibition rate (%) = (A-B) x 100/(A-1)

A represents the mean value of the Cell Index values in wells without antibody addition (containing only the target cells and human PBMCs), and B represents the mean value of the Cell Index values in each well. The examinations were performed in triplicate.

When peripheral blood mononuclear cells (PBMCs) prepared from human blood were used as the effector cell to measure the cytotoxicity of GPC3_ERY22_rCE115, a very strong activity was observed (Fig. 2).

[Example 2] Humanization of the H chain of the anti-CD3 antibody, rCE115, and sharing of a common L chain

(2-1) Design of hCE115HA, the humanized rCE115 H-chain variable region

The H-chain variable region of the rCE115 anti-CD3 antibody (SEQ ID NO: 42) was humanized. CDR and FR were determined as defined by Kabat (Kabat numbering).

First, a human FR sequence was selected by comparing the human antibody variable region sequences in a database to the rCE115 rat variable region sequence. The IMGT Database (http://www.imgt.org/) and NCBI GenBank (http://www.ncbi.nlm.nih.gov/genbank/) were used for the database. A humanized H-chain variable region sequence was designed by linking the H-chain CDR sequence of the rCE115 variable region with the selected human FR sequence. This yielded a humanized H-chain variable region sequence, hCE115HL (SEQ ID NO: 51).

The amino acid residue at position 93 indicated by Kabat numbering is Ala in the selected human H-chain FR3 sequence, but is Arg in the rCE115 variable region sequence. Using the database of rat and human germline sequences (IMGT Database (http://www.imgt.org/)), only few sequences were found to contain Arg at this site. It is reported that the amino acid residue at position 94 indicated by Kabat numbering contributes to stabilization of the antibody structure by upper core formation (Ewert *et al.* Methods. 2004 Oct;34(2):184-99). Based on such information, a humanized H-chain variable region sequence, in which the amino acid residues at Kabat positions 93 and 94 in the H-chain FR3 were substituted with those residues present in the rCE115 variable region sequence, was newly designed. This was the humanized H-chain variable region sequence, hCE115HA (SEQ ID NO: 52).

(2-2) Design of the common L chain, L0000, for the rCE115 anti-CD3 antibody and the anti-GPC3 antibody

The FR/CDR shuffling of the L-chain variable region rCE115L (SEQ ID NO: 43) of the rCE115 anti-CD3 antibody and the L-chain variable region GL4 (SEQ ID NO: 41) of the anti-GPC3 antibody was performed.

The FR sequence of GL4 was selected as the L-chain FR sequence. L-chain CDR2 was the same for rCE115L and GL4. The L-chain CDR1 was selected from the CDR sequences of GL4, and the L-chain CDR3 was selected from the CDR sequences of rCE115L, respectively. Furthermore, the L-chain CDR3 produced by substituting the amino acid residue Asp at Kabat position 94 of the selected L-chain CDR3 with the Val residue present in GL4 was newly designed.

A humanized L chain variable region sequence was designed by linking FR and CDR selected above. This yielded a humanized L-chain variable region sequence, L0000 (SEQ ID NO: 53).

(2-3) Evaluation of the affinity for human GPC3

The activity to bind human GPC3 when using GL4 (SEQ ID NO: 41) and L0000 (SEQ ID NO: 53) as the L-chain variable regions was evaluated. This was performed using the molecular form of a single-arm antibody having a single Fab at the Fc region of a human IgG1 heterodimerized by the knobs-into-hole technique. H0000 (SEQ ID NO: 40) was used for the anti-GPC3 antibody H-chain variable region.

The affinity and binding rate constants of an anti-GPC3 antibody for an antigen were measured by the multi-cycle kinetics method of a surface plasmon resonance assay using Biacore™-T200 (GE Healthcare Japan). HBS-EP+ (GE Healthcare Japan) was used for the

running buffer, and an amine coupling kit (GE Healthcare Japan) was used to covalently bind Protein A/G to the CM5 chip (carboxymethyl dextran-coated chip). Each anti-GPC3 antibody was prepared so that approximately 100 RU will be captured by Protein A/G. Human GPC3 used as the analyte was prepared at 8, 16, 32, 64, and 128 nM using HBS-EP+. Measurements were carried out by first allowing Protein A/G to capture the antibody solution, and then injecting the human GPC3 solution at a flow rate of 30 μL/min for three minutes to allow reaction to take place. Then, the solution was switched to HBS-EP+ and the dissociation phase was measured for 15 minutes. After completion of the dissociation phase measurement, the sensor chip was regenerated by washing with 10 mM Gly-HCl at pH 1.5. Measurement at the concentration of 0 was similarly carried out by allowing Protein A/G to capture the antibody solution, performing a three-minute HBS-EP+ injection to allow reaction to take place, and then switching to HBS-EP+ to measure the dissociation phase for 15 minutes. After completion of the dissociation phase measurement, the sensor chip was regenerated by washing with 10 mM Gly-HCl at pH 1.5. A data analysis software exclusively for Biacore, Biacore T200 Evaluation Software Version 1.0, was used to perform kinetic analyses to calculate the binding rate constant (ka), dissociation rate constant (kd), and the rate constant ratio from the obtained sensorgrams. The results are shown in Table 6.

Table 6

Variable region		Affinity for human GPC3		
H-chain variable region	L-chain variable region	KD (M)	ka (1/Ms)	kd (1/s)
H0000	GL4	$4.2x10^{-9}$	$4.3x10^{5}$	$1.8x10^{-3}$
H0000	L0000	$3.6x10^{-8}$	$3.0x10^{5}$	$1.1x10^{-2}$

(2-4) Evaluation of the affinity for human CD3

The activity to bind human CD3 when using hCE115HA (SEQ ID NO: 52) as the H chain variable region and L0000 (SEQ ID NO: 53) as the L-chain variable region was evaluated. This was performed using the molecular form of a single-arm antibody having a single Fab at the Fc region of a human IgG1 heterodimerized by the knobs-into-hole technique.

The affinity and binding rate constants of an anti-CD3 antibody for an antigen were measured by the single-cycle kinetics method of a surface plasmon resonance assay using Biacore™-T200 (GE Healthcare Japan). HBS-EP+ (GE Healthcare Japan) was used for the running buffer, and an amine coupling kit (GE Healthcare Japan) was used to covalently bind human CD3 to the CM4 chip (carboxymethyl dextran-coated chip). The anti-CD3 antibody used as the analyte was prepared at 5 and 20 μg/mL using HBS-EP+. Measurements were carried out by first injecting each of the 5- and 20-μg/mL anti-CD3 antibody solutions for three minutes

continuously at a flow rate of 20 μL/min to allow reaction to take place. Then, the solution was switched to HBS-EP+ and the dissociation phase was measured for 3 minutes. After completion of the dissociation phase measurement, the sensor chip was regenerated by washing with 10 mM Gly-HCl at pH 1.5. Measurement at the concentration of 0 was carried out by performing each of the three-minute HBS-EP+ injections twice successively to allow reaction to take place, and then switching to HBS-EP+ to measure the dissociation phase for 3 minutes. After completion of the dissociation phase measurement, the sensor chip was regenerated by washing with 10 mM Gly-HCl at pH 1.5. A data analysis software exclusively for Biacore, Biacore T200 Evaluation Software Version 1.0, was used to perform kinetic analyses to calculate the binding rate constant (ka), dissociation rate constant (kd), and the rate constant ratio from the obtained sensorgrams. The results are shown in Table 7.

Table 7

Variable region		Affinity for human CD3		
H-chain variable region	L-chain variable region	KD (M)	ka (1/Ms)	kd (1/s)
rCE115H	rCE115L	$1.0x10^{-7}$	$5.9x10^{4}$	$6.0x10^{-3}$
hCE115HA	L0000	$1.2x10^{-7}$	$1.9x10^{5}$	$2.3x10^{-2}$

(2-5) Preparation of GPC3_ERY27_hCE115

The IgG4 against a cancer antigen (GPC3) was used as the basic structure to produce the ERY27 molecule (Fig. 1b), in which the H-chain variable region of one of the Fabs has been replaced with a CD3 epsilon-binding domain, and the L chain is common to both Fabs. In this case, the IgG4 Fc used as the basic structure was a silent Fc with attenuated affinity for FcgR (an Fcγ receptor). H0000 (SEQ ID NO: 40) was used as the H-chain variable region of the GPC3-binding domain, and hCE115HA (SEQ ID NO: 52) was used as the H-chain variable region of the CD3-binding domain. L0000 (SEQ ID NO: 53) was used as the L-chain variable region. The D356K and K439E mutations introduced into the respective H chains were introduced for efficient heteromer formation of each H chain when producing heterodimeric antibodies comprising two types of H chains (WO2006/106905). H435R is a modification that interrupts binding to Protein A, and was introduced for efficient separation of the heteromer and homomer (WO/2011/078332).

A series of expression vectors inserted with a polynucleotide encoding each of H0000-ERY27_HK (SEQ ID NO: 54), hCE115HA-ERY27_HE (SEQ ID NO: 55), and L0000-k0 (SEQ ID NO: 56) were produced by well-known methods.

The following combination of expression vectors were introduced into FreeStyle 293-F cells for transient expression of each target molecule.

Target molecule: GPC3_ERY27_hCE115

Polypeptides encoded by the polynucleotides inserted into the expression vectors: H0000-ERY27_HK, hCE115HA-ERY27_HE, and L0000-k0

(2-6) Purification of GPC3_ERY27_hCE115

Each molecule of interest was purified by the method described in Example 1-2.

(2-7) Measurement of cytotoxic activity using human peripheral blood mononuclear cells

(2-7-1) Preparation of a human peripheral blood mononuclear cell (PBMC) solution

The solution was prepared by the method described in Example 1-3-1.

(2-7-2) Measurement of cytotoxic activity

Cytotoxic activity was measured by the method described in Example 1-3-2.

When PBMCs prepared from human blood were used as the effector cell to measure the cytotoxicity of GPC3_ERY27_hCE115, reduction of the activity was observed as a result of humanization of the H chain of rCE115 and sharing of a common L chain (Fig. 2).

[Example 3] Production and evaluation of humanized bispecific antibody variants for improvement of various properties

The T-cell-dependent cytotoxic activity of the humanized anti-human CD3ε (CD3 epsilon) chain and anti-human GPC3 bispecific antibody obtained in Example 2, GPC3_ERY27_hCE115 (SEQ ID NOs: 54, 55, and 56), was lower than the T-cell-dependent cytotoxic activity of GPC3_ERY22_rCE115 (SEQ ID NOs: 47, 48, 49, and 50). This may be due to attenuation of affinity for GPC3 and the CD3ε chain as a result of humanization and sharing of a common L chain. Regarding GPC3 and CD3ε-chain antigens which have independent sequences, there has been no report so far on humanized bispecific antibodies whose T-cell dependent cytotoxic activity has been enhanced and whose affinity for both antigens has been improved by using a common antibody L chain. Therefore, it has been considered difficult to obtain humanized antibodies with dual specificity that show a drug efficacy equivalent to or greater than that of GPC3_ERY22_rCE115.

Under such circumstances, the Applicants produced modified humanized bispecific antibodies with modified affinity for human GPC3 and human CD3ε chain by methods known to those skilled in the art, which involves comprehensively substituting amino acid residues encoded by the antibody gene to produce antibody variants against both the human GPC3 and human CD3ε-chain antigens, and by performing various evaluations by screening. Furthermore, similar methods were used to produce modified humanized bispecific antibodies with modified physicochemical properties. Furthermore, by combining substitutions of amino acid residues

effective for modifying affinity and physicochemical properties, optimized bispecific antibodies having a TDCC activity equivalent to or greater than the T-cell dependent cellular cytotoxicity of GPC3_ERY22_rCE115 prior to humanization were produced.

Introduction of point mutations, expression and purification of antibodies, antigen affinity measurements, and determination of T-cell dependent cellular cytotoxicity in the optimization of humanized bispecific antibodies were performed by methods similar to those in Examples 1 and 2. CDR and FR were determined according to the Kabat definition (Kabat numbering).

Depending on the objective, the following were used as the antibody H-chain constant regions (the numbers indicate EU numbering): E22Hh (SEQ ID NO: 57) produced by introducing L234A/L235A/N297A/D356C/T366S/L368A/Y407V/G446 deletion/K447 deletion mutations into human IgG1; E22Hk (SEQ ID NO: 58) produced by introducing L234A/L235A/N297A/Y349C/T366W/G446 deletion/K447 deletion mutations and a Ser-Ser insertion mutation immediately before position 118 into human IgG1; G1dh produced by introducing D356C/T366S/L368A/Y407V/G446 deletion/K447 deletion mutations into human IgG1; none-Hi-Kn010G3 produced by introducing 118-215 deletion and C220S/Y349C/T366W/H435R mutations into human IgG1; E2702GsKsc (SEQ ID NO: 60) produced by introducing L235R/S239K/N297A/E356K/R409K/H435R/L445P/G446 deletion/K447 deletion mutations into human IgG4; E2704sEpsc (SEQ ID NO: 61) produced by introducing K196Q/L235R/S239K/N297A/R409K/K439E/L445P/G446 deletion/K447 deletion mutations into human IgG4; and E2702sKsc (SEQ ID NO: 62) produced by introducing L235R/S239K/N297A/E356K/R409K/L445P/G446 deletion/K447 deletion mutations into human IgG4. Furthermore, human κ (kappa) chain k0 (SEQ ID NO: 63) and E22L (SEQ ID NO: 432) produced by introducing R108A/T109S mutations into human κ chain were used as the antibody L-chain constant regions.

The mutation that substitutes Cys for Asp at EU numbering position 356, the mutation that substitutes Ser for The at EU numbering position 366, the mutation that substitutes Ala for Leu at EU numbering position 368, the mutation that substitutes Val for Tyr at EU numbering position 407, the mutation that substitutes Cys for Tyr at EU numbering position 349, the mutation that substitutes Trp for Thr at EU numbering position 366, and the mutation that inserts Ser-Ser immediately before position 118 are mutations for efficient formation of heterodimeric molecules for each H chain when producing heteromeric antibodies. Similarly, the mutation that substitutes Lys for Glu at EU numbering position 356 and the mutation that substitutes Glu for Lys at EU numbering position 439 are also mutations for efficient formation of heterodimeric molecules for each H chain when producing heteromeric antibodies. They are expected to improve the efficiency of bispecific antibody production.

The mutation that substitutes Ala for Leu at EU numbering position 234, the mutation that substitutes Ala or Arg for Leu at EU numbering position 235, the mutation that substitutes Lys for Ser at EU numbering position 239, and the mutation that substitutes Ala for Asn at EU numbering position 297 are mutations for attenuating affinity for an Fcγ receptor and a complement (C1q). They are expected to suppress the binding of Fab to CD3 and Fc-mediated crosslinking of an Fcγ receptor or a complement, and avoid cytokine release syndrome that accompanies enhancement of non-specific effector functions.

The H chain introduced with deletion mutations at EU numbering positions 118 to 215 can be combined with a full-length H chain sequence to produce an antibody that has only one Fab (monovalent antibody), and it is useful for affinity evaluation.

The mutation that substitutes Lys for Arg at EU numbering position 409 and the mutation that substitutes Arg for His at EU numbering position 435 are mutations for modifying the antibody properties to be close to the properties of human IgG1 and human IgG3, respectively.

(3-1) Modifying the affinity of a humanized anti-CD3 antibody by point mutations

First, point mutations were introduced into FR1, FR2, FR3, CDR1, CDR2, and CDR3 of the humanized anti-human CD3ε chain antibody sequence produced in Example 2, hCE115HA-ERY27_HE (SEQ ID NO: 55), to prepare modified antibodies. Next, the affinity of these modified antibodies for the soluble human CD3ε chain was determined. Combining sites that have an affinity-enhancing effect yielded modified antibodies having the affinities shown in Table 8.

Table 8

Antibody name	KD (Human CD3)
hCE115HA-E22Hh//-Hi-Kn010G3/L0000-k0	1.43E-07
TR01H083-E22Hh/none-Hi-Kn010G3/L0212-k0	5.86E-11
TR01H040-E22Hh/none-Hi-Kn010G3/L0240-k0	2.17E-09
TR01H002-E22Hh/GLS3108-k0/GL4-E22Hk/H0610-E22L	2.04E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0212-k0	2.17E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0235-k0	2.81E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0238-k0	2.91E-09
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L016-k0	2.52E-09
TR01H083-E22Hh/none-Hi-Kn010G3/L0262-k0	2.45E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0207-k0	2.60E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0241-k0	3.48E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0242-k0	3.58E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0206-k0	2.90E-09
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L019-k0	3.20E-09
TR01H080-E22Hh/none-Hi-Kn010G3/L0000-k0	3.25E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0211-k0	3.22E-09
TR01H002-E22Hh//-Hi-Kn010G3/GLC3108-k0	4.61E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0209-k0	4.25E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0208-k0	4.16E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0224-k0	5.06E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0236-k0	5.64E-09
TR01H083-E22Hh/none-Hi-Kn010G3/L0201-k0	4.42E-09
TR01H084-E2702GsKsc/none-Hi-E2704sE/L0011-k0	4.14E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0210-k0	5.06E-09
TR01H114-E2702GsKsc/none-Hi-E2704sE/L0011-k0	4.22E-09
CE115HA236-E22Hh/GLS3108-k0/GL4-E22Hk/H0610-E22L	6.08E-09
TR01H077-E22Hh/none-Hi-Kn010G3/L0200-k0	6.12E-09
TR01H071-E22Hh/none-Hi-Kn010G3/L0200-k0	6.13E-09
TR01H111-E2702GsKsc/none-Hi-E2704sE/L0011-k0	4.91E-09
TR01H081-E22Hh/none-Hi-Kn010G3/L0262-k0	5.76E-09
TR01H001-E22Hh//-Hi-Kn010G3/GLC3108-k0	8.22E-09
CE115HA179-G1dh//-Hi-Kn010G3/L0000-k0	8.35E-09
TR01H112-E2702GsKsc/none-Hi-E2704sE/L0011-k0	5.12E-09
TR01H113-E2702GsKsc/none-Hi-E2704sE/L0011-k0	5.14E-09
TR01H082-E22Hh/none-Hi-Kn010G3/L0212-k0	4.75E-09
CE115HA236-E22Hh//-Hi-Kn010G3/GLC3108-k0	9.10E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0231-k0	7.75E-09
TR01H037-E22Hh/none-Hi-Kn010G3/L0000-k0	6.93E-09
CE115HA252-E22Hh//-Hi-Kn010G3/L0000-k0	9.48E-09
TR01H083-E22Hh/none-Hi-Kn010G3/L0011-k0	6.70E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0223-k0	8.15E-09
TR01H083-E22Hh/none-Hi-Kn010G3/L0000-k0	6.83E-09
TR01H071-E22Hh/none-Hi-Kn010G3/L0000-k0	8.85E-09
TR01H067-E22Hh/none-Hi-Kn010G3/L0212-k0	5.88E-09
CE115HA178-G1dh//-Hi-Kn010G3/L0000-k0	1.09E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0237-k0	1.02E-08
TR01H083-E22Hh/none-Hi-Kn010G3/L0222-k0	9.42E-09
TR01H084-E22Hh/none-Hi-Kn010G3/L0262-k0	8.51E-09
TR01H071-E22Hh/none-Hi-Kn010G3/L0215-k0	9.51E-09
TR01H040-E22Hh/none-Hi-Kn010G3/L0218-k0	8.20E-09
TR01H081-E22Hh/none-Hi-Kn010G3/L0201-k0	9.46E-09
TR01H071-E22Hh/none-Hi-Kn010G3/L0222-k0	1.04E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0220-k0	9.15E-09
TR01H067-E22Hh/none-Hi-Kn010G3/TR01L016-k0	1.09E-08
TR01H002-E22Hh/GLS3108-k0/GL4-E22Hk/H0000-E22L	4.78E-09
TR01H067-E22Hh/none-Hi-Kn010G3/TR01L019-k0	1.21E-08
TR01H038-E22Hh/none-Hi-Kn010G3/L0000-k0	1.24E-08
TR01H061-E22Hh/none-Hi-Kn010G3/L0200-k0	1.27E-08
TR01H082-E2702GsKsc/none-Hi-E2704sE/L0011-k0	1.01E-08
CE115HA180-G1dh//-Hi-Kn010G3/L0000-k0	1.68E-08
CE115HA251-E22Hh/L0000-k0/GL4-E22Hk/H0610-E22L	1.37E-08
TR01H100-E2702GsKsc/none-Hi-E2704sE/L0011-k0	1.11E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0228-k0	1.60E-08
TR01H081-E22Hh/none-Hi-Kn010G3/L0011-k0	1.35E-08
TR01H061-E22Hh/none-Hi-Kn010G3/L0215-k0	1.54E-08
TR01H110-E2702GsKsc/none-Hi-E2704sE/L0011-k0	1.26E-08
TR01H043-E22Hh/none-Hi-Kn010G3/L0000-k0	1.52E-08
TR01H081-E22Hh/none-Hi-Kn010G3/L0000-k0	1.56E-08
CE115HA251-E22Hh//-Hi-Kn010G3/L0000-k0	2.23E-08
TR01H091-E2702GsKsc/none-Hi-E2704sE/L0011-k0	1.39E-08
CE115HA236-E22Hh/GLS3108-k0/GL4-E22Hk/H0000-E22L	6.95E-09
TR01H084-E22Hh/none-Hi-Kn010G3/L0201-k0	1.65E-08
TR01H072-E22Hh/none-Hi-Kn010G3/L0000-k0	2.03E-08
TR01H099-E2702GsKsc/none-Hi-E2704sE/L0011-k0	1.46E-08
TR01H061-E22Hh/none-Hi-Kn010G3/L0222-k0	1.88E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0239-k0	2.31E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0262-k0	1.81E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0234-k0	2.40E-08
TR01H012-E22Hh/none-Hi-Kn010G3/L0000-k0	7.94E-09
TR01H061-E22Hh/none-Hi-Kn010G3/L0000-k0	1.71E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0243-k0	2.46E-08
TR01H109-E2702GsKsc/none-Hi-E2704sE/L0011-k0	1.64E-08
TR01H047-E22Hh/none-Hi-Kn010G3/L0000-k0	2.04E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0267-k0	2.29E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0266-k0	2.29E-08
TR01H084-E22Hh/none-Hi-Kn010G3/L0011-k0	1.98E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0250-k0	2.15E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0204-k0	2.21E-08
TR01H084-E22Hh/none-Hi-Kn010G3/L0000-k0	2.13E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0213-k0	2.01E-08

Antibody name	KD (Human CD3)
hCE115HA-E22Hh//-Hi-Kn010G3/L0000-k0	1.43E-07
TR01H040-E22Hh/none-Hi-Kn010G3/L0214-k0	2.02E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0217-k0	2.07E-08
TR01H071-E22Hh/none-Hi-Kn010G3/L0226-k0	2.51E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0200-k0	2.87E-08
TR01H074-E22Hh/none-Hi-Kn010G3/L0000-k0	2.91E-08
TR01H039-E22Hh/none-Hi-Kn010G3/L0000-k0	2.61E-08
CE115HA177-G1dh//-Hi-Kn010G3/L0000-k0	3.55E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0201-k0	2.81E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0263-k0	3.09E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0000-k0	3.60E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0216-k0	2.53E-08
TR01H051-E22Hh/none-Hi-Kn010G3/L0000-k0	2.91E-08
TR01H003-E22Hh//-Hi-Kn010G3/L0000-k0	4.03E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0264-k0	3.44E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0232-k0	3.86E-08
TR01H041-E22Hh/none-Hi-Kn010G3/L0000-k0	3.16E-08
CE115HA122-E22Hh//-Hi-Kn010G3/L0000-k0	4.28E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0233-k0	4.01E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0215-k0	3.37E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0203-k0	3.24E-08
TR01H015-E2702GsKsc/GCH019-E2704sEpsc/L0000-k0	2.96E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L008-k0	2.93E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0205-k0	3.42E-08
TR01H015-E22Hh/L0000-k0/GL4-E22Hk/H0610-E22L	3.57E-08
TR01H064-E22Hh/none-Hi-Kn010G3/L0000-k0	3.07E-08
TR01H044-E22Hh/none-Hi-Kn010G3/L0000-k0	3.52E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0262-k0	3.98E-08
TR01H062-E22Hh/none-Hi-Kn010G3/L0000-k0	3.13E-08
CE115HA251-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L	1.48E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0011-k0	3.48E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0222-k0	4.65E-08
CE115HA192-E22Hh//-Hi-Kn010G3/L0000-k0	5.05E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L010-k0	3.28E-08
TR01H025-E22Hh/none-Hi-Kn010G3/L0000-k0	3.86E-08
TR01H082-E22Hh/none-Hi-Kn010G3/TR01L023-k0	4.25E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L015-k0	3.95E-08
TR01H055-E22Hh/none-Hi-Kn010G3/L0000-k0	3.88E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0260-k0	4.53E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L009-k0	3.56E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L011-k0	3.57E-08
TR01H017-E22Hh/none-Hi-Kn010G3/L0000-k0	3.50E-08
CE115HA122-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L	1.69E-08
TR01H076-E22Hh/none-Hi-Kn010G3/L0000-k0	4.78E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0258-k0	4.70E-08
TR01H046-E22Hh/none-Hi-Kn010G3/L0000-k0	4.23E-08
rCE115H-G1dh//-Hi-Kn010G3/L0000-k0	5.76E-08
TR01H082-E22Hh/none-Hi-Kn010G3/TR01L024-k0	4.76E-08
TR01H016-E22Hh/none-Hi-Kn010G3/L0000-k0	3.69E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L018-k0	4.51E-08
TR01H084-E22Hh/none-Hi-Kn010G3/L0271-k0	2.76E-08
TR01H084-E22Hh/none-Hi-Kn010G3/L0270-k0	2.76E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0000vk1-k0	4.69E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0219-k0	3.94E-08
TR01H014-E22Hh/none-Hi-Kn010G3/L0000-k0	3.87E-08
TR01H061-E22Hh/none-Hi-Kn010G3/L0226-k0	4.71E-08
TR01H048-E22Hh/none-Hi-Kn010G3/L0000-k0	4.52E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0259-k0	5.07E-08
TR01H028-E22Hh/none-Hi-Kn010G3/L0000-k0	4.80E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0201-k0	4.49E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L013-k0	4.15E-08
TR01H033-E22Hh/none-Hi-Kn010G3/L0000-k0	4.88E-08
hCE115HA-G1dh//-Hi-Kn010G3/L0000-k0	6.50E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L012-k0	4.22E-08
TR01H065-E22Hh/none-Hi-Kn010G3/L0000-k0	4.31E-08
TR01H079-E22Hh/none-Hi-Kn010G3/L0000-k0	5.05E-08
TR01H042-E22Hh/none-Hi-Kn010G3/L0000-k0	4.48E-08
TR01H063-E22Hh/none-Hi-Kn010G3/L0000-k0	4.35E-08
TR01H084-E22Hh/none-Hi-Kn010G3/L0272-k0	3.10E-08
CE115HA121-E22Hh//-Hi-Kn010G3/L0000-k0	6.76E-08
TR01H026-E22Hh/none-Hi-Kn010G3/L0000-k0	5.12E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0262-k0	4.92E-08
TR01H073-E22Hh/none-Hi-Kn010G3/L0000-k0	5.97E-08
TR01H045-E22Hh/none-Hi-Kn010G3/L0000-k0	5.22E-08
TR01H007-E22Hh/none-Hi-Kn010G3/L0000-k0	2.17E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0203-k0	4.07E-08
TR01H032-E22Hh/none-Hi-Kn010G3/L0000-k0	5.73E-08
TR01H006-E22Hh/none-Hi-Kn010G3/L0000-k0	2.30E-08
TR01H013-E22Hh/none-Hi-Kn010G3/L0000-k0	4.94E-08
TR01H050-E22Hh/none-Hi-Kn010G3/L0000-k0	5.76E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0200-k0	6.03E-08
TR01H015-E22Hh/none-Hi-Kn010G3/L0000-k0	6.13E-08
hCE115HA-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L	6.16E-08
hCE115HA-E22stHh/none-Hi-stKn010G3/L0000-k0	5.17E-08
TR01H069-E22Hh/none-Hi-Kn010G3/L0000-k0	7.11E-08
TR01H015-E22Hh/none-Hi-Kn010G3/TR01L003-k0	6.34E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0202-k0	6.19E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0201-k0	5.93E-08
TR01H020-E22Hh/none-Hi-Kn010G3/L0000-k0	6.48E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0011-k0	5.95E-08

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hCE115HA-E22Hh//-Hi-Kn010G3/L0000-k0	1.43E-07
TR01H082-E22Hh/none-Hi-Kn010G3/TR01L018-k0	4.72E-08
TR01H015-E22Hh/none-Hi-Kn010G3/TR01L005-k0	6.53E-08
TR01H052-E22Hh/none-Hi-Kn010G3/L0000-k0	6.27E-08
TR01H036-E22Hh/none-Hi-Kn010G3/L0000-k0	6.50E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0203-k0	4.79E-08
TR01H030-E22Hh/none-Hi-Kn010G3/L0000-k0	6.54E-08
TR01H015-E22Hh/none-Hi-Kn010G3/TR01L001-k0	6.56E-08
TR01H100-E22Hh/none-Hi-Kn010G3/L0011-k0	6.25E-08
TR01H029-E22Hh/none-Hi-Kn010G3/L0000-k0	6.70E-08
TR01H019-E22Hh/none-Hi-Kn010G3/L0000-k0	6.85E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0000-k0	7.37E-08
TR01H018-E22Hh/none-Hi-Kn010G3/L0000-k0	6.93E-08
TR01H027-E22Hh/none-Hi-Kn010G3/L0000-k0	6.95E-08
TR01H049-E22Hh/none-Hi-Kn010G3/L0000-k0	6.79E-08
TR01H066-E22Hh/none-Hi-Kn010G3/L0000-k0	6.02E-08
TR01H091-E22Hh/none-Hi-Kn010G3/L0011-k0	6.67E-08
rCE115H-E22Hh/none-Hi-Kn010G3/L0000-k0	8.00E-08
TR01H015-E22Hh/none-Hi-Kn010G3/TR01L002-k0	7.14E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0226-k0	8.01E-08
TR01H067-E22Hh/none-Hi-Kn010G3/TR01L018-k0	5.26E-08
TR01H093-E22Hh/none-Hi-Kn010G3/L0011-k0	6.80E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0215-k0	7.41E-08
TR01H015-E22Hh/none-Hi-Kn010G3/TR01L004-k0	7.34E-08
TR01H107-E22Hh/none-Hi-Kn010G3/L0011-k0	6.91E-08
TR01H105-E22Hh/none-Hi-Kn010G3/L0011-k0	6.95E-08
TR01H090-E22Hh/none-Hi-Kn010G3/L0011-k0	6.95E-08
TR01H108-E22Hh/none-Hi-Kn010G3/L0011-k0	6.98E-08
TR01H094-E22Hh/none-Hi-Kn010G3/L0011-k0	7.00E-08
TR01H109-E22Hh/none-Hi-Kn010G3/L0011-k0	7.06E-08
TR01H056-E22Hh/none-Hi-Kn010G3/L0000-k0	7.32E-08
TR01H031-E22Hh/none-Hi-Kn010G3/L0000-k0	7.55E-08
TR01H022-E22Hh/none-Hi-Kn010G3/L0000-k0	7.58E-08
TR01H092-E22Hh/none-Hi-Kn010G3/L0011-k0	7.21E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0000-k0	7.15E-08
TR01H067-E22Hh/none-Hi-Kn010G3/L0011-k0	7.18E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0248-k0	7.89E-08
TR01H009-E22Hh/none-Hi-Kn010G3/L0000-k0	3.15E-08
TR01H023-E22Hh/none-Hi-Kn010G3/L0000-k0	7.94E-08
TR01H096-E22Hh/none-Hi-Kn010G3/L0011-k0	7.47E-08
TR01H040-E22Hh/none-Hi-Kn010G3/TR01L007-k0	6.82E-08
TR01H054-E22Hh/none-Hi-Kn010G3/L0000-k0	7.79E-08
TR01H021-E22Hh/none-Hi-Kn010G3/L0000-k0	8.05E-08
TR01H103-E22Hh/none-Hi-Kn010G3/L0011-k0	7.72E-08
TR01H099-E22Hh/none-Hi-Kn010G3/L0011-k0	7.74E-08
rCE115H-E22Hh/none-Hi-Kn010G3/L0000vk1-k0	8.52E-08
TR01H101-E22Hh/none-Hi-Kn010G3/L0011-k0	7.87E-08
TR01H053-E22Hh/none-Hi-Kn010G3/L0000-k0	8.23E-08
TR01H035-E22Hh/none-Hi-Kn010G3/L0000-k0	8.49E-08
TR01H067-E22Hh/none-Hi-Kn010G3/TR01L015-k0	8.64E-08
TR01H104-E22Hh/none-Hi-Kn010G3/L0011-k0	8.26E-08
TR01H075-E22Hh/none-Hi-Kn010G3/L0000-k0	9.88E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0227-k0	1.01E-07
TR01H102-E22Hh/none-Hi-Kn010G3/L0011-k0	8.54E-08
TR01H034-E22Hh/none-Hi-Kn010G3/L0000-k0	9.11E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0222-k0	1.01E-07
rCE115H-E22Hh/rCE115L-k0/GL4-E22Hk/H0000-E22L	9.37E-08
TR01H015-E22Hh/none-Hi-Kn010G3/TR01L006-k0	9.30E-08
TR01H040-E22Hh/none-Hi-Kn010G3/L0246-k0	9.28E-08
TR01H097-E22Hh/none-Hi-Kn010G3/L0011-k0	8.76E-08
TR01H011-E22Hh/none-Hi-Kn010G3/L0000-k0	3.71E-08
TR01H010-E22Hh/none-Hi-Kn010G3/L0000-k0	3.73E-08
TR01H095-E22Hh/none-Hi-Kn010G3/L0011-k0	9.09E-08
TR01H082-E22Hh/none-Hi-Kn010G3/TR01L020-k0	1.06E-07
TR01H098-E22Hh/none-Hi-Kn010G3/L0011-k0	9.14E-08
TR01H082-E22Hh/none-Hi-Kn010G3/TR01L017-k0	1.09E-07
TR01H040-E22Hh/none-Hi-Kn010G3/L0247-k0	1.00E-07
rCE115H-E22Hh/none-Hi-Kn010G3/rCE115L-k0	1.24E-07
TR01H004-E22Hh//-Hi-Kn010G3/L0000-k0	1.35E-07
TR01H067-E22Hh/none-Hi-Kn010G3/L0222-k0	7.63E-08
rCE115H-E22Hh//-Hi-Kn010G3/rCE115L-k0	1.38E-07
TR01H008-E22Hh/none-Hi-Kn010G3/L0000-k0	4.22E-08
TR01H070-E22Hh/none-Hi-Kn010G3/L0000-k0	1.20E-07
TR01H106-E22Hh/none-Hi-Kn010G3/L0011-k0	1.00E-07
TR01H024-E22Hh/none-Hi-Kn010G3/L0000-k0	1.08E-07
CE115HA124-E22Hh//-Hi-Kn010G3/L0000-k0	1.43E-07
TR01H040-E22Hh/none-Hi-Kn010G3/L0249-k0	1.11E-07
TR01H082-E22Hh/none-Hi-Kn010G3/L0271-k0	6.82E-08
TR01H057-E22Hh/none-Hi-Kn010G3/L0000-k0	1.12E-07
TR01H058-E22Hh/none-Hi-Kn010G3/L0000-k0	1.15E-07
TR01H068-E22Hh/none-Hi-Kn010G3/L0000-k0	1.01E-07
TR01H082-E22Hh/none-Hi-Kn010G3/L0270-k0	7.42E-08
TR01H082-E22Hh/none-Hi-Kn010G3/L0272-k0	7.44E-08
hCE115HA-E22Hh/none-Hi-Kn010G3/L0000-k0	1.24E-07
TR01H082-E22Hh/none-Hi-Kn010G3/L0268-k0	1.36E-07
hCE115HAa-E22Hh/none-Hi-Kn010G3/L0000-k0	1.08E-07
TR01H067-E22Hh/none-Hi-Kn010G3/L0226-k0	1.32E-07
TR01H067-E22Hh/none-Hi-Kn010G3/L0248-k0	1.39E-07

(3-2) Modifying the affinity of a humanized anti-GPC3 antibody

First, point mutations were introduced into CDR1, CDR2, and CDR3 of the anti-human GPC3 bispecific antibody sequence produced in Example 2, H0000-ERY27_HK (SEQ ID NO: 54), to prepare modified antibodies. Next, the affinity of these modified antibodies for soluble human GPC3 was determined. Combining sites that have an affinity-enhancing effect yielded modified antibodies having the affinities shown in Table 9.

Table 9

Antibody name	KD (Human GPC3)
H0610-G1dh/none-Hi-Kn010G3/L0000-k0	3.97E-09
H0610-G1dh/none-Hi-Kn010G3/L0222-k0	1.40E-13
H0610-G1dh/none-Hi-Kn010G3/L0258-k0	3.52E-13
GCH054-G1dh/none-Hi-Kn010G3/L0262-k0	5.25E-13
GCH060-G1dh/none-Hi-Kn010G3/L0222-k0	6.42E-13
H0610-G1dh/none-Hi-Kn010G3/L0246-k0	1.21E-12
GCH057-G1dh/none-Hi-Kn010G3/L0222-k0	1.85E-12
GCH054-G1dh/none-Hi-Kn010G3/L0249-k0	3.61E-12
GCH055-G1dh/none-Hi-Kn010G3/L0222-k0	3.90E-12
GCH094-G1dh/none-Hi-Kn010G3/L0246-k0	4.12E-12
H0610-G1dh/none-Hi-Kn010G3/L0249-k0	6.86E-12
H0610-G1dh/none-Hi-Kn010G3/TR01L017-k0	8.27E-12
H0610-G1dh/none-Hi-Kn010G3/L0265-k0	8.70E-12
H0610-G1dh/none-Hi-Kn010G3/L0261-k0	1.07E-11
GCH065-G1dh/none-Hi-Kn010G3/L0262-k0	1.18E-11
GCH056-G1dh/none-Hi-Kn010G3/L0262-k0	1.19E-11
H0610-G1dh/none-Hi-Kn010G3/L0268-k0	1.69E-11
H0610-G1dh/none-Hi-Kn010G3/TR01L020-k0	2.24E-11
GCH054-G1dh/none-Hi-Kn010G3/L0246-k0	3.15E-11
GCH054-G1dh/none-Hi-Kn010G3/L0222-k0	3.15E-11
GCH073-G1dh/none-Hi-Kn010G3/L0201-k0	3.50E-11
H0610-G1dh/none-Hi-Kn010G3/L0248-k0	5.55E-11
GCH065-G1dh/none-Hi-Kn010G3/L0201-k0	7.74E-11
H0610-G1dh/none-Hi-Kn010G3/L0226-k0	9.30E-11
H0610-G1dh/none-Hi-Kn010G3/L0093-k0	1.06E-10
GCH098-G1dh/none-Hi-Kn010G3/L0201-k0	1.11E-10
H0610-G1dh/none-Hi-Kn010G3/L0267-k0	1.79E-10
H0610-G1dh/none-Hi-Kn010G3/L0228-k0	2.02E-10
H0610-G1dh/none-Hi-Kn010G3/L0262-k0	2.11E-10
H0610-G1dh/none-Hi-Kn010G3/L0266-k0	2.13E-10
H0610-G1dh/none-Hi-Kn010G3/L0264-k0	2.19E-10
H0610-G1dh/none-Hi-Kn010G3/L0224-k0	2.43E-10
H0610-G1dh/none-Hi-Kn010G3/L0167-k0	2.11E-10
CE115HA251-E22Hh/L0000-k0/GL4-E22Hk/H0610-E22L	2.36E-10
TR01H015-E22Hh/L0000-k0/GL4-E22Hk/H0610-E22L	2.63E-10
CE115HA236-E22Hh/GLS3108-k0/GL4-E22Hk/H0610-E22L	2.67E-10
H0610-G1dh/none-Hi-Kn010G3/L0259-k0	3.34E-10
H0610-G1dh/none-Hi-Kn010G3/L0227-k0	4.08E-10
GCH065-G1dh/none-Hi-Kn010G3/L0272-k0	3.93E-10
H0610-G1dh/none-Hi-Kn010G3/L0269-k0	4.59E-10
H0610-G1dh/none-Hi-Kn010G3/L0223-k0	4.75E-10
TR01H002-E22Hh/GLS3108-k0/GL4-E22Hk/H0610-E22L	4.75E-10
GCH054-G1dh/none-Hi-Kn010G3/L0212-k0	5.17E-10
H0610-G1dh/none-Hi-Kn010G3/L0208-k0	5.30E-10
H0610-G1dh/none-Hi-Kn010G3/L0263-k0	5.64E-10
H0610-G1dh/none-Hi-Kn010G3/L0231-k0	5.89E-10
H0610-G1dh/none-Hi-Kn010G3/L0143-k0	5.73E-10
GCH055-G1dh/none-Hi-Kn010G3/L0212-k0	6.14E-10
H0610-G1dh/none-Hi-Kn010G3/L0211-k0	6.47E-10
H0610-G1dh/none-Hi-Kn010G3/L0238-k0	6.37E-10
H0610-G1dh/none-Hi-Kn010G3/L0214-k0	6.57E-10
H0610-G1dh/none-Hi-Kn010G3/L0243-k0	6.49E-10
GCH025-G1dh/none-Hi-Kn010G3/L0204-k0	6.70E-10
GCH054-G1dh/none-Hi-Kn010G3/TR01L016-k0	7.63E-10
H0610-G1dh/none-Hi-Kn010G3/L0168-k0	6.99E-10
GCH094-G1dh/none-Hi-Kn010G3/L0271-k0	6.92E-10
GCH054-G1dh/none-Hi-Kn010G3/TR01L019-k0	8.71E-10
H0610-G1dh/none-Hi-Kn010G3/L0234-k0	7.78E-10
GCH098-G1dh/none-Hi-Kn010G3/L0011-k0	8.02E-10
H0610-G1dh/none-Hi-Kn010G3/L0204-k0	7.27E-10
H0610-G1dh/none-Hi-Kn010G3/L0240-k0	8.48E-10
H0610-G1dh/none-Hi-Kn010G3/L0239-k0	8.74E-10
H0610-G1dh/none-Hi-Kn010G3/L0212-k0	9.94E-10
GCH065-G1dh/none-Hi-Kn010G3/L0011-k0	8.84E-10
H0610-G1dh/none-Hi-Kn010G3/L0200-k0	1.04E-09
H0610-G1dh/none-Hi-Kn010G3/L0124-k0	9.72E-10
GCH073-G1dh/none-Hi-Kn010G3/L0011-k0	9.10E-10
H0610-G1dh/none-Hi-Kn010G3/TR01L016-k0	1.08E-09
GCH054-G1dh/none-Hi-Kn010G3/L0201-k0	1.08E-09
H0610-G1dh/none-Hi-Kn010G3/L0090-k0	1.12E-09
H0610-G1dh/none-Hi-Kn010G3/L0209-k0	1.12E-09
H0610-G1dh/none-Hi-Kn010G3/L0201-k0	1.13E-09
H0610-G1dh/none-Hi-Kn010G3/L0161-k0	9.73E-10
H0610-G1dh/none-Hi-Kn010G3/L0206-k0	8.65E-10
H0610-G1dh/none-Hi-Kn010G3/L0186-k0	1.08E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L019-k0	1.15E-09
H0610-G1dh/none-Hi-Kn010G3/L0085-k0	1.17E-09
GCH055-G1dh/none-Hi-Kn010G3/L0200-k0	1.13E-09
H0610-G1dh/none-Hi-Kn010G3/L0154-k0	1.01E-09
H0610-G1dh/none-Hi-Kn010G3/L0229-k0	1.20E-09
GCH054-G1dh/none-Hi-Kn010G3/L0200-k0	1.18E-09
GCH094-G1dh/none-Hi-Kn010G3/L0201-k0	1.17E-09

Antibody name	KD (Human GPC3)
H0610-G1dh/none-Hi-Kn010G3/L0000-k0	3.97E-09
H0610-G1dh/none-Hi-Kn010G3/L0205-k0	1.01E-09
GCH099-G1dh/none-Hi-Kn010G3/L0201-k0	1.29E-09
H0610-G1dh/none-Hi-Kn010G3/L0242-k0	1.19E-09
GCH056-G1dh/none-Hi-Kn010G3/L0201-k0	1.16E-09
H0610-G1dh/none-Hi-Kn010G3/L0213-k0	1.25E-09
GCH060-G1dh/none-Hi-Kn010G3/L0200-k0	1.34E-09
GCH065-G1dh/none-Hi-Kn010G3/L0000-k0	1.41E-09
GCH100-G1dh/none-Hi-Kn010G3/L0201-k0	1.37E-09
H0610-G1dh/none-Hi-Kn010G3/L0015-k0	1.31E-09
H0610-G1dh/none-Hi-Kn010G3/L0151-k0	1.25E-09
H0610-G1dh/none-Hi-Kn010G3/L0237-k0	1.31E-09
H0610-G1dh/none-Hi-Kn010G3/L0220-k0	1.36E-09
H0610-G1dh/none-Hi-Kn010G3/L0155-k0	1.28E-09
GCH055-G1dh/none-Hi-Kn010G3/L0215-k0	1.52E-09
H0610-G1dh/none-Hi-Kn010G3/L0202-k0	1.22E-09
GCH056-G1dh/none-Hi-Kn010G3/L0215-k0	1.59E-09
H0610-G1dh/none-Hi-Kn010G3/L0012-k0	1.55E-09
GCH054-G1dh/none-Hi-Kn010G3/L0215-k0	1.62E-09
H0610-G1dh/none-Hi-Kn010G3/L0215-k0	1.64E-09
GCH098-G1dh/none-Hi-Kn010G3/L0000-k0	1.77E-09
H0610-G1dh/none-Hi-Kn010G3/L0125-k0	1.71E-09
GCH057-G1dh/none-Hi-Kn010G3/L0215-k0	1.83E-09
H0610-G1dh/none-Hi-Kn010G3/L0217-k0	1.79E-09
H0610-G1dh/none-Hi-Kn010G3/L0014-k0	1.82E-09
H0610-G1dh/none-Hi-Kn010G3/L0216-k0	1.86E-09
TR01H015-E2702GsKsc/GCH019-E2704sEpsc/L0000-k0	1.64E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L015-k0	2.16E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L018-k0	2.17E-09
H0610-G1dh/none-Hi-Kn010G3/L0218-k0	1.99E-09
H0610-G1dh/none-Hi-Kn010G3/L0000vk1-k0	2.16E-09
H0610-G1dh/none-Hi-Kn010G3/L0160-k0	2.12E-09
H0610-G1dh/none-Hi-Kn010G3/L0047-k0	2.23E-09
GCH073-G1dh/none-Hi-Kn010G3/L0000-k0	2.00E-09
GCH054-G1dh/none-Hi-Kn010G3/TR01L015-k0	2.45E-09
H0610-G1dh/none-Hi-Kn010G3/L0219-k0	2.28E-09
GCH094-G1dh/none-Hi-Kn010G3/L0272-k0	2.10E-09
H0610-G1dh/none-Hi-Kn010G3/L0149-k0	2.16E-09
GCH054-G1dh/none-Hi-Kn010G3/TR01L018-k0	2.59E-09
GCH054-G1dh/none-Hi-Kn010G3/L0203-k0	2.48E-09
H0610-G1dh/none-Hi-Kn010G3/L0122-k0	2.42E-09
H0610-G1dh/none-Hi-Kn010G3/L0134-k0	2.53E-09
H0610-G1dh/none-Hi-Kn010G3/L0152-k0	2.36E-09
H0610-G1dh/none-Hi-Kn010G3/L0203-k0	2.11E-09
H0610-G1dh/none-Hi-Kn010G3/L0075-k0	2.85E-09
H0610-G1dh/none-Hi-Kn010G3/L0038-k0	2.75E-09
H0610-G1dh/none-Hi-Kn010G3/L0011-k0	2.76E-09
H0610-G1dh/none-Hi-Kn010G3/L0157-k0	2.60E-09
H0610-G1dh/none-Hi-Kn010G3/L0145-k0	2.66E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L010-k0	2.92E-09
H0610-G1dh/none-Hi-Kn010G3/L0009-k0	2.99E-09
GCH099-G1dh/none-Hi-Kn010G3/L0011-k0	2.78E-09
H0610-G1dh/none-Hi-Kn010G3/L0006-k0	3.04E-09
H0610-G1dh/none-Hi-Kn010G3/L0173-k0	2.83E-09
H0610-G1dh/none-Hi-Kn010G3/L0127-k0	3.12E-09
H0610-G1dh/none-Hi-Kn010G3/L0082-k0	3.43E-09
H0610-G1dh/none-Hi-Kn010G3/L0064-k0	3.37E-09
H0610-G1dh/none-Hi-Kn010G3/L0008-k0	3.30E-09
H0610-G1dh/none-Hi-Kn010G3/L0013-k0	3.35E-09
H0610-G1dh/none-Hi-Kn010G3/L0140-k0	3.38E-09
H0610-G1dh/none-Hi-Kn010G3/L0039-k0	3.41E-09
GCH043-G1dh/none-Hi-Kn010G3/L0000-k0	3.74E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L008-k0	3.48E-09
H0610-G1dh/none-Hi-Kn010G3/L0148-k0	3.28E-09
GCH062-G1dh/none-Hi-Kn010G3/L0000-k0	3.73E-09
H0610-G1dh/none-Hi-Kn010G3/L0163-k0	3.38E-09
H0610-G1dh/none-Hi-Kn010G3/L0233-k0	3.55E-09
H0610-G1dh/none-Hi-Kn010G3/L0230-k0	4.00E-09
GCH006-G1dh/none-Hi-Kn010G3/L0000-k0	4.06E-09
H0610-G1dh/none-Hi-Kn010G3/L0032-k0	3.72E-09
H0610-G1dh/none-Hi-Kn010G3/L0181-k0	3.51E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L009-k0	3.81E-09
H0610-G1dh/none-Hi-Kn010G3/L0141-k0	3.86E-09
H0610-G1dh/none-Hi-Kn010G3/L0079-k0	4.23E-09
GCH094-G1dh/none-Hi-Kn010G3/L0270-k0	3.60E-09
GCH066-G1dh/none-Hi-Kn010G3/L0000-k0	4.29E-09
GCH064-G1dh/none-Hi-Kn010G3/L0000-k0	4.14E-09
H0610-G1dh/none-Hi-Kn010G3/L0066-k0	4.20E-09
GCH027-G1dh/none-Hi-Kn010G3/L0000-k0	3.83E-09
H0610-G1dh/none-Hi-Kn010G3/L0003-k0	4.01E-09
H0610-G1dh/none-Hi-Kn010G3/L0042-k0	4.27E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L011-k0	4.02E-09

Antibody name	KD (Human GPC3)
H0610-G1dh/none-Hi-Kn010G3/L0000-k0	3.97E-09
GCH015-G1dh/none-Hi-Kn010G3/L0000-k0	4.14E-09
H0610-G1dh/none-Hi-Kn010G3/L0175-k0	3.84E-09
GCH100-G1dh/none-Hi-Kn010G3/L0011-k0	3.81E-09
GCH014-G1dh/none-Hi-Kn010G3/L0000-k0	4.20E-09
GCH053-G1dh/none-Hi-Kn010G3/L0000-k0	4.05E-09
hCE115HA-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L	4.28E-09
GCH094-G1dh/none-Hi-Kn010G3/L0011-k0	3.88E-09
GCH045-G1dh/none-Hi-Kn010G3/L0000-k0	4.63E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L012-k0	4.25E-09
H0610-G1dh/none-Hi-Kn010G3/L0115-k0	4.34E-09
H0610-G1dh/none-Hi-Kn010G3/L0044-k0	4.57E-09
H0610-G1dh/none-Hi-Kn010G3/L0107-k0	4.38E-09
H0610-G1dh/none-Hi-Kn010G3/L0007-k0	4.39E-09
GCH013-G1dh/none-Hi-Kn010G3/L0000-k0	4.44E-09
H0610-G1dh/none-Hi-Kn010G3/L0045-k0	4.66E-09
GCH010-G1dh/none-Hi-Kn010G3/L0000-k0	4.12E-09
GCH040-G1dh/none-Hi-Kn010G3/L0000-k0	4.80E-09
H0610-G1dh/none-Hi-Kn010G3/L0002-k0	4.43E-09
H0610-G1dh/none-Hi-Kn010G3/L0016-k0	4.44E-09
GCH007-G1dh/none-Hi-Kn010G3/L0000-k0	4.93E-09
GCH042-G1dh/none-Hi-Kn010G3/L0000-k0	4.89E-09
rCE115H-E22Hh/rCE115L-k0/GL4-E22Hk/H0000-E22L	4.57E-09
H0610-G1dh/none-Hi-Kn010G3/L0120-k0	4.54E-09
H0610-G1dh/none-Hi-Kn010G3/L0065-k0	4.79E-09
GCH016-G1dh/none-Hi-Kn010G3/L0000-k0	4.59E-09
GCH035-G1dh/none-Hi-Kn010G3/L0000-k0	4.94E-09
GCH039-G1dh/none-Hi-Kn010G3/L0000-k0	4.95E-09
GCH099-G1dh/none-Hi-Kn010G3/L0000-k0	4.24E-09
H0610-G1dh/none-Hi-Kn010G3/L0041-k0	4.85E-09
GCH019-G1dh/none-Hi-Kn010G3/L0000-k0	4.36E-09
GCH029-G1dh/none-Hi-Kn010G3/L0000-k0	5.01E-09
GCH056-G1dh/none-Hi-Kn010G3/L0011-k0	4.31E-09
H0610-G1dh/none-Hi-Kn010G3/L0147-k0	4.38E-09
GCH034-G1dh/none-Hi-Kn010G3/L0000-k0	5.09E-09
GCH003-G1dh/none-Hi-Kn010G3/L0000-k0	5.20E-09
H0610-G1dh/none-Hi-Kn010G3/L0139-k0	4.78E-09
H0610-G1dh/none-Hi-Kn010G3/L0089-k0	5.24E-09
H0610-G1dh/none-Hi-Kn010G3/L0113-k0	4.82E-09
H0610-G1dh/none-Hi-Kn010G3/L0180-k0	4.48E-09
GCH005-G1dh/none-Hi-Kn010G3/L0000-k0	5.32E-09
GCH067-G1dh/none-Hi-Kn010G3/L0000-k0	5.24E-09
H0610-G1dh/none-Hi-Kn010G3/L0187-k0	4.92E-09
H0610-G1dh/none-Hi-Kn010G3/L0043-k0	5.14E-09
H0610-G1dh/none-Hi-Kn010G3/L0117-k0	4.92E-09
GCH061-G1dh/none-Hi-Kn010G3/L0000-k0	5.13E-09
GCH022-G1dh/none-Hi-Kn010G3/L0000-k0	4.92E-09
H0610-G1dh/none-Hi-Kn010G3/L0091-k0	5.43E-09
GCH023-G1dh/none-Hi-Kn010G3/L0000-k0	4.94E-09
H0610-G1dh/none-Hi-Kn010G3/L0062-k0	5.28E-09
H0610-G1dh/none-Hi-Kn010G3/L0136-k0	5.04E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L003-k0	5.08E-09
H0610-G1dh/none-Hi-Kn010G3/L0069-k0	5.32E-09
H0610-G1dh/none-Hi-Kn010G3/L0123-k0	5.08E-09
GCH025-G1dh/none-Hi-Kn010G3/L0000-k0	5.05E-09
GCH100-G1dh/none-Hi-Kn010G3/L0000-k0	5.39E-09
H0610-G1dh/none-Hi-Kn010G3/L0046-k0	5.45E-09
H0610-G1dh/none-Hi-Kn010G3/L0144-k0	4.84E-09
GCH026-G1dh/none-Hi-Kn010G3/L0000-k0	5.17E-09
H0610-G1dh/none-Hi-Kn010G3/L0138-k0	5.24E-09
GCH056-G1dh/none-Hi-Kn010G3/L0000-k0	5.03E-09
H0610-G1dh/none-Hi-Kn010G3/L0129-k0	5.28E-09
GCH032-G1dh/none-Hi-Kn010G3/L0000-k0	5.74E-09
H0610-G1dh/none-Hi-Kn010G3/TR01L005-k0	5.37E-09
GCH012-G1dh/none-Hi-Kn010G3/L0000-k0	5.40E-09
GCH055-G1dh/none-Hi-Kn010G3/L0000-k0	5.60E-09
H0610-G1dh/none-Hi-Kn010G3/L0104-k0	5.90E-09
GCH059-G1dh/none-Hi-Kn010G3/L0000-k0	5.70E-09
GCH054-G1dh/none-Hi-Kn010G3/L0000-k0	5.30E-09
GCH008-G1dh/none-Hi-Kn010G3/L0000-k0	5.55E-09
H0610-G1dh/none-Hi-Kn010G3/L0232-k0	5.38E-09
H0610-G1dh/none-Hi-Kn010G3/L0126-k0	5.62E-09
GCH094-G1dh/none-Hi-Kn010G3/L0000-k0	5.89E-09
H0610-G1dh/none-Hi-Kn010G3/L0132-k0	5.65E-09
H0610-G1dh/none-Hi-Kn010G3/L0106-k0	5.66E-09
GCH054-G1dh/none-Hi-Kn010G3/L0011-k0	5.25E-09
H0610-G1dh/none-Hi-Kn010G3/L0109-k0	5.70E-09
H0610-G1dh/none-Hi-Kn010G3/L0063-k0	6.03E-09
GCH068-G1dh/none-Hi-Kn010G3/L0000-k0	6.23E-09
GCH057-G1dh/none-Hi-Kn010G3/L0000-k0	5.61E-09
H0610-G1dh/none-Hi-Kn010G3/L0137-k0	5.87E-09

(3-3) Modification of pI by point mutations

In commercial production of bispecific antibodies, a high level of purity is required. When using ion-exchange chromatography, modifying the molecular isoelectric point (pI) has been reported to be effective (PLoS One. 2013;8(2):e57479). Therefore, point mutations for pI modifications were introduced into CDR1, CDR2, and CDR3 of the humanized anti-human GPC3 antibody sequence produced in Example 2, H0000-ERY27_HK (SEQ ID NO: 54), to prepare modified antibodies. Next, the affinity of these modified antibodies for soluble human GPC3 was determined.

As a result, amino acid modifications that can lower the pI while maintaining the affinity for human GPC3 were found to be amino acids at positions 19, 43, 53, and 61 according to Kabat numbering.

Combination of sites showing effects of maintaining the affinity for human GPC3 and lowering the pI yielded antibodies having the affinities and pI values shown in Table 10.

Table 10

Antibody name (homomeric antibody)	Calculated pI value (homomeric antibody)	Antibody name (single-arm antibody)	human GPC3 KD (single-arm antibody)	Mutation sites based on H0610-E2704sEpsc
H0610-E2704sEpsc/L0000-k0	7.8	H0610-G1dh/none-Hi-Kn010G3/L0000-k0	4.16E-09	-
GCH054-E2704sEpsc/L0011-k0	6.2	GCH054-G1dh/none-Hi-Kn010G3/L0011-k0	5.25E-09	K19T/Q43E/P52aG/K53E/G55P/Q61E
GCH065-E2704sEpsc/L0011-k0	6.4	GCH065-G1dh/none-Hi-Kn010G3/L0011-k0	8.84E-10	K19T/Q43E/P52aG/K53P/G55P/Q61E
GCH094-E2704sEpsc/L0011-k0	6.2	GCH094-G1dh/none-Hi-Kn010G3/L0011-k0	4.54E-09	K19T/I37V/P40A/Q43E/I48M/P52aG/K53E/G55P/Q61E

(3-4) Modifying the extracellular matrix-binding ability by point mutation

It has been reported that non-specific binding to the extracellular matrix (ECM) and such may have effects on pharmacokinetics (MAbs. 2012 Nov-Dec;4(6):753-60). Therefore, the ECM-binding ability of the modified antibodies obtained in the Examples was determined by the method described in Reference Example 4. As a result, the humanized anti-human CD3ε chain and anti-human GPC3 bispecific antibody, GPC3_ERY27_hCE115 (SEQ ID NOs: 54, 55, and 56), were confirmed to have high ECM-binding abilities. Therefore, any of the point mutations examined in Examples 3-1, 3-2, and 3-3 for the humanized anti-human CD3ε chain antibody sequence hCE115HA-ERY27_HE (SEQ ID NO: 55) was investigated to be a combination for reducing the ECM-binding ability. As a result, amino acids at positions 11, 16, 52a, 53, 98, and 100 by Kabat numbering were found to contribute to the maintenance of affinity for CD3ε and to have influence on the reduction of the ECM-binding ability, and antibodies with a reduced ECM-binding ability in comparison to that of an antibody variant of the humanized anti-human CD3ε chain and anti-human GPC3 bispecific antibody, GPC3_ERY27_hCE115, were obtained (Table 11).

Table 11

Antibody name	ECM binding ratio (standard = 1)
GPC3_ERY22_CE115 (rCE115H-E22Hh/rCE115L-k0/GL4-E22Hk/H0000-E22L)	4.0
GPC3_ERY27 (hCE115HA-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L)	50.9
CE115HA236-E22Hh/GLS3108-k0/GL4-E22Hk/H0610-E22L	429.9
CE115HA236-E22Hh/GLS3108-k0/GL4-E22Hk/H0000-E22L	414.8
CE115HA251-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L	346.9
CE115HA251-E22Hh/L0000-k0/GL4-E22Hk/H0610-E22L	334.4
TR01H002-E22Hh/GLS3108-k0/GL4-E22Hk/H0610-E22L	301.1
TR01H002-E22Hh/GLS3108-k0/GL4-E22Hk/H0000-E22L	216.9
TR01H015-E22Hh/L0000-k0/GL4-E22Hk/H0610-E22L	185.7
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0208-k0	50.4
CE115HA122-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L	47.0
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0211-k0	15.5
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0206-k0	15.4
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0209-k0	7.4
rCE115H-E22Hh/rCE115L-k0/GL4-E22Hk/H0610-E22L	4.6
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0204-k0	4.4
TR01H067-E2702GsKsc/GCH054-E2704sEpsc/L0212-k0	3.3
TR01H113-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0	2.5
TR01H082-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0	1.7
TR01H113-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0	1.6
rCE115H-E22Hh/rCE115L-k0/L0000-E22Hk/H0610-E22L	1.4
TR01H084-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0	1.3
TR01H084-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0	1.2
TR01H082-E2702GsKsc/GCH094-E2704sEpsc/L0201-k0	1.1
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0000-k0	0.8
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0201-k0	0.8
TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0203-k0	0.8
TR01H082-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0	0.7
TR01H109-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0	0.7
TR01H067-E2702GsKsc/GCH054-E2704sEpsc/L0222-k0	0.6
TR01H067-E2702GsKsc/GCH054-E2704sEpsc/L0201-k0	0.5
TR01H109-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0	0.4
TR01H113-E2702sKsc/GCH065-E2704sEpsc/L0011-k0	0.3
MRAH-G1d/MRAL-k0(standard)	1

(3-5) Modifying the binding ability to the SuRe™ ligand by point mutations

An example where the binding of an antibody to Protein A depends on its variable region sequence (VH3) is known (J Biomol Tech. 2011 Jul; 22(2):50-2). In the Protein A purification of the humanized anti-human CD3ε chain and anti-human GPC3 bispecific antibody, removal of the homomeric anti-CD3 antibody is important for suppressing non-specific reactions *via* CD3. Therefore, it is considered desirable to suppress the binding of the homomeric anti-CD3 antibody to Protein A. Presumably, the SuRe™ ligand will be used in commercial production, and thus point mutations for SuRe™ ligand binding were introduced into CDR2 of

the humanized anti-CD3 antibody H-chain variants, TR01H082-E2702GsKsc and TR01H084-E2702GsKsc (SEQ ID NO: 398 and 399), to prepare modified antibodies. The binding ability of these modified antibodies to the SuRe™ ligand was determined by the method described in Reference Example 5. As a result, amino acids at positions 19, 57, and 59 by Kabat numbering were found to contribute to the maintenance of the affinity for CD3ε and to have influence on the Sure™ ligand-binding ability, and antibodies with a reduced Sure™ ligand-binding ability in comparison to that of TR01H082-E2702GsKsc/L0011-k0 (SEQ ID NOs: 398 and 410) or TR01H084-E2702GsKsc/L0011-k0 (SEQ ID NOs: 399 and 410) were obtained (Table 12).

Table 12

Antibody name	SuRe™ binding (RU)	Mutation sites based on CE115HA000
TR01H084-E2702GsKsc/L0011-k0	5065.8	R16G/A52aD/N53Q/D72A/L78I/G98A/Y100G/A102I
TR01H082-E2702GsKsc/L0011-k0	4469.2	V11L/A52aD/N53Q/G98A/Y100G
TR01H090-E2702GsKsc/L0011-k0	3606.3	V11L/R16G/A52aD/N53Q/G98A/Y100G
TR01H093-E2702GsKsc/L0011-k0	2459.7	V11L/A52aD/N53Q/K64Q/G98A/Y100G
TR01H094-E2702GsKsc/L0011-k0	2351.9	V11L/A52aD/N53Q/K64S/G98A/Y100G
TR01H114-E2702GsKsc/L0011-k0	1485.5	R16G/A52aD/N53Q/T57S/D72A/L78I/G98A/Y100G/A102I
TR01H092-E2702GsKsc/L0011-k0	1159.5	V11L/A52aD/N53Q/K64A/G98A/Y100G
TR01H100-E2702GsKsc/L0011-k0	383.0	V11L/A52aD/N53Q/T57S/G98A/Y100G
TR01H111-E2702GsKsc/L0011-k0	50.7	R16G/R19K/A52aD/N53Q/D72A/L78I/G98A/Y100G/A102I
TR01H110-E2702GsKsc/L0011-k0	29.5	R19K/A52aD/N53Q/G98A/Y100G
TR01H091-E2702GsKsc/L0011-k0	27.5	V11L/R19K/A52aD/N53Q/G98A/Y100G
TR01H091-E2702GsKsc/L0011-k0	15.0	V11L/R19K/A52aD/N53Q/G98A/Y100G
TR01H112-E2702GsKsc/L0011-k0	8.8	R16G/A52aD/N53Q/T57Q/D72A/L78I/G98A/Y100G/A102I
TR01H113-E2702GsKsc/L0011-k0	7.0	R16G/A52aD/N53Q/Y59V/D72A/L78I/G98A/Y100G/A102I
TR01H096-E2702GsKsc/L0011-k0	2.7	V11L/A52aD/N53Q/T57G/G98A/Y100G
TR01H109-E2702GsKsc/L0011-k0	2.2	V11L/A52aD/N53Q/Y59V/G98A/Y100G
TR01H098-E2702GsKsc/L0011-k0	1.6	V11L/A52aD/N53Q/T57P/G98A/Y100G
TR01H107-E2702GsKsc/L0011-k0	1.4	V11L/A52aD/N53Q/Y59Q/G98A/Y100G
TR01H103-E2702GsKsc/L0011-k0	1.4	V11L/A52aD/N53Q/Y59G/G98A/Y100G
TR01H104-E2702GsKsc/L0011-k0	1.0	V11L/A52aD/N53Q/Y59I/G98A/Y100G
TR01H105-E2702GsKsc/L0011-k0	0.8	V11L/A52aD/N53Q/Y59L/G98A/Y100G
TR01H099-E2702GsKsc/L0011-k0	0.6	V11L/A52aD/N53Q/T57Q/G98A/Y100G
TR01H102-E2702GsKsc/L0011-k0	0.5	V11L/A52aD/N53Q/Y59F/G98A/Y100G
TR01H101-E2702GsKsc/L0011-k0	0.5	V11L/A52aD/N53Q/T57V/G98A/Y100G
TR01H108-E2702GsKsc/L0011-k0	0.4	V11L/A52aD/N53Q/Y59T/G98A/Y100G
TR01H097-E2702GsKsc/L0011-k0	0.1	V11L/A52aD/N53Q/T57L/G98A/Y100G
TR01H106-E2702GsKsc/L0011-k0	0.0	V11L/A52aD/N53Q/Y59P/G98A/Y100G
TR01H095-E2702GsKsc/L0011-k0	-0.2	V11L/A52aD/N53Q/T57F/G98A/Y100G

(3-6) Production of optimized bispecific antibodies by combining point mutations that lead to improvement of various properties

Optimized modified antibodies can be produced by combining the point mutations that lead to improvement of various properties as described in Examples 3-1 to 3-5. As examples of such modified antibodies, the antibodies described in Table 13 were produced, and they were subjected to the T-cell-dependent cellular cytotoxicity (TDCC) evaluation using methods similar to those of Example 1. The results are shown in Figs. 4 to 9. As a result, optimized humanized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies showing a T-cell-dependent

cellular cytotoxicity equivalent to or greater than that of GPC3_ERY22_rCE115 prior to humanization were obtained.

Table 13

Sample number in TDCC assay	Antibody name
1	GPC3_ERY22_CE115 (rCE115H-E22Hh/rCE115L-k0/GL4-E22Hk/H0000-E22L)
2	GPC3_ERY27 (hCE115HA-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L)
3	CE115HA251-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L
4	CE115HA236-E22Hh/GLS3108-k0/GL4-E22Hk/H0000-E22L
5	TR01H002-E22Hh/GLS3108-k0/GL4-E22Hk/H0000-E22L
6	CE115HA122-E22Hh/L0000-k0/GL4-E22Hk/H0000-E22L
7	rCE115H-E22Hh/rCE115L-k0/L0000-E22Hk/H0610-E22L
8	rCE115H-E22Hh/rCE115L-k0/GL4-E22Hk/H0610-E22L
13	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0000-k0
14	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0201-k0
15	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0203-k0
16	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0204-k0
17	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0206-k0
18	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0208-k0
19	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0209-k0
20	TR01H040-E2702GsKsc/H0610-E2704sEpsc/L0211-k0
21	rCE115H-E2702GsKsc/H0610-E2704sEpsc/L0000-k0
22	TR01H061-E2702GsKsc/H0610-E2704sEpsc/L0000-k0
23	TR01H068-E2702GsKsc/H0610-E2704sEpsc/L0000-k0
24	TR01H071-E2702GsKsc/H0610-E2704sEpsc/L0000-k0
25	TR01H067-E2702GsKsc/GCH054-E2704sEpsc/L0201-k0
26	TR01H067-E2702GsKsc/GCH054-E2704sEpsc/L0212-k0
27	TR01H067-E2702GsKsc/GCH054-E2704sEpsc/L0222-k0
28	TR01H067-E2702GsKsc/ GCH054-E2704sEpsc/L0000-k0
29	TR01H082-E2702GsKsc/GCH094-E2704sEpsc/L0201-k0
30	TR01H082-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0
31	TR01H084-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0
32	TR01H084-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0
33	TR01H082-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0
34	TR01H109-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0
35	TR01H109-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0
36	TR01H113-E2702GsKsc/GCH094-E2704sEpsc/L0011-k0
37	TR01H113-E2702GsKsc/GCH065-E2704sEpsc/L0011-k0
38	TR01H113-E2702sKsc/GCH065-E2704sEpsc/L0011-k0

Examples 3-1 to 3-6 showed that the following amino acid residues, for example, are important for maintaining the properties of the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies showing a T-cell-dependent cellular cytotoxicity equivalent to or greater than that of GPC3_ERY22_rCE115 prior to humanization.

In anti-human CD3ε chain antibodies, the examples are Leu at position 11, Gly at position 16, Asp at position 52a, Gln at position 53, Ala at position 72, Ile at position 78, Ala at position 98, Gly at position 100, and Ile at position 102. In anti-human GPC3 antibodies, the examples are Thr at position 19, Glu at position 43, Gly at position 52a, Pro or Glu at position 53, Pro at position 55, and Glu at position 61. Furthermore, in common antibody L chains, the

examples are Pro at position 25, Pro at position 27a, Pro at position 27b, Ile at position 33, Gln at position 34, Arg or Trp at position 56, and Tyr at position 89. (All positions are indicated by Kabat numbering).

[Example 4] Evaluation of the *in vivo* efficacy

Some of the above-described antibodies were evaluated for their *in vivo* efficacy using tumor-bearing models.

Evaluation of the *in vivo* efficacy was carried out on representative antibodies from among those shown in Table 13, which have been confirmed to have cytotoxic activities from the *in vitro* assay described in Example 3-6. In the *in vivo* efficacy evaluation, any influence caused by differences in the microenvironment due to tumor aggregate formation on the evaluation results was taken into consideration. Therefore, two types of human cancer cell lines having different sensitivities to the antibody drug efficacy, i.e., PC-10 and NCI-H446, were used for the evaluation, even though the GPC3 expression levels of these cell lines were nearly equal. The cell lines were transplanted into the NOD scid mice, and the NOD scid mice with confirmed tumor formation were subjected to transplantation of T cells grown by *in vitro* culturing of human PBMCs. The mice (referred to as a T-cell injected model) were treated by administration of the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies.

More specifically, in drug efficacy tests of the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies using the PC-10 T-cell injected model, the tests below were performed. T cells were expansively cultured using PBMCs separated from blood collected from healthy volunteers and T cell activation/ expansion kit/ human (MACS Miltenyi biotec). The human cancer cell line PC-10 (1×10^7 cells) was mixed with Matrigel™ Basement Membrane Matrix (BD), and transplanted to the inguinal subcutaneous region of NOD scid mice (CLEA Japan, female, 6W). The day of transplantation was defined as day 0. On the day before transplantation, the anti-asialo-GM1 antibody (Wako Pure Chemicals) was administered intraperitoneally to the mice at 0.2 mg/mouse. On days 13 to 15 after the transplantation, the mice were separated into groups according to their body weight and tumor size, and the anti-asialo-GM1 antibody was administered again intraperitoneally to the mice at 0.2 mg/mouse. On the following day, T cells obtained by the aforementioned expansive culturing were transplanted intraperitoneally at 3×10^7 cells/mouse. Four hours after T-cell transplantation, the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies were administered intravenously through the caudate vein at 1 mg/kg. The optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies were administered only once.

As a result, anti-tumor activities were more clearly observed in the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibody-administered group than in the solvent-administered group (Fig. 10a, b).

Drug efficacy tests for the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies on the NCI-H446 T-cell injected model were performed by similar methods. The optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibodies were administered once intravenously through the caudate vein at 5 mg/kg against NCI-H446.

As a result, anti-tumor activities were more clearly observed in the optimized anti-human CD3ε chain and anti-human GPC3 bispecific antibody-administered group than in the solvent-administered group (Fig. 11a, b).

Reference Examples

[Reference Example 1] Production of antibody expression vectors, and antibody expression and purification

Amino acid substitutions were introduced by methods known to those skilled in the art such as using the QuikChange Site-Directed Mutagenesis Kit (Stratagene), PCR, or the In-fusion Advantage PCR cloning kit (TAKARA) to construct expression vectors. Nucleotide sequences of the obtained expression vectors were determined by a method known to those skilled in the art. The produced plasmids were transiently introduced into cells of the human embryonic kidney cancer-derived cell line HEK293H (Invitrogen) or FreeStyle293 (Invitrogen) to express antibodies. From the obtained culture supernatants, antibodies were purified using the rProtein A Sepharose™ Fast Flow (GE Healthcare) by a method known to those skilled in the art. Absorbance at 280 nm of the purified antibody solutions was measured using a spectrophotometer, and antibody concentrations were calculated from the determined values using an absorption coefficient calculated by the PACE method (Protein Science 1995; 4: 2411-2423).

[Reference Example 2] The ADCC activity of each test antibody using human peripheral blood mononuclear cells as the effector cell

The ADCC activity of each test antibody was determined according to the method below.

Human peripheral blood mononuclear cells (hereinafter referred to as human PBMC) were used as the effector cell to measure the ADCC activity of each test antibody as below.

(1) Preparation of a human PBMC solution

From a healthy volunteer (adult male) of Chugai Pharmaceutical Co. Ltd., 50 mL of peripheral blood was collected using a syringe preloaded with 200 μL of a 1000 unit/mL heparin solution (Novo-Heparin Injection 5000 units, Novo Nordisk). The peripheral blood was diluted two-fold with PBS(-), divided into four aliquots, and added into a Leucosep lymphocyte separation tube (Greiner Bio-one) that had been loaded with 15 mL of Ficoll-Paque PLUS and subjected to centrifugation in advance. This separation tube containing aliquots of peripheral blood was centrifuged at 2150 rpm for ten minutes at room temperature, and then the mononuclear cell fraction was collected. The cells in each fraction were washed once with Dulbecco's Modified Eagle's Medium (SIGMA) containing 10% FBS (hereinafter referred to as 10% FBS/D-MEM) and then suspended in 10% FBS/D-MEM at a cell density of 5×10^6 cells/mL. After incubation in an incubator at 37°C for one hour, the cells were washed once with 10% FBS/D-MEM, and the cells were suspended in 10% FBS/D-MEM to produce a cell density of 2×10^5 cells/mL. The cell suspension was subjected to the experiment below as the target cell.

(2) Chromium release assay (ADCC activity)

The ADCC activity was evaluated from the specific chromium release rate according to the chromium release method. First, antibody solutions prepared at each concentration (0, 0.004, 0.04, 0.4, 4, and 40 μg/mL) were added to a 96-well U-bottomed plate at 50 μL per well. Next, the target cells were seeded at 50 μL per well (1×10^4 cells/well), and this was allowed to stand at room temperature for 15 minutes. The human PBMC solution prepared in (1) was added at 100 μL per well (5×10^5 cells/well), and the plate was left to stand in a 5% carbon dioxide gas incubator at 37°C for four hours, followed by centrifugation. The radioactivity of 100 μL of culture supernatant in each well of the plate was measured using a gamma counter. The specific chromium release rate was determined based on the following equation:

Specific chromium release rate (%) = (A-C) x 100 / (B-C)

In this equation, A represents the mean value of radioactivity (cpm) of 100 μL of culture supernatant in each well; B represents the mean value of radioactivity (cpm) of 100 μL of culture supernatant in the well where 100 μL of a 2% aqueous NP-40 solution (Nonidet P-40, Nacalai Tesque) and 50 μL of 10% FBS/D-MEM had been added to the target cells; and C represents the mean value of radioactivity (cpm) of 100 μL of culture supernatant in the well where 150 μL of 10% FBS/D-MEM had been added to the target cells. The examinations were performed in triplicate and the mean values and standard deviations of the specific chromium release rates (%) in the above-mentioned examination reflecting the ADCC activity were calculated for each of the test antibodies.

[Reference Example 3] Assessment of Tm of the modified antibodies by differential scanning fluorimetry

In this examination, the Tm (thermal denaturation temperature) value of the modified antibodies was assessed by differential scanning fluorimetry using Rotor-Gene Q (QIAGEN). It has been reported that this method has a favorable correlation with Tm assessment using a differential scanning calorimeter widely known as a method for evaluating thermal stability of antibodies (Journal of Pharmaceutical Science 2010; 4: 1707-1720).

The 5000x-concentrated SYPRO™ orange (Molecular Probes) was diluted with PBS (Sigma), and then admixed with the antibody solutions to prepare measurement samples. Twenty-μL aliquots of each sample were placed into measurement tubes, and the temperature was increased from 30 °C to 99 °C at a temperature elevation rate of 240°C/hr. Changes in fluorescence accompanying the temperature elevation were detected at 470 nm (excitation wavelength) / 555 nm (fluorescence wavelength).

The data were analyzed using the Rotor-Gene Q Series software (QIAGEN) to calculate the temperature at which fluorescence transition was observed, and this temperature was defined as the Tm.

[Reference Example 4] Assessment of the ECM-binding ability

The assessment was carried out according to the method described in WO2012093704. Specifically, BD Matrigel (BD Biosciences, #356237) was prepared at 2 mg/mL using TBS (Takara, #T903), and this was dispensed into a 96-well measurement plate (Meso Scale Discovery, #L15XB-3(High Bind)) at 5 μL per well and then allowed to stand overnight in a cool place. Then, 150 μL of an ECL blocking buffer (PBS containing 0.05% Tween20, 0.5% BSA, and 0.01% sodium azide) was dispensed into each well of the plate, and this was allowed to stand at room temperature for two hours or more.

A goat anti-human IgG(γ) (Invitrogen, #628400) was ruthenium-labeled with MSD SULFO-TAG NHS Ester (Meso Scale Discovery, #R91AN-2) by following the attached instructions. This was diluted in an ECL dilution buffer (PBS containing 0.01% Tween20, 0.1% BSA, and 0.01% sodium azide) to have a final concentration of 2 μg/mL. Furthermore, the standard antibody and the test antibodies were diluted in PBS-T (PBS containing 0.05% Tween 20 and 0.01% sodium azide) to have a final concentration of 3 μg/mL.

To a 96-well reaction plate (Thermo scientific, Nunc #145399), 10 μL of the ECL dilution buffer, 20 μL of the standard antibody and test antibody (3 μg/mL), and 30 μL of the ruthenium-labeled antibody (2 μg/mL) were added sequentially, and this was allowed to react for one hour at room temperature with stirring in the dark.

The ECL blocking buffer was removed from the 96-well measurement plate by tilting, 50 μL of the sample solution from the 96-well reaction plate was added, and this was allowed to stand in the dark at room temperature for one hour. This was followed by removal of the sample solution from the 96-well measurement plate by tilting, and immediately after addition of 150 μL of 2x T buffer (4x MSD Read Buffer T (Meso Scale Discovery) diluted two-fold using the ECL dilution buffer), ECL measurements were taken. SECTOR Imager 2400 (Meso Scale Discovery) was used for taking the measurements.

Analyses were carried out by dividing the fluorescence intensity of the test antibody by the fluorescence intensity of the standard antibody to calculate and compare the intensities by defining the value for the standard antibody to be 1.

[Reference Example 5] Assessment of the SuRe™ ligand-binding ability

The ability to bind to the SuRe™ ligand was assessed by using Biacore™-T200 (GE Healthcare Japan). HBS-EP+ (GE Healthcare Japan) was used for the running buffer, and an amine coupling kit (GE Healthcare Japan) was used to covalently bind the Mab Select SuRe™ Ligand (GE Healthcare Japan) to the CM5 chip (carboxymethyl dextran-coated chip). The antibody used as the analyte was prepared at 5 μg/mL using HBS-EP+. Measurements were carried out by first injecting the 5-μg/mL antibody solution at a flow rate of 10 μL/min for 3 minutes, then switching to HBS-EP+, and measuring the response (RU) after allowing the flow to continue for 0.5 minutes. After completion of the measurements, the sensor chip was regenerated by washing with 10 mM Gly-HCl at pH 1.5 . For the control flow cell, a similar experiment was performed without covalent bonding of the ligand to the chip, and the affinity for the SuRe™ ligand was analyzed by taking the difference between the responses (RU).

Sequences corresponding to the SEQ ID NOs mentioned herein are shown in the Table below.

Table 14

SEQ ID NO:	Name
1	GPC3 nucleotide sequence (NM_001164617.1)
2	GPC3 amino acid sequence (NP_001158089.1)
3	Signal sequence
4	T cell receptor α-chain peptide (CAA26636.1)
5	T cell receptor β-chain peptide (C25777)
6	T cell receptor γ1-chain peptide (A26659)
7	T cell receptor γ2-chain peptide (AAB63312.1)
8	T cell receptor δ-chain peptide (AAA61033.1)
9	CD3 γ-chain nucleotide (NM_000073.2)
10	CD3 δ-chain nucleotide (NM_000732.4)
11	CD3 ε-chain nucleotide (NM_000733.3)
12	CD3 γ-chain peptide (NP_000064.1)
13	CD3 δ-chain peptide (NP_000723.1)
14	CD3 ε-chain peptide (NP_000724.1)
15~22	Peptide linker
23	Human Cγ1
24	Human Cγ2
25	Human Cγ3
26	Human Cγ4
27	FcγRI nucleotide (NM_000566.3)
28	FcγRI peptide (NP_000557.1)
29	FcγRIIA nucleotide (BC020823.1)
30	FcγRIIA peptide (AAH20823.1)
31	FcγRIIB nucleotide (BC146678.1)
32	FcγRIIB peptide (AAI46679.1)
33	FcγRIIIA nucleotide (BC033678.1)
34	FcγRIIIA peptide (AAH33678.1)
35	FcγRIIIB nucleotide (BC128562.1)
36	FcγRIIIB peptide (AAI28563.1)
37	Fc region (addition of A to the N terminus of RefSeq accession number AAC82527.1)
38	Fc region (addition of A to the N terminus of RefSeq accession number AAB59393.1)
39	Fc region (addition of A to the N terminus of RefSeq accession number AAB59394.1)
40	H0000, GPC3 H-chain variable region
41	GL4, GPC3 L-chain variable region
42	rCE115H, CE115 H-chain variable region
43	rCE115L, CE115 L-chain variable region
44	G1dh
45	ERY22_Hk
46	ERY22_Hh
47	GL4-ERY22_Hk
48	H0000-ERY22_L
49	rCE115H-ERY22_Hh
50	rCE115L-k0
51	hCE115HL (Heavy chain of humanized CE115)
52	hCE115HA (Heavy chain of humanized CE115)
53	L0000 (Light chain of humanized CE115)
54	H0000-ERY27_HK
55	hCE115HA-ERY27_HE
56	L0000-k0
57	E22Hh
58	E22Hk
59	Hi-Kn010G3
60	E2702GsKsc
61	E2704sEpsc
62	E2702sKsc
63	k0
64	CE115HA177
65	CE115HA178
66	CE115HA179
67	CE115HA180
68	hCE115HAa
69	TR01H006
70	TR01H007
71	TR01H008
72	TR01H009
73	TR01H010
74	TR01H011
75	TR01H012
76	TR01H013
77	TR01H014
78	TR01H015
79	TR01H016
80	TR01H017
81	TR01H018
82	TR01H019
83	TR01H020
84	TR01H021
85	TR01H022
86	TR01H023
87	TR01H024
88	TR01H025
89	TR01H026
90	TR01H027
91	TR01H028
92	TR01H029
93	TR01H030
94	TR01H031
95	TR01H032
96	TR01H033
97	TR01H034
98	TR01H035
99	TR01H036
100	TR01H037
101	TR01H038
102	TR01H039
103	TR01H040
104	TR01H041
105	TR01H042
106	TR01H043
107	TR01H044
108	TR01H045
109	TR01H046
110	TR01H047
111	TR01H048
112	TR01H049
113	TR01H050
114	TR01H051
115	TR01H052
116	TR01H053
117	TR01H054
118	TR01H055
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126	TR01H065
127	TR01H066
128	TR01H067
129	TR01H068
130	TR01H069
131	TR01H070
132	TR01H071
133	TR01H072
134	TR01H073
135	TR01H074
136	TR01H075
137	TR01H076
138	TR01H077
139	TR01H079
140	TR01H080
141	TR01H081
142	TR01H082
143	TR01H083
144	TR01H084
145	TR01H090
146	TR01H091
147	TR01H092
148	TR01H093
149	TR01H094
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157	TR01H102
158	TR01H103
159	TR01H104
160	TR01H105
161	TR01H106
162	TR01H107
163	TR01H108
164	TR01H109
165	TR01H110
166	TR01H111
167	TR01H112
168	TR01H113
169	TR01H114
170	GCH003
171	GCH005
172	GCH006
173	GCH007
174	GCH008
175	GCH010
176	GCH012
177	GCH013
178	GCH014
179	GCH015
180	GCH016
181	GCH019
182	GCH022
183	GCH023
184	GCH025
185	GCH026
186	GCH027
187	GCH029
188	GCH032
189	GCH034
190	GCH035
191	GCH039
192	GCH040
193	GCH042
194	GCH043
195	GCH045
196	GCH053
197	GCH054
198	GCH055
199	GCH056
200	GCH057
201	GCH059
202	GCH060
203	GCH061
204	GCH062
205	GCH064
206	GCH065
207	GCH066
208	GCH067
209	GCH068
210	GCH073
211	GCH094
212	GCH098
213	GCH099
214	GCH100
215	H0610
216	L0000vk1
217	L0002
218	L0003
219	L0006
220	L0007
221	L0008
222	L0009
223	L0011
224	L0012
225	L0013
226	L0014

SEQ ID NO:	Name
227	L0015
228	L0016
229	L0032
230	L0038
231	L0039
232	L0041
233	L0042
234	L0043
235	L0044
236	L0045
237	L0046
238	L0047
239	L0062
240	L0063
241	L0064
242	L0065
243	L0066
244	L0069
245	L0075
246	L0079
247	L0082
248	L0085
249	L0089
250	L0090
251	L0091
252	L0093
253	L0104
254	L0106
255	L0107
256	L0109
257	L0113
258	L0115
259	L0117
260	L0120
261	L0122
262	L0123
263	L0124
264	L0125
265	L0126
266	L0127
267	L0129
268	L0132
269	L0134
270	L0136
271	L0137
272	L0138
273	L0139
274	L0140
275	L0141
276	L0143
277	L0144
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279	L0147
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281	L0149
282	L0151
283	L0152
284	L0154
285	L0155
286	L0157
287	L0160
288	L0161
289	L0163
290	L0167
291	L0168
292	L0173
293	L0175
294	L0180
295	L0181
296	L0186
297	L0187
298	L0200
299	L0201

SEQ ID NO:	Name
300	L0202
301	L0203
302	L0204
303	L0205
304	L0206
305	L0207
306	L0208
307	L0209
308	L0210
309	L0211
310	L0212
311	L0213
312	L0214
313	L0215
314	L0216
315	L0217
316	L0218
317	L0219
318	L0220
319	L0222
320	L0223
321	L0224
322	L0226
323	L0227
324	L0228
325	L0229
326	L0230
327	L0231
328	L0232
329	L0233
330	L0234
331	L0235
332	L0236
333	L0237
334	L0238
335	L0239
336	L0240
337	L0241
338	L0242
339	L0243
340	L0246
341	L0247
342	L0248
343	L0249
344	L0250
345	L0258
346	L0259
347	L0260
348	L0261
349	L0262
350	L0263
351	L0264
352	L0265
353	L0266
354	L0267
355	L0268
356	L0269
357	L0270
358	L0271
359	L0272
360	TR01L001
361	TR01L002
362	TR01L003
363	TR01L004
364	TR01L005
365	TR01L006
366	TR01L007
367	TR01L008
368	TR01L009
369	TR01L010
370	TR01L011
371	TR01L012
372	TR01L013

SEQ ID NO:	Name
373	TR01L015
374	TR01L016
375	TR01L017
376	TR01L018
377	TR01L019
378	TR01L020
379	TR01L023
380	TR01L024
381	CE115HA122-E22Hh
382	CE115HA236-E22Hh
383	CE115HA251-E22Hh
384	GCH054-E2704sEpsc
385	GCH065-E2704sEpsc
386	GCH094-E2704sEpsc
387	H0610-E2704sEpsc
388	hCE115HA-E22Hh
389	rCE115H-E22Hh
390	rCE115H-E2702GsKsc
391	TR01H002-E22Hh
392	TR01H015-E22Hh
393	TR01H040-E2702GsKsc
394	TR01H061-E2702GsKsc
395	TR01H067-E2702GsKsc
396	TR01H068-E2702GsKsc
397	TR01H071-E2702GsKsc
398	TR01H082-E2702GsKsc
399	TR01H084-E2702GsKsc
400	TR01H109-E2702GsKsc
401	TR01H113-E2702GsKsc
402	TR01H113-E2702sKsc
403	GL4-E22Hk
404	L0000-E22Hk
405	H0000-E22L
406	H0610-E22L
407	rCE115L-k0
408	GLS3108-k0
409	L0000-k0
410	L0011-k0
411	L0201-k0
412	L0203-k0
413	L0204-k0
414	L0206-k0
415	L0208-k0
416	L0209-k0
417	L0211-k0
418	L0212-k0
419	L0222-k0
420	TR01H001
421	TR01H002
422	TR01H003
423	TR01H004
424	rCE115H
425	CE115HA121
426	CE115HA122
427	CE115HA124
428	CE115HA192
429	CE115HA236
430	CE115HA251
431	CE115HA252
432	E22L

Industrial Applicability

The present invention provides novel multispecific antigen-binding molecules that maintain the strong anti-tumor activity possessed by BiTE and the excellent safety property of not inducing a cytokine storm or such independently from cancer antigen, and also have long half-lives in blood. Cytotoxicity-inducing agents that comprise an antigen-binding molecule of the present invention as an active ingredient can target glypican 3-expressing cells and tumor tissues containing these cells and induce cell injury. Administration of a multispecific antigen-binding molecule of the present invention to patients makes it possible to have a desirable treatment which not only has a high level of safety but also a reduced physical burden, and is highly convenient.

CLAIMS

1. A multispecific antigen-binding molecule that comprises:
(1) a domain comprising an antibody variable region having glypican 3-binding activity,
(2) a domain comprising an antibody variable region having T-cell receptor complex-binding activity, and
(3) a domain comprising an Fc region with reduced binding activity towards an Fcγ receptor,
wherein the L chain variable regions comprised in the variable region of (1) and the variable region of (2) have a common amino acid sequence; wherein the multispecific antigen-binding molecule has a cytotoxic activity equivalent to or greater than that of a bispecific antibody comprising a glypican 3-binding domain comprising SEQ ID NOs: 47 and 48, and a T-cell receptor complex-binding domain comprising SEQ ID NOs: 49 and 50.

2. The multispecific antigen-binding molecule of claim 1, wherein the cytotoxic activity is T-cell-dependent cytotoxic activity.

3. The multispecific antigen-binding molecule of claim 1 or 2, wherein the T-cell receptor complex-binding activity is binding activity towards a T-cell receptor.

4. The multispecific antigen-binding molecule of any one of claims 1 to 3, wherein the T-cell receptor complex-binding activity is binding activity towards a CD3ε chain.

5. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable region of (1) in claim 1 is an antibody variable region that comprises any one of the combinations of H-chain CDR1, CDR2, and CDR3 selected from (a1) to (a5) below, or an antibody variable region functionally equivalent thereto:
(a1) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40;
(a2) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197;
(a3) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206;
(a4) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and

(a5) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215.

6. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable region of (2) in claim 1 is an antibody variable region that comprises any one of the combinations of H-chain CDR1, CDR2, and CDR3 amino acid sequences selected from (b1) to (b15) below, or an antibody variable region functionally equivalent thereto:

(b1) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 52;

(b2) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103;

(b3) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 122;

(b4) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128;

(b5) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 129;

(b6) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 132;

(b7) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142;

(b8) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144;

(b9) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164;

(b10) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168;

(b11) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 421;

(b12) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 424;

(b13) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 426;

(b14) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 429; and

(b15) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 430.

7. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable regions of (1) and (2) in claim 1 are antibody variable regions comprising any one of the combinations of H-chain CDR1, CDR2, and CDR3 selected from the following (c1) to (c19), or antibody variable regions functionally equivalent thereto:

(c1) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 52;

(c2) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 421;

(c3) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 426;

(c4) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 429;

(c5) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 40; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 430;

(c6) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2)

in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128;

(c7) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142;

(c8) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144;

(c9) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164;

(c10) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168;

(c11) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142;

(c12) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144;

(c13) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2)

in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164;

(c14) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168;

(c15) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103;

(c16) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 122;

(c17) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 129;

(c18) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 132; and

(c19) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 424.

8. The multispecific antigen-binding molecule of any one of claims 5 to 7, wherein CDR1, CDR2, and CDR3 are CDR1, CDR2, and CDR3 regions based on Kabat numbering.

9. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable region of (1) in claim 1 is an antibody variable region comprising any one of the H-chain variable regions selected from (a1) to (a5) below, or an antibody variable region functionally equivalent thereto:

(a1) an H-chain variable region having the amino acid sequence of SEQ ID NO: 40;
(a2) an H-chain variable region having the amino acid sequence of SEQ ID NO: 197;
(a3) an H-chain variable region having the amino acid sequence of SEQ ID NO: 206;
(a4) an H-chain variable region having the amino acid sequence of SEQ ID NO: 211; and
(a5) an H-chain variable region having the amino acid sequence of SEQ ID NO: 215.

10. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable region of (2) in claim 1 is an antibody variable region comprising any one of the H-chain variable regions selected from (b1) to (b15) below, or an antibody variable region functionally equivalent thereto:

(b1) an H-chain variable region having the amino acid sequence of SEQ ID NO: 52;
(b2) an H-chain variable region having the amino acid sequence of SEQ ID NO: 103;
(b3) an H-chain variable region having the amino acid sequence of SEQ ID NO: 122;
(b4) an H-chain variable region having the amino acid sequence of SEQ ID NO: 128;
(b5) an H-chain variable region having the amino acid sequence of SEQ ID NO: 129;
(b6) an H-chain variable region having the amino acid sequence of SEQ ID NO: 132;
(b7) an H-chain variable region having the amino acid sequence of SEQ ID NO: 142;
(b8) an H-chain variable region having the amino acid sequence of SEQ ID NO: 144;
(b9) an H-chain variable region having the amino acid sequence of SEQ ID NO: 164;
(b10) an H-chain variable region having the amino acid sequence of SEQ ID NO: 168;
(b11) an H-chain variable region having the amino acid sequence of SEQ ID NO: 421;
(b12) an H-chain variable region having the amino acid sequence of SEQ ID NO: 424;
(b13) an H-chain variable region having the amino acid sequence of SEQ ID NO: 426;
(b14) an H-chain variable region having the amino acid sequence of SEQ ID NO: 429; and
(b15) an H-chain variable region having the amino acid sequence of SEQ ID NO: 430.

11. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable regions of (1) and (2) in claim 1 are antibody variable regions comprising any one of the combinations of H-chain variable regions selected from (c1) to (c19) below, or antibody variable regions functionally equivalent thereto:

(c1) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region

comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 52;

(c2) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 421;

(c3) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 426;

(c4) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 429;

(c5) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 40; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 430;

(c6) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 197; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 128;

(c7) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 142;

(c8) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 144;

(c9) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 164;

(c10) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 206; and an H-chain variable region

comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 168;

(c11) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 142;

(c12) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 144;

(c13) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 164;

(c14) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 211; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 168;

(c15) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 103;

(c16) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 122;

(c17) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 129;

(c18) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 132; and

(c19) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 which has the amino acid sequence of SEQ ID NO: 215; and an H-chain variable region

comprised in the antibody variable region of (2) in claim 1 which has the amino acid sequence of SEQ ID NO: 424.

12. The multispecific antigen-binding molecule of any one of claims 1 to 11, wherein the common L chain of claim 1 is a common L chain comprising any one of the combinations of CDR1, CDR2, and CDR3 selected from (d1) to (d11) below, or a common L chain functionally equivalent thereto:

(d1) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(d2) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(d3) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(d4) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 301;

(d5) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 302;

(d6) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 304;

(d7) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 306;

(d8) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 307;

(d9) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 309;

(d10) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 310; and

(d11) CDR1, CDR2, and CDR3 identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 319.

13. The multispecific antigen-binding molecule of any one of claims 1 to 11, wherein the L chain variable region of claim 1 is a variable region of any one of the L chain amino acid sequences selected from(d1) to (d11) below:

(d1) an L chain comprising the amino acid sequence of SEQ ID NO: 53;

(d2) an L chain comprising the amino acid sequence of SEQ ID NO: 223;

(d3) an L chain comprising the amino acid sequence of SEQ ID NO: 299;

(d4) an L chain comprising the amino acid sequence of SEQ ID NO: 301;
(d5) an L chain comprising the amino acid sequence of SEQ ID NO: 302;
(d6) an L chain comprising the amino acid sequence of SEQ ID NO: 304;
(d7) an L chain comprising the amino acid sequence of SEQ ID NO: 306;
(d8) an L chain comprising the amino acid sequence of SEQ ID NO: 307;
(d9) an L chain comprising the amino acid sequence of SEQ ID NO: 309;
(d10) an L chain comprising the amino acid sequence of SEQ ID NO: 310; and
(d11) an L chain comprising the amino acid sequence of SEQ ID NO: 319.

14. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable regions of (1) and (2) of claim 1 and the common L chain variable region are antibody variable regions comprising any one of the combinations of H-chain CDR1, CDR2, and CDR3 and L-chain CDR1, CDR2, and CDR3 selected from (e1) to (e25) below, or antibody variable regions functionally equivalent thereto:

(e1) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e2) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(e3) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 310;

(e4) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 197; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 128; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 319;

(e5) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e6) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e7) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e8) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e9) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e10) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(e11) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e12) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 164; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e13) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223;

(e14) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e15) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 299;

(e16) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 301;

(e17) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 302;

(e18) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 304;

(e19) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 306;

(e20) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 307;

(e21) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 103; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 309;

(e22) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 122; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e23) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 129; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53;

(e24) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 132; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53; and

(e25) CDR1, CDR2, and CDR3 comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 215; CDR1, CDR2, and CDR3 comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 424; and CDR1, CDR2, and CDR3 comprised in the antibody variable region of the common L chain and identical to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 53.

15. The multispecific antigen-binding molecule of any one of claims 1 to 4, wherein the antibody variable regions of (1) and (2) of claim 1 and the common L chain variable region are antibody variable regions comprising any one of the combinations of variable regions selected from (f1) to (f26) below, or antibody variable regions functionally equivalent thereto:

(f1) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f2) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 299;

(f3) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 310;

(f4) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 197; an H-chain variable region

comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 128; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 319;

(f5) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 142; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f6) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 144; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f7) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 164; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f8) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 206; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 168; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f9) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 142; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f10) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 142; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 299;

(f11) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid

sequence of SEQ ID NO: 144; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f12) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 164; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f13) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 211; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 168; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 223;

(f14) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f15) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 299;

(f16) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 301;

(f17) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 302;

(f18) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid

sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 304;

(f19) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 306;

(f20) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 307;

(f21) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 103; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 309;

(f22) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 122; and an antibody variable region of the common L chain identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f23) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 129; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f24) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 132; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53;

(f25) an H-chain variable region comprised in the antibody variable region of (1) in claim 1 and identical to the amino acid sequence of SEQ ID NO: 215; an H-chain variable region comprised in the antibody variable region of (2) in claim 1 and identical to the amino acid

sequence of SEQ ID NO: 424; and an antibody variable region of the common L chain and identical to the amino acid sequence of the variable region comprised in SEQ ID NO: 53; and

(f26) multispecific antigen-binding molecule that binds to an epitope overlapping with each of the epitopes on glypican 3 and T-cell receptor complex bound by the multispecific antigen-binding molecule of any one of (f1) to (f25), and which has a common L chain.

16. The multispecific antigen-binding molecule of any one of claims 1 to 15, wherein the Fc region of (3) in claim 1 is an Fc region with an amino acid mutation at any of the Fc region-constituting amino acids of SEQ ID NOs: 23 to 26 (IgG1 to IgG4).

17. The multispecific antigen-binding molecule of claim 16, wherein the Fc region of (3) in claim 1 is an Fc region with mutation of at least one amino acid selected from the following amino acid positions specified by EU numbering:
position 220, position 226, position 229, position 231, position 232, position 233, position 234, position 235, position 236, position 237, position 238, position 239, position 240, position 264, position 265, position 266, position 267, position 269, position 270, position 295, position 296, position 297, position 298, position 299, position 300, position 325, position 327, position 328, position 329, position 330, position 331, and position 332.

18. The multispecific antigen-binding molecule of claim 16, wherein the Fc region of (3) in claim 1 is an Fc region comprising at least one amino acid selected from the following amino acids specified by EU numbering:
Arg at amino acid position 234, Ala or Arg at amino acid position 235, Lys at amino acid position 239, and Ala at amino acid position 297.

19. The multispecific antigen-binding molecule of any one of claims 16 to 18, wherein the Fc region of (3) in claim 1 further comprises an amino acid mutation for promoting formation of a heterodimeric Fc region.

20. The multispecific antigen-binding molecule of claim 19, wherein the heterodimeric Fc region is the amino acid sequence combination of (g1) or (g2) below:
(g1) a combination of an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 57, and an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 58; and
(g2) a combination of an amino acid sequence identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 60 or 62, and an amino acid sequence

identical to the Fc region of a constant region comprising the amino acid sequence of SEQ ID NO: 61.

21. The multispecific antigen-binding molecule of any one of claims 1 to 20, wherein the multispecific antigen-binding molecule is a bispecific antibody.

22. A bispecific antibody of any one of (h1) to (h25) below:

(h1) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 424 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h2) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h3) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 299;

(h4) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 301;

(h5) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 302;

(h6) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 304;

(h7) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 306;

(h8) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 307;

(h9) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 103 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 309;

(h10) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 122 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h11) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 129 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h12) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 215 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 132 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h13) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 299;

(h14) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 310;

(h15) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 319;

(h16) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 197 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 128 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 53;

(h17) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 142 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 299;

(h18) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 142 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h19) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 144 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h20) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 144 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h21) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 142 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h22) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 164 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h23) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 206 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 168 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223;

(h24) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 164 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223; and

(h25) a bispecific antibody having an antibody H chain having glypican 3-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 211 and a constant region having the amino acid sequence of SEQ ID NO: 61; an antibody H chain having T-cell receptor complex-binding activity that comprises an antibody H-chain variable region having the amino acid sequence of SEQ ID NO: 168 and a constant region having the amino acid sequence of SEQ ID NO: 60 or 62; and a common antibody L chain having the amino acid sequence of SEQ ID NO: 223.

23. A nucleic acid that encodes the multispecific antigen-binding molecule of any one of claims 1 to 20 or the bispecific antibody of claim 21 or 22.

24. A vector into which the nucleic acid of claim 23 is introduced.

25. A cell comprising the nucleic acid of claim 23 or the vector of claim 24.

26. A method for producing the multispecific antigen-binding molecule of any one of claims 1 to 20 or the bispecific antibody of claim 21 or 22 by culturing the cell of claim 25.

27. A multispecific antigen-binding molecule or a bispecific antibody produced by the method of claim 26.

28. A pharmaceutical composition comprising the multispecific antigen-binding molecule of any one of claims 1 to 20 or the bispecific antibody of claim 21 or 22, and a pharmaceutically acceptable carrier.

29. The pharmaceutical composition of claim 28, which induces cytotoxicity.

30. The pharmaceutical composition of claim 29, wherein the cytotoxicity is T-cell-dependent cytotoxicity.

31. The pharmaceutical composition of claim 28, which is for administration to a patient in need of the multispecific antigen-binding molecule of any one of claims 1 to 20 or the bispecific antibody of claim 21 or 22.

SEQUENCE LISTING

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tgaagggccc tgagccagtg gtcagtcaaa ttattgacaa actgaagcac attaaccagc 1680

tcctgagaac catgtctatg cccaaaggta gagttctgga taaaaacctg gatgaggaag 1740

ggtttgaaag tggagactgc ggtgatgatg aagatgagtg cattggaggc tctggtgatg 1800

gaatgataaa agtgaagaat cagctccgct tccttgcaga actggcctat gatctggatg 1860

tggatgatgc gcctggaaac agtcagcagg caactccgaa ggacaacgag ataagcacct 1920

ttcacaacct cgggaacgtt cattccccgc tgaagcttct caccagcatg gccatctcgg 1980

tggtgtgctt cttcttcctg gtgcactgac tgcctggtgc ccagcacatg tgctgcccta 2040

cagcaccctg tggtcttcct cgataaaggg aaccactttc ttatttttt ctatttttt 2100

ttttttgtta tcctgtatac ctcctccagc catgaagtag aggactaacc atgtgttatg 2160

ttttcgaaaa tcaaatggta tcttttggag gaagatacat tttagtggta gcatatagat 2220

tgtccttttg caaagaaaga aaaaaaacca tcaagttgtg ccaaattatt ctcctatgtt 2280

tggctgctag aacatggtta ccatgtcttt ctctctcact ccctcccttt ctatcgttct 2340

ctctttgcat ggatttcttt gaaaaaaaat aaattgctca aataaaaaaa aaaaaaaa 2398

<210> 2
<211> 603
<212> PRT

<213> Homo sapiens

<400> 2

```
Met Ala Gly Thr Val Arg Thr Ala Cys Leu Val Val Ala Met Leu Leu
1               5                  10                  15

Ser Leu Asp Phe Pro Gly Gln Ala Gln Pro Pro Pro Pro Pro Pro Asp
            20                  25                  30

Ala Thr Cys His Gln Val Arg Ser Phe Phe Gln Arg Leu Gln Pro Gly
        35                  40                  45

Leu Lys Trp Val Pro Glu Thr Pro Val Pro Gly Ser Asp Leu Gln Val
    50                  55                  60

Cys Leu Pro Lys Gly Pro Thr Cys Cys Ser Arg Lys Met Glu Glu Lys
65                  70                  75                  80

Tyr Gln Leu Thr Ala Arg Leu Asn Met Glu Gln Leu Leu Gln Ser Ala
                85                  90                  95

Ser Met Glu Leu Lys Phe Leu Ile Ile Gln Asn Ala Ala Val Phe Gln
            100                 105                 110

Glu Ala Phe Glu Ile Val Val Arg His Ala Lys Asn Tyr Thr Asn Ala
        115                 120                 125
```

```
Met Phe Lys Asn Asn Tyr Pro Ser Leu Thr Pro Gln Ala Phe Glu Phe
    130                 135                 140

Val Gly Glu Phe Phe Thr Asp Val Ser Leu Tyr Ile Leu Gly Ser Asp
145                 150                 155                 160

Ile Asn Val Asp Asp Met Val Asn Glu Leu Phe Asp Ser Leu Phe Pro
                165                 170                 175

Val Ile Tyr Thr Gln Leu Met Asn Pro Gly Leu Pro Asp Ser Ala Leu
            180                 185                 190

Asp Ile Asn Glu Cys Leu Arg Gly Ala Arg Arg Asp Leu Lys Val Phe
        195                 200                 205

Gly Asn Phe Pro Lys Leu Ile Met Thr Gln Val Ser Lys Ser Leu Gln
    210                 215                 220

Val Thr Arg Ile Phe Leu Gln Ala Leu Asn Leu Gly Ile Glu Val Ile
225                 230                 235                 240

Asn Thr Thr Asp His Leu Lys Phe Ser Lys Asp Cys Gly Arg Met Leu
                245                 250                 255

Thr Arg Met Trp Tyr Cys Ser Tyr Cys Gln Gly Leu Met Met Val Lys
            260                 265                 270
```

```
Pro Cys Gly Gly Tyr Cys Asn Val Val Met Gln Gly Cys Met Ala Gly
        275                 280                 285

Val Val Glu Ile Asp Lys Tyr Trp Arg Glu Tyr Ile Leu Ser Leu Glu
    290                 295                 300

Glu Leu Val Asn Gly Met Tyr Arg Ile Tyr Asp Met Glu Asn Val Leu
305                 310                 315                 320

Leu Gly Leu Phe Ser Thr Ile His Asp Ser Ile Gln Tyr Val Gln Lys
                325                 330                 335

Asn Ala Gly Lys Leu Thr Thr Thr Glu Thr Glu Lys Lys Ile Trp His
            340                 345                 350

Phe Lys Tyr Pro Ile Phe Phe Leu Cys Ile Gly Leu Asp Leu Gln Ile
        355                 360                 365

Gly Lys Leu Cys Ala His Ser Gln Gln Arg Gln Tyr Arg Ser Ala Tyr
    370                 375                 380

Tyr Pro Glu Asp Leu Phe Ile Asp Lys Lys Val Leu Lys Val Ala His
385                 390                 395                 400

Val Glu His Glu Glu Thr Leu Ser Ser Arg Arg Arg Glu Leu Ile Gln
                405                 410                 415
```

Lys Leu Lys Ser Phe Ile Ser Phe Tyr Ser Ala Leu Pro Gly Tyr Ile
420 425 430

Cys Ser His Ser Pro Val Ala Glu Asn Asp Thr Leu Cys Trp Asn Gly
435 440 445

Gln Glu Leu Val Glu Arg Tyr Ser Gln Lys Ala Ala Arg Asn Gly Met
450 455 460

Lys Asn Gln Phe Asn Leu His Glu Leu Lys Met Lys Gly Pro Glu Pro
465 470 475 480

Val Val Ser Gln Ile Ile Asp Lys Leu Lys His Ile Asn Gln Leu Leu
485 490 495

Arg Thr Met Ser Met Pro Lys Gly Arg Val Leu Asp Lys Asn Leu Asp
500 505 510

Glu Glu Gly Phe Glu Ser Gly Asp Cys Gly Asp Asp Glu Asp Glu Cys
515 520 525

Ile Gly Gly Ser Gly Asp Gly Met Ile Lys Val Lys Asn Gln Leu Arg
530 535 540

Phe Leu Ala Glu Leu Ala Tyr Asp Leu Asp Val Asp Asp Ala Pro Gly
545 550 555 560

Asn Ser Gln Gln Ala Thr Pro Lys Asp Asn Glu Ile Ser Thr Phe His
565 570 575

Asn Leu Gly Asn Val His Ser Pro Leu Lys Leu Leu Thr Ser Met Ala
580 585 590

Ile Ser Val Val Cys Phe Phe Phe Leu Val His
595 600

<210> 3
<211> 19
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 3

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser

<210> 4
<211> 141
<212> PRT
<213> Homo sapiens

<400> 4

```
Asp Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu Arg Asp Ser Lys
1               5                  10                  15

Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe Asp Ser Gln Thr
            20                  25                  30

Asn Val Ser Gln Ser Lys Asp Ser Asp Val Tyr Ile Thr Asp Lys Thr
        35                  40                  45

Val Leu Asp Met Arg Ser Met Asp Phe Lys Ser Asn Ser Ala Val Ala
    50                  55                  60

Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala Asn Ala Phe Asn Asn Ser
65                  70                  75                  80

Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Pro Glu Ser Ser Cys Asp
                85                  90                  95

Val Lys Leu Val Glu Lys Ser Phe Glu Thr Asp Thr Asn Leu Asn Phe
            100                 105                 110

Gln Asn Leu Ser Val Ile Gly Phe Arg Ile Leu Leu Leu Lys Val Ala
        115                 120                 125

Gly Phe Asn Leu Leu Met Thr Leu Arg Leu Trp Ser Ser
    130                 135                 140
```

<210> 5
<211> 179
<212> PRT
<213> Homo sapiens

<400> 5

Glu Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro
1 5 10 15

Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu
20 25 30

Ala Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp Val Asn
35 40 45

Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys
50 55 60

Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu
65 70 75 80

Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys
85 90 95

Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp
100 105 110

Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg
115 120 125

Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr Gln Gln Gly Val Leu Ser
130 135 140

Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala
145 150 155 160

Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp
165 170 175

Ser Arg Gly

<210> 6
<211> 173
<212> PRT
<213> Homo sapiens

<400> 6

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

Pro Ser Ile Ala Glu Thr Lys Leu Gln Lys Ala Gly Thr Tyr Leu Cys
20 25 30

Leu Leu Glu Lys Phe Phe Pro Asp Val Ile Lys Ile His Trp Gln Glu

35 40 45

Lys Lys Ser Asn Thr Ile Leu Gly Ser Gln Glu Gly Asn Thr Met Lys
50 55 60

Thr Asn Asp Thr Tyr Met Lys Phe Ser Trp Leu Thr Val Pro Glu Lys
65 70 75 80

Ser Leu Asp Lys Glu His Arg Cys Ile Val Arg His Glu Asn Asn Lys
85 90 95

Asn Gly Val Asp Gln Glu Ile Ile Phe Pro Pro Ile Lys Thr Asp Val
100 105 110

Ile Thr Met Asp Pro Lys Asp Asn Cys Ser Lys Asp Ala Asn Asp Thr
115 120 125

Leu Leu Leu Gln Leu Thr Asn Thr Ser Ala Tyr Tyr Met Tyr Leu Leu
130 135 140

Leu Leu Leu Lys Ser Val Val Tyr Phe Ala Ile Ile Thr Cys Cys Leu
145 150 155 160

Leu Arg Arg Thr Ala Phe Cys Cys Asn Gly Glu Lys Ser
165 170

<210> 7

<211> 204
<212> PRT
<213> Homo sapiens

<400> 7

```
Lys Gln Leu Asp Ala Asp Val Ser Pro Lys Pro Thr Ile Phe Leu Pro
1               5                  10                  15

Ser Ile Ala Glu Thr Lys Leu Gln Lys Ala Gly Thr Tyr Leu Cys Leu
            20                  25                  30

Leu Glu Lys Phe Phe Pro Asp Ile Ile Lys Ile His Trp Gln Glu Lys
        35                  40                  45

Lys Ser Asn Thr Ile Leu Gly Ser Gln Glu Gly Asn Thr Met Lys Thr
    50                  55                  60

Asn Asp Thr Tyr Met Lys Phe Ser Trp Leu Thr Val Pro Glu Glu Ser
65                  70                  75                  80

Leu Asp Lys Glu His Arg Cys Ile Val Arg His Glu Asn Asn Lys Asn
                85                  90                  95

Gly Ile Asp Gln Glu Ile Ile Phe Pro Pro Ile Lys Thr Asp Val Thr
            100                 105                 110

Thr Val Asp Pro Lys Asp Ser Tyr Ser Lys Asp Ala Asn Asp Val Thr
        115                 120                 125
```

```
Thr Val Asp Pro Lys Tyr Asn Tyr Ser Lys Asp Ala Asn Asp Val Ile
    130                 135                 140

Thr Met Asp Pro Lys Asp Asn Trp Ser Lys Asp Ala Asn Asp Thr Leu
145                 150                 155                 160

Leu Leu Gln Leu Thr Asn Thr Ser Ala Tyr Tyr Met Tyr Leu Leu Leu
                165                 170                 175

Leu Leu Lys Ser Val Val Tyr Phe Ala Ile Ile Thr Cys Cys Leu Leu
            180                 185                 190

Gly Arg Thr Ala Phe Cys Cys Asn Gly Glu Lys Ser
        195                 200
```

<210> 8
<211> 177
<212> PRT
<213> Homo sapiens

<400> 8

```
Pro Ser Tyr Thr Gly Gly Tyr Ala Asp Lys Leu Ile Phe Gly Lys Gly
1               5                   10                  15

Thr Arg Val Thr Val Glu Pro Arg Ser Gln Pro His Thr Lys Pro Ser
            20                  25                  30
```

Val Phe Val Met Lys Asn Gly Thr Asn Val Ala Cys Leu Val Lys Glu
35 40 45

Phe Tyr Pro Lys Asp Ile Arg Ile Asn Leu Val Ser Ser Lys Lys Ile
50 55 60

Thr Glu Phe Asp Pro Ala Ile Val Ile Ser Pro Ser Gly Lys Tyr Asn
65 70 75 80

Ala Val Lys Leu Gly Lys Tyr Glu Asp Ser Asn Ser Val Thr Cys Ser
85 90 95

Val Gln His Asp Asn Lys Thr Val His Ser Thr Asp Phe Glu Val Lys
100 105 110

Thr Asp Ser Thr Asp His Val Lys Pro Lys Glu Thr Glu Asn Thr Lys
115 120 125

Gln Pro Ser Lys Ser Cys His Lys Pro Lys Ala Ile Val His Thr Glu
130 135 140

Lys Val Asn Met Met Ser Leu Thr Val Leu Gly Leu Arg Met Leu Phe
145 150 155 160

Ala Lys Thr Val Ala Val Asn Phe Leu Leu Thr Ala Lys Leu Phe Phe
165 170 175

Leu

<210> 9
<211> 1311
<212> DNA
<213> Homo sapiens

<400> 9
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gccggaggac agagactgac atggaacagg ggaagggcct ggctgtcctc atcctggcta 120

tcattcttct tcaaggtact ttggcccagt caatcaaagg aaaccacttg gttaaggtgt 180

atgactatca agaagatggt tcggtacttc tgacttgtga tgcagaagcc aaaaatatca 240

catggtttaa agatgggaag atgatcggct tcctaactga agataaaaaa aaatggaatc 300

tgggaagtaa tgccaaggac cctcgaggga tgtatcagtg taaaggatca cagaacaagt 360

caaaaccact ccaagtgtat tacagaatgt gtcagaactg cattgaacta aatgcagcca 420

ccatatctgg ctttctcttt gctgaaatcg tcagcatttt cgtccttgct gttggggtct 480

acttcattgc tggacaggat ggagttcgcc agtcgagagc ttcagacaag cagactctgt 540

tgcccaatga ccagctctac cagcccctca aggatcgaga agatgaccag tacagccacc 600

ttcaaggaaa ccagttgagg aggaattgaa ctcaggactc agagtagtcc aggtgttctc 660

ctcctattca gttcccagaa tcaaagcaat gcattttgga aagctcctag cagagagact 720

ttcagcccta aatctagact caaggttccc agagatgaca aatggagaag aaaggccatc 780

agagcaaatt tgggggtttc tcaaataaaa taaaaataaa aacaaatact gtgtttcaga 840

agcgccacct attggggaaa attgtaaaag aaaaatgaaa agatcaaata acccccctgga 900

tttgaatata atttttgtg ttgtaatttt tatttcgttt ttgtataggt tataattcac 960

atggctcaaa tattcagtga aagctctccc tccaccgcca tcccctgcta cccagtgacc 1020

ctgttgccct cttcagagac aaattagttt ctctttttt ttttttttt ttttttttg 1080

agacagtctg gctctgtcac ccaggctgaa atgcagtggc accatctcgg ctcactgcaa 1140

cctctgcctc ctgggttcaa gcgattctcc tgcctcagcc tcccgggcag ctgggattac 1200

aggcacacac taccacacct ggctaatttt tgtatttta gtagagacag ggttttgctc 1260

tgttggccaa gctggtctcg aactcctgac ctcaagtgat ccgcccgcct c 1311

<210> 10
<211> 771
<212> DNA
<213> Homo sapiens

<400> 10
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gctaggggag ggcagctctc acccaggctg atagttcggt gacctggctt tatctactgg 120

atgagttccg ctgggagatg gaacatagca cgtttctctc tggcctggta ctggctaccc 180

ttctctcgca agtgagcccc ttcaagatac ctatagagga acttgaggac agagtgtttg 240

tgaattgcaa taccagcatc acatgggtag agggaacggt gggaacactg ctctcagaca 300

ttacaagact ggacctggga aaacgcatcc tggacccacg aggaatatat aggtgtaatg 360

ggacagatat atacaaggac aaagaatcta ccgtgcaagt tcattatcga atgtgccaga 420

gctgtgtgga gctggatcca gccaccgtgg ctggcatcat tgtcactgat gtcattgcca 480

ctctgctcct tgctttggga gtcttctgct ttgctggaca tgagactgga aggctgtctg 540

gggctgccga cacacaagct ctgttgagga atgaccaggt ctatcagccc ctccgagatc 600

gagatgatgc tcagtacagc caccttggag gaaactgggc tcggaacaag tgaacctgag 660

actggtggct tctagaagca gccattacca actgtacctt cccttcttgc tcagccaata 720

aatatatcct ctttcactca gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 771

<210> 11
<211> 1534
<212> DNA
<213> Homo sapiens

<400> 11
tattgtcaga gtcctcttgt ttggccttct aggaaggctg tgggacccag ctttcttcaa 60

ccagtccagg tggaggcctc tgccttgaac gtttccaagt gaggtaaaac ccgcaggccc 120

agaggcctct ctacttcctg tgtggggttc agaaaccctc ctcccctccc agcctcaggt 180

gcctgcttca gaaaatgaag tagtaagtct gctggcctcc gccatcttag taaagtaaca 240

gtcccatgaa acaaagatgc agtcgggcac tcactggaga gttctgggcc tctgcctctt 300

atcagttggc gtttgggggc aagatggtaa tgaagaaatg ggtggtatta cacagacacc 360

atataaagtc tccatctctg gaaccacagt aatattgaca tgccctcagt atcctggatc 420

tgaaatacta tggcaacaca atgataaaaa cataggcggt gatgaggatg ataaaaacat 480

aggcagtgat gaggatcacc tgtcactgaa ggaattttca gaattggagc aaagtggtta 540

ttatgtctgc taccccagag gaagcaaacc agaagatgcg aacttttatc tctacctgag 600

ggcaagagtg tgtgagaact gcatggagat ggatgtgatg tcggtggcca caattgtcat 660

agtggacatc tgcatcactg ggggcttgct gctgctggtt tactactgga gcaagaatag 720

aaaggccaag gccaagcctg tgacacgagg agcgggtgct ggcggcaggc aaaggggaca 780

aaacaaggag aggccaccac ctgttcccaa cccagactat gagcccatcc ggaaaggcca 840

gcgggacctg tattctggcc tgaatcagag acgcatctga ccctctggag aacactgcct 900

cccgctggcc caggtctcct ctccagtccc cctgcgactc cctgtttcct gggctagtct 960

tggaccccac gagagagaat cgttcctcag cctcatggtg aactcgcgcc ctccagcctg 1020

atcccccgct ccctcctccc tgccttctct gctggtaccc agtcctaaaa tattgctgct 1080

tcctcttcct ttgaagcatc atcagtagtc acaccctcac agctggcctg ccctcttgcc 1140

aggatattta tttgtgctat tcactccctt ccctttggat gtaacttctc cgttcagttc 1200

cctccttttc ttgcatgtaa gttgtccccc atcccaaagt attccatcta cttttctatc 1260

gccgtcccct tttgcagccc tctctgggga tggactgggt aaatgttgac agaggccctg 1320

ccccgttcac agatcctggc cctgagccag ccctgtgctc ctccctcccc caacactccc 1380

taccaacccc ctaatcccct actccctcca ccccccctcc actgtaggcc actggatggt 1440

catttgcatc tccgtaaatg tgctctgctc ctcagctgag agagaaaaaa ataaactgta 1500

tttggctgca agaaaaaaaa aaaaaaaaaa aaaa 1534

<210> 12
<211> 182
<212> PRT
<213> Homo sapiens

<400> 12

Met Glu Gln Gly Lys Gly Leu Ala Val Leu Ile Leu Ala Ile Ile Leu
1 5 10 15

Leu Gln Gly Thr Leu Ala Gln Ser Ile Lys Gly Asn His Leu Val Lys
20 25 30

Val Tyr Asp Tyr Gln Glu Asp Gly Ser Val Leu Leu Thr Cys Asp Ala
35 40 45

Glu Ala Lys Asn Ile Thr Trp Phe Lys Asp Gly Lys Met Ile Gly Phe
50 55 60

Leu Thr Glu Asp Lys Lys Lys Trp Asn Leu Gly Ser Asn Ala Lys Asp
65 70 75 80

Pro Arg Gly Met Tyr Gln Cys Lys Gly Ser Gln Asn Lys Ser Lys Pro
85 90 95

Leu Gln Val Tyr Tyr Arg Met Cys Gln Asn Cys Ile Glu Leu Asn Ala

100 105 110

Ala Thr Ile Ser Gly Phe Leu Phe Ala Glu Ile Val Ser Ile Phe Val
115 120 125

Leu Ala Val Gly Val Tyr Phe Ile Ala Gly Gln Asp Gly Val Arg Gln
130 135 140

Ser Arg Ala Ser Asp Lys Gln Thr Leu Leu Pro Asn Asp Gln Leu Tyr
145 150 155 160

Gln Pro Leu Lys Asp Arg Glu Asp Asp Gln Tyr Ser His Leu Gln Gly
165 170 175

Asn Gln Leu Arg Arg Asn
180

<210> 13
<211> 171
<212> PRT
<213> Homo sapiens

<400> 13

Met Glu His Ser Thr Phe Leu Ser Gly Leu Val Leu Ala Thr Leu Leu
1 5 10 15

Ser Gln Val Ser Pro Phe Lys Ile Pro Ile Glu Glu Leu Glu Asp Arg
20 25 30

Val Phe Val Asn Cys Asn Thr Ser Ile Thr Trp Val Glu Gly Thr Val
35 40 45

Gly Thr Leu Leu Ser Asp Ile Thr Arg Leu Asp Leu Gly Lys Arg Ile
50 55 60

Leu Asp Pro Arg Gly Ile Tyr Arg Cys Asn Gly Thr Asp Ile Tyr Lys
65 70 75 80

Asp Lys Glu Ser Thr Val Gln Val His Tyr Arg Met Cys Gln Ser Cys
85 90 95

Val Glu Leu Asp Pro Ala Thr Val Ala Gly Ile Ile Val Thr Asp Val
100 105 110

Ile Ala Thr Leu Leu Leu Ala Leu Gly Val Phe Cys Phe Ala Gly His
115 120 125

Glu Thr Gly Arg Leu Ser Gly Ala Ala Asp Thr Gln Ala Leu Leu Arg
130 135 140

Asn Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp Asp Ala Gln Tyr
145 150 155 160

Ser His Leu Gly Gly Asn Trp Ala Arg Asn Lys
165 170

<210> 14
<211> 207
<212> PRT
<213> Homo sapiens

<400> 14

```
Met Gln Ser Gly Thr His Trp Arg Val Leu Gly Leu Cys Leu Leu Ser
1               5                  10                  15

Val Gly Val Trp Gly Gln Asp Gly Asn Glu Glu Met Gly Gly Ile Thr
            20                  25                  30

Gln Thr Pro Tyr Lys Val Ser Ile Ser Gly Thr Thr Val Ile Leu Thr
        35                  40                  45

Cys Pro Gln Tyr Pro Gly Ser Glu Ile Leu Trp Gln His Asn Asp Lys
    50                  55                  60

Asn Ile Gly Gly Asp Glu Asp Asp Lys Asn Ile Gly Ser Asp Glu Asp
65                  70                  75                  80

His Leu Ser Leu Lys Glu Phe Ser Glu Leu Glu Gln Ser Gly Tyr Tyr
                85                  90                  95

Val Cys Tyr Pro Arg Gly Ser Lys Pro Glu Asp Ala Asn Phe Tyr Leu
            100                 105                 110
```

Tyr Leu Arg Ala Arg Val Cys Glu Asn Cys Met Glu Met Asp Val Met
115 120 125

Ser Val Ala Thr Ile Val Ile Val Asp Ile Cys Ile Thr Gly Gly Leu
130 135 140

Leu Leu Leu Val Tyr Tyr Trp Ser Lys Asn Arg Lys Ala Lys Ala Lys
145 150 155 160

Pro Val Thr Arg Gly Ala Gly Ala Gly Gly Arg Gln Arg Gly Gln Asn
165 170 175

Lys Glu Arg Pro Pro Pro Val Pro Asn Pro Asp Tyr Glu Pro Ile Arg
180 185 190

Lys Gly Gln Arg Asp Leu Tyr Ser Gly Leu Asn Gln Arg Arg Ile
195 200 205

<210> 15
<211> 4
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 15

Gly Gly Gly Ser

1

<210> 16
<211> 4
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 16

Ser Gly Gly Gly
1

<210> 17
<211> 5
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 17

Gly Gly Gly Gly Ser
1 5

<210> 18
<211> 5
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 18

Ser Gly Gly Gly Gly
1 5

<210> 19
<211> 6
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 19

Gly Gly Gly Gly Gly Ser
1 5

<210> 20
<211> 6
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 20

Ser Gly Gly Gly Gly Gly
1 5

<210> 21
<211> 7
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 21

Gly Gly Gly Gly Gly Gly Ser
1 5

<210> 22
<211> 7
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 22

Ser Gly Gly Gly Gly Gly Gly
1 5

<210> 23
<211> 330
<212> PRT
<213> Homo sapiens

<400> 23

```
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                  10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140
```

```
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285
```

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 24
<211> 326
<212> PRT
<213> Homo sapiens

<400> 24

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr

65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
100 105 110

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
130 135 140

Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
145 150 155 160

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
165 170 175

Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp
180 185 190

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
195 200 205

Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu

210 215 220

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
225 230 235 240

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
245 250 255

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
260 265 270

Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
275 280 285

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
290 295 300

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
305 310 315 320

Ser Leu Ser Pro Gly Lys
325

<210> 25
<211> 377
<212> PRT
<213> Homo sapiens

<400> 25

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1               5                  10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Thr Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Arg Val Glu Leu Lys Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro
            100                 105                 110

Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg
        115                 120                 125

Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys
    130                 135                 140
```

```
Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
145                 150                 155                 160

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
                165                 170                 175

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            180                 185                 190

Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Lys Trp Tyr
        195                 200                 205

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    210                 215                 220

Gln Tyr Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Leu His
225                 230                 235                 240

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                245                 250                 255

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys 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 Ser Gly Gln Pro Glu Asn Asn
305                 310                 315                 320

Tyr Asn Thr Thr Pro Pro Met 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 Ile
            340                 345                 350

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Phe Thr Gln
        355                 360                 365

Lys Ser Leu Ser Leu Ser Pro Gly Lys
    370                 375
```

<210> 26
<211> 327
<212> PRT
<213> Homo sapiens

<400> 26

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1               5                   10                  15
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```
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65                  70                  75                  80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
            100                 105                 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145                 150                 155                 160
```

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 27
<211> 2268
<212> DNA
<213> Homo sapiens

<400> 27
aatatcttgc atgttacaga tttcactgct cccaccagct tggagacaac atgtggttct 60

tgacaactct gctcctttgg gttccagttg atgggcaagt ggacaccaca aaggcagtga 120

tcactttgca gcctccatgg gtcagcgtgt tccaagagga aaccgtaacc ttgcactgtg 180

aggtgctcca tctgcctggg agcagctcta cacagtggtt tctcaatggc acagccactc 240

agacctcgac ccccagctac agaatcacct ctgccagtgt caatgacagt ggtgaataca 300

ggtgccagag aggtctctca gggcgaagtg accccataca gctggaaatc cacagaggct 360

ggctactact gcaggtctcc agcagagtct tcacggaagg agaacctctg gccttgaggt 420

gtcatgcgtg gaaggataag ctggtgtaca atgtgcttta ctatcgaaat ggcaaagcct 480

ttaagttttt ccactggaat tctaacctca ccattctgaa aaccaacata agtcacaatg 540

gcacctacca ttgctcaggc atgggaaagc atcgctacac atcagcagga atatctgtca 600

ctgtgaaaga gctatttcca gctccagtgc tgaatgcatc tgtgacatcc ccactcctgg 660

aggggaatct ggtcaccctg agctgtgaaa caaagttgct cttgcagagg cctggtttgc 720

agctttactt ctccttctac atgggcagca agaccctgcg aggcaggaac acatcctctg 780

aataccaaat actaactgct agaagagaag actctgggtt atactggtgc gaggctgcca 840

cagaggatgg aaatgtcctt aagcgcagcc ctgagttgga gcttcaagtg cttggcctcc 900

agttaccaac tcctgtctgg tttcatgtcc ttttctatct ggcagtggga ataatgtttt 960

tagtgaacac tgttctctgg gtgacaatac gtaaagaact gaaaagaaag aaaaagtggg 1020

atttagaaat ctctttggat tctggtcatg agaagaaggt aatttccagc cttcaagaag 1080

acagacattt agaagaagag ctgaaatgtc aggaacaaaa agaagaacag ctgcaggaag 1140

gggtgcaccg gaaggagccc caggggggca cgtagcagcg gctcagtggg tggccatcga 1200

tctggaccgt cccctgccca cttgctcccc gtgagcactg cgtacaaaca tccaaaagtt 1260

caacaacacc agaactgtgt gtctcatggt atgtaactct taaagcaaat aaatgaactg 1320

acttcaactg ggatacattt ggaaatgtgg tcatcaaaga tgacttgaaa tgaggcctac 1380

tctaaagaat tcttgaaaaa cttacaagtc aagcctagcc tgataatcct attacatagt 1440

ttgaaaaata gtattttatt tctcagaaca aggtaaaaag gtgagtgggt gcatatgtac 1500

agaagattaa gacagagaaa cagacagaaa gagacacaca cacagccagg agtgggtaga 1560

tttcagggag acaagaggga atagtataga caataaggaa ggaaatagta cttacaaatg 1620

actcctaagg gactgtgaga ctgagagggc tcacgcctct gtgttcagga tacttagttc 1680

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gcctccagag atttgcttta ccttcctgat tttctggtta ctaattagct tcaggatacg 2040

ctgctctcat acttgggctg tagtttggag acaaaatatt ttcctgccac tgtgtaacat 2100

agctgaggta aaaactgaac tatgtaaatg actctactaa aagtttaggg aaaaaaaaca 2160

ggaggagtat gacacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2220

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa 2268

<210> 28
<211> 374
<212> PRT
<213> Homo sapiens

<400> 28

Met Trp Phe Leu Thr Thr Leu Leu Leu Trp Val Pro Val Asp Gly Gln
1 5 10 15

Val Asp Thr Thr Lys Ala Val Ile Thr Leu Gln Pro Pro Trp Val Ser
20 25 30

Val Phe Gln Glu Glu Thr Val Thr Leu His Cys Glu Val Leu His Leu

35 40 45

Pro Gly Ser Ser Ser Thr Gln Trp Phe Leu Asn Gly Thr Ala Thr Gln
50 55 60

Thr Ser Thr Pro Ser Tyr Arg Ile Thr Ser Ala Ser Val Asn Asp Ser
65 70 75 80

Gly Glu Tyr Arg Cys Gln Arg Gly Leu Ser Gly Arg Ser Asp Pro Ile
85 90 95

Gln Leu Glu Ile His Arg Gly Trp Leu Leu Leu Gln Val Ser Ser Arg
100 105 110

Val Phe Thr Glu Gly Glu Pro Leu Ala Leu Arg Cys His Ala Trp Lys
115 120 125

Asp Lys Leu Val Tyr Asn Val Leu Tyr Tyr Arg Asn Gly Lys Ala Phe
130 135 140

Lys Phe Phe His Trp Asn Ser Asn Leu Thr Ile Leu Lys Thr Asn Ile
145 150 155 160

Ser His Asn Gly Thr Tyr His Cys Ser Gly Met Gly Lys His Arg Tyr
165 170 175

Thr Ser Ala Gly Ile Ser Val Thr Val Lys Glu Leu Phe Pro Ala Pro

180 185 190

Val Leu Asn Ala Ser Val Thr Ser Pro Leu Leu Glu Gly Asn Leu Val
195 200 205

Thr Leu Ser Cys Glu Thr Lys Leu Leu Leu Gln Arg Pro Gly Leu Gln
210 215 220

Leu Tyr Phe Ser Phe Tyr Met Gly Ser Lys Thr Leu Arg Gly Arg Asn
225 230 235 240

Thr Ser Ser Glu Tyr Gln Ile Leu Thr Ala Arg Arg Glu Asp Ser Gly
245 250 255

Leu Tyr Trp Cys Glu Ala Ala Thr Glu Asp Gly Asn Val Leu Lys Arg
260 265 270

Ser Pro Glu Leu Glu Leu Gln Val Leu Gly Leu Gln Leu Pro Thr Pro
275 280 285

Val Trp Phe His Val Leu Phe Tyr Leu Ala Val Gly Ile Met Phe Leu
290 295 300

Val Asn Thr Val Leu Trp Val Thr Ile Arg Lys Glu Leu Lys Arg Lys
305 310 315 320

Lys Lys Trp Asp Leu Glu Ile Ser Leu Asp Ser Gly His Glu Lys Lys

325 330 335

Val Ile Ser Ser Leu Gln Glu Asp Arg His Leu Glu Glu Glu Leu Lys
340 345 350

Cys Gln Glu Gln Lys Glu Glu Gln Leu Gln Glu Gly Val His Arg Lys
355 360 365

Glu Pro Gln Gly Ala Thr
370

<210> 29
<211> 1396
<212> DNA
<213> Homo sapiens

<400> 29
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caaccattga cagttttgct gctgctggct tctgcagaca gtcaagctgc tcccccaaag 120

gctgtgctga aacttgagcc cccgtggatc aacgtgctcc aggaggactc tgtgactctg 180

acatgccagg gggctcgcag ccctgagagc gactccattc agtggttcca caatgggaat 240

ctcattccca cccacacgca gcccagctac aggttcaagg ccaacaacaa tgacagcggg 300

gagtacacgt gccagactgg ccagaccagc ctcagcgacc ctgtgcatct gactgtgctt 360

tccgaatggc tggtgctcca gacccctcac ctggagttcc aggagggaga aaccatcatg 420

ctgaggtgcc acagctggaa ggacaagcct ctggtcaagg tcacattctt ccagaatgga 480

aaatcccaga aattctccca tttggatccc accttctcca tcccacaagc aaaccacagt 540

cacagtggtg attaccactg cacaggaaac ataggctaca cgctgttctc atccaagcct 600

gtgaccatca ctgtccaagt gcccagcatg ggcagctctt caccaatggg ggtcattgtg 660

gctgtggtca ttgcgactgc tgtagcagcc attgttgctg ctgtagtggc cttgatctac 720

tgcaggaaaa agcggatttc agccaattcc actgatcctg tgaaggctgc ccaatttgag 780

ccacctggac gtcaaatgat tgccatcaga aagagacaac ttgaagaaac caacaatgac 840

tatgaaacag ctgacggcgg ctacatgact ctgaacccca gggcacctac tgacgatgat 900

aaaaacatct acctgactct tcctcccaac gaccatgtca acagtaataa ctaaagagta 960

acgttatgcc atgtggtcat actctcagct tgctgagtgg atgacaaaaa gaggggaatt 1020

gttaaaggaa aatttaaatg gagactggaa aaatcctgag caaacaaaac cacctggccc 1080

ttagaaatag ctttaacttt gcttaaacta caaacacaag caaaacttca cggggtcata 1140

ctacatacaa gcataagcaa aacttaactt ggatcatttc tggtaaatgc ttatgttaga 1200

aataagacaa ccccagccaa tcacaagcag cctactaaca tataattagg tgactaggga 1260

ctttctaaga agatacctac ccccaaaaaa caattatgta attgaaaacc aaccgattgc 1320

ctttattttg cttccacatt ttcccaataa atacttgcct gtgactaaaa aaaaaaaaaa 1380

aaaaaaaaaa aaaaaa 1396

<210> 30
<211> 316

<212> PRT
<213> Homo sapiens

<400> 30

Met Thr Met Glu Thr Gln Met Ser Gln Asn Val Cys Pro Arg Asn Leu
1 5 10 15

Trp Leu Leu Gln Pro Leu Thr Val Leu Leu Leu Leu Ala Ser Ala Asp
20 25 30

Ser Gln Ala Ala Pro Pro Lys Ala Val Leu Lys Leu Glu Pro Pro Trp
35 40 45

Ile Asn Val Leu Gln Glu Asp Ser Val Thr Leu Thr Cys Gln Gly Ala
50 55 60

Arg Ser Pro Glu Ser Asp Ser Ile Gln Trp Phe His Asn Gly Asn Leu
65 70 75 80

Ile Pro Thr His Thr Gln Pro Ser Tyr Arg Phe Lys Ala Asn Asn Asn
85 90 95

Asp Ser Gly Glu Tyr Thr Cys Gln Thr Gly Gln Thr Ser Leu Ser Asp
100 105 110

Pro Val His Leu Thr Val Leu Ser Glu Trp Leu Val Leu Gln Thr Pro
115 120 125

```
His Leu Glu Phe Gln Glu Gly Glu Thr Ile Met Leu Arg Cys His Ser
    130                 135                 140

Trp Lys Asp Lys Pro Leu Val Lys Val Thr Phe Phe Gln Asn Gly Lys
145                 150                 155                 160

Ser Gln Lys Phe Ser His Leu Asp Pro Thr Phe Ser Ile Pro Gln Ala
                165                 170                 175

Asn His Ser His Ser Gly Asp Tyr His Cys Thr Gly Asn Ile Gly Tyr
            180                 185                 190

Thr Leu Phe Ser Ser Lys Pro Val Thr Ile Thr Val Gln Val Pro Ser
        195                 200                 205

Met Gly Ser Ser Ser Pro Met Gly Val Ile Val Ala Val Val Ile Ala
    210                 215                 220

Thr Ala Val Ala Ala Ile Val Ala Ala Val Val Ala Leu Ile Tyr Cys
225                 230                 235                 240

Arg Lys Lys Arg Ile Ser Ala Asn Ser Thr Asp Pro Val Lys Ala Ala
                245                 250                 255

Gln Phe Glu Pro Pro Gly Arg Gln Met Ile Ala Ile Arg Lys Arg Gln
            260                 265                 270
```

Leu Glu Glu Thr Asn Asn Asp Tyr Glu Thr Ala Asp Gly Gly Tyr Met
275 280 285

Thr Leu Asn Pro Arg Ala Pro Thr Asp Asp Asp Lys Asn Ile Tyr Leu
290 295 300

Thr Leu Pro Pro Asn Asp His Val Asn Ser Asn Asn
305 310 315

<210> 31
<211> 1497
<212> DNA
<213> Homo sapiens

<400> 31
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ttacctgtcc ttgccactga gagtgactgg gctgactgca agtcccccca gccttggggt 120

catatgcttc tgtggacagc tgtgctattc ctggctcctg ttgctgggac acctgcagct 180

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aatgggaatc tcattcccac ccacacgcag cccagctaca ggttcaaggc caacaacaat 360

gacagcgggg agtacacgtg ccagactggc cagaccagcc tcagcgaccc tgtgcatctg 420

actgtgcttt ctgagtggct ggtgctccag acccctcacc tggagttcca ggagggagaa 480

accatcgtgc tgaggtgcca cagctggaag gacaagcctc tggtcaaggt cacattcttc 540

cagaatggaa aatccaagaa attttcccgt tcggatccca acttctccat cccacaagca 600

aaccacagtc acagtggtga ttaccactgc acaggaaaca taggctacac gctgtactca 660

tccaagcctg tgaccatcac tgtccaagct cccagctctt caccgatggg gatcattgtg 720

gctgtggtca ctgggattgc tgtagcggcc attgttgctg ctgtagtggc cttgatctac 780

tgcaggaaaa agcggatttc agccaatccc actaatcctg atgaggctga caaagttggg 840

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gaccagaacc gtatttagtc tccattgtct tgcattggga tttgagaaga aaatcagaga 960

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tattaacaga taatagcaac ttgggaaatg cttatgttac aggttacgtg agaacaatca 1260

tgtaaatcta tatgatttca gaaatgttaa aatagactaa cctctaccag cacattaaaa 1320

gtgattgttt ctgggtgata aaattattga tgatttttat tttctttatt tttctataaa 1380

gatcatatat tacttttata ataaaacatt ataaaaacaa aaaaaaaaaa aaaaaaaaaa 1440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 1497

<210> 32
<211> 291

<212> PRT
<213> Homo sapiens

<400> 32

Met Gly Ile Leu Ser Phe Leu Pro Val Leu Ala Thr Glu Ser Asp Trp
1 5 10 15

Ala Asp Cys Lys Ser Pro Gln Pro Trp Gly His Met Leu Leu Trp Thr
20 25 30

Ala Val Leu Phe Leu Ala Pro Val Ala Gly Thr Pro Ala Ala Pro Pro
35 40 45

Lys Ala Val Leu Lys Leu Glu Pro Gln Trp Ile Asn Val Leu Gln Glu
50 55 60

Asp Ser Val Thr Leu Thr Cys Arg Gly Thr His Ser Pro Glu Ser Asp
65 70 75 80

Ser Ile Gln Trp Phe His Asn Gly Asn Leu Ile Pro Thr His Thr Gln
85 90 95

Pro Ser Tyr Arg Phe Lys Ala Asn Asn Asn Asp Ser Gly Glu Tyr Thr
100 105 110

Cys Gln Thr Gly Gln Thr Ser Leu Ser Asp Pro Val His Leu Thr Val
115 120 125

Leu Ser Glu Trp Leu Val Leu Gln Thr Pro His Leu Glu Phe Gln Glu
130 135 140

Gly Glu Thr Ile Val Leu Arg Cys His Ser Trp Lys Asp Lys Pro Leu
145 150 155 160

Val Lys Val Thr Phe Phe Gln Asn Gly Lys Ser Lys Lys Phe Ser Arg
165 170 175

Ser Asp Pro Asn Phe Ser Ile Pro Gln Ala Asn His Ser His Ser Gly
180 185 190

Asp Tyr His Cys Thr Gly Asn Ile Gly Tyr Thr Leu Tyr Ser Ser Lys
195 200 205

Pro Val Thr Ile Thr Val Gln Ala Pro Ser Ser Ser Pro Met Gly Ile
210 215 220

Ile Val Ala Val Val Thr Gly Ile Ala Val Ala Ala Ile Val Ala Ala
225 230 235 240

Val Val Ala Leu Ile Tyr Cys Arg Lys Lys Arg Ile Ser Ala Asn Pro
245 250 255

Thr Asn Pro Asp Glu Ala Asp Lys Val Gly Ala Glu Asn Thr Ile Thr
260 265 270

Tyr Ser Leu Leu Met His Pro Asp Ala Leu Glu Glu Pro Asp Asp Gln
275 280 285

Asn Arg Ile
290

<210> 33
<211> 2137
<212> DNA
<213> Homo sapiens

<400> 33
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tagtttcagc tggcatgcgg actgaagatc tcccaaaggc tgtggtgttc ctggagcctc 120

aatggtacag ggtgctcgag aaggacagtg tgactctgaa gtgccaggga gcctactccc 180

ctgaggacaa ttccacacag tggtttcaca atgagagcct catctcaagc caggcctcga 240

gctacttcat tgacgctgcc acagttgacg acagtggaga gtacaggtgc cagacaaacc 300

tctccaccct cagtgacccg gtgcagctag aagtccatat cggctggctg ttgctccagg 360

cccctcggtg ggtgttcaag gaggaagacc ctattcacct gaggtgtcac agctggaaga 420

acactgctct gcataaggtc acatatttac agaatggcaa aggcaggaag tattttcatc 480

ataattctga cttctacatt ccaaaagcca cactcaaaga cagcggctcc tacttctgca 540

gggggcttgt tgggagtaaa aatgtgtctt cagagactgt gaacatcacc atcactcaag 600

gtttgtcagt gtcaaccatc tcatcattct ttccacctgg gtaccaagtc tctttctgct 660

tggtgatggt actccttttt gcagtggaca caggactata tttctctgtg aagacaaaca 720

ttcgaagctc aacaagagac tggaaggacc ataaatttaa atggagaaag gaccctcaag 780

acaaatgacc cccatcccat gggggtaata agagcagtag cagcagcatc tctgaacatt 840

tctctggatt tgcaacccca tcatcctcag gcctctctac aagcagcagg aaacatagaa 900

ctcagagcca gatcccttat ccaactctcg acttttcctt ggtctccagt ggaagggaaa 960

agcccatgat cttcaagcag ggaagcccca gtgagtagct gcattcctag aaattgaagt 1020

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caggctaggg atggtaatcc tttaaacata caaaaattgc tcgtgttata aattacccag 1140

tttagagggg aaaaaaaaac aattattcct aaataaatgg ataagtagaa ttaatggttg 1200

aggcaggacc atacagagtg tgggaactgc tggggatcta gggaattcag tgggaccaat 1260

gaaagcatgg ctgagaaata gcaggtagtc caggatagtc taagggaggt gttcccatct 1320

gagcccagag ataagggtgt cttcctagaa cattagccgt agtggaatta acaggaaatc 1380

atgagggtga cgtagaattg agtcttccag gggactctat cagaactgga ccatctccaa 1440

gtatataacg atgagtcctc ttaatgctag gagtagaaaa tggtcctagg aaggggactg 1500

aggattgcgg tgggggggtgg ggtggaaaag aaagtacaga acaaaccctg tgtcactgtc 1560

ccaagttgct aagtgaacag aactatctca gcatcagaat gagaaagcct gagaagaaag 1620

aaccaaccac aagcacacag gaaggaaagc gcaggaggtg aaaatgcttt cttggccagg 1680

gtagtaagaa ttagaggtta atgcagggac tgtaaaacca ccttttctgc ttcaatatct 1740

aattcctgtg tagctttgtt cattgcattt attaaacaaa tgttgtataa ccaatactaa 1800

atgtactact gagcttcgct gagttaagtt atgaaacttt caaatccttc atcatgtcag 1860

ttccaatgag gtggggatgg agaagacaat tgttgcttat gaaagaaagc tttagctgtc 1920

tctgttttgt aagctttaag cgcaacattt cttggttcca ataaagcatt ttacaagatc 1980

ttgcatgcta ctcttagata gaagatggga aaaccatggt aataaaatat gaatgataaa 2040

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 2137

<210> 34
<211> 254
<212> PRT
<213> Homo sapiens

<400> 34

Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu

50 55 60

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

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145 150 155 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
165 170 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
180 185 190

Gly Leu Ser Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln

195 200 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
210 215 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225 230 235 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
245 250

<210> 35
<211> 820
<212> DNA
<213> Homo sapiens

<400> 35
cactccagtg tggcatcatg tggcagctgc tcctcccaac tgctctgcta cttctagttt 60

cagctggcat gcggactgaa gatctcccaa aggctgtggt gttcctggag cctcaatggt 120

acagcgtgct tgagaaggac agtgtgactc tgaagtgcca gggagcctac tcccctgagg 180

acaattccac acagtggttt cacaatgaga gcctcatctc aagccaggcc tcgagctact 240

tcattgacgc tgccacagtc aacgacagtg gagagtacag gtgccagaca aacctctcca 300

ccctcagtga cccggtgcag ctagaagtcc atatcggctg gctgttgctc caggcccctc 360

ggtgggtgtt caaggaggaa gaccctattc acctgaggtg tcacagctgg aagaacactg 420

ctctgcataa ggtcacatat ttacagaatg gcaaagacag gaagtatttt catcataatt 480

ctgacttcca cattccaaaa gccacactca aagatagcgg ctcctacttc tgcaggggggc 540

ttgttgggag taaaaatgtg tcttcagaga ctgtgaacat caccatcact caaggtttgg 600

cagtgtcaac catctcatca ttctctccac ctgggtacca agtctctttc tgcttggtga 660

tggtactcct ttttgcagtg gacacaggac tatatttctc tgtgaagaca aacatttgaa 720

gctcaacaag agactggaag gaccataaac ttaaatggag aaaggaccct caagacaaat 780

gacccccatc ccatgggagt aataagagca gtggcagcag 820

<210> 36
<211> 233
<212> PRT
<213> Homo sapiens

<400> 36

Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Ser Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

```
Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asn Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205
```

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
210 215 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225 230

<210> 37
<211> 330
<212> PRT
<213> Homo sapiens

<400> 37

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

```
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
```

<210> 38
<211> 326
<212> PRT
<213> Homo sapiens

<400> 38

```
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
```

1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
100 105 110

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
130 135 140

Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly

145 150 155 160

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
165 170 175

Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp
180 185 190

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
195 200 205

Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu
210 215 220

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
225 230 235 240

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
245 250 255

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
260 265 270

Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
275 280 285

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys

290 295 300

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
305 310 315 320

Ser Leu Ser Pro Gly Lys
325

<210> 39
<211> 327
<212> PRT
<213> Homo sapiens

<400> 39

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

```
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
            100                 105                 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145                 150                 155                 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220
```

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 40
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 40

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Pro Lys Thr Gly Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 41
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 41

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Asn
85 90 95

Thr His Val Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 42
<211> 122
<212> PRT
<213> Rattus norvegicus

<400> 42

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

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

Trp Met His Trp Val Arg Gln Ser Pro Glu Lys Gln Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Asn
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Glu Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 43
<211> 112
<212> PRT
<213> Rattus norvegicus

<400> 43

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

Gly Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Asn
20 25 30

Asn Gly Asn Thr Tyr Val Ser Trp Tyr Ile Gln Lys Pro Ser Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Ile Ser
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Pro Asp Asp Leu Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Asp Pro Tyr Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 44
<211> 328
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 44

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

```
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Cys Glu
225                 230                 235                 240
```

Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro
325

<210> 45
<211> 338
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 45

```
Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
1               5                  10                  15

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
            20                  25                  30

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
        35                  40                  45

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
    50                  55                  60

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
65                  70                  75                  80

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
                85                  90                  95

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
            100                 105                 110

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
        115                 120                 125

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    130                 135                 140
```

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
145 150 155 160

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
165 170 175

Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr
180 185 190

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
195 200 205

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
210 215 220

Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg
225 230 235 240

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
245 250 255

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
260 265 270

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
275 280 285

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
290 295 300

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
305 310 315 320

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro His His His His His His
325 330 335

His His

<210> 46
<211> 336
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 46

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

```
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190
```

```
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Cys Glu
225                 230                 235                 240

Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
                325                 330                 335
```

<210> 47
<211> 450
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 47

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Asn
85 90 95

Thr His Val Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

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

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
130 135 140

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
145 150 155 160

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

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

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

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
210 215 220

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
225 230 235 240

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

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

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

Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr
290 295 300

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

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

Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg
340 345 350

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
355 360 365

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
370 375 380

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

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
405 410 415

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
420 425 430

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

His His
450

<210> 48
<211> 222
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 48

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

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

```
Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Pro Lys Thr Gly Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
        115                 120                 125

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
    130                 135                 140

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
145                 150                 155                 160

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
                165                 170                 175
```

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
180 185 190

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
195 200 205

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 49
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 49

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

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

Trp Met His Trp Val Arg Gln Ser Pro Glu Lys Gln Leu Glu Trp Val
35 40 45

```
Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Asn
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Glu Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

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

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
```

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

```
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

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

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

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
    450                 455
```

<210> 50
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 50

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

Gly Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Asn
20 25 30

Asn Gly Asn Thr Tyr Val Ser Trp Tyr Ile Gln Lys Pro Ser Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Ile Ser
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Pro Asp Asp Leu Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Asp Pro Tyr Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

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

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 51
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 51

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Ala Arg Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 52
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 52

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 53
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 53

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 54
<211> 448
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 54

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Pro Lys Thr Gly Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

```
Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

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

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
    130                 135                 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145                 150                 155                 160

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

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

Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
    210                 215                 220

Pro Ala Pro Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro
225                 230                 235                 240
```

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

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
260 265 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
275 280 285

Glu Gln Phe Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
290 295 300

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

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
325 330 335

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

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
355 360 365

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
370 375 380

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
385 390 395 400

Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
405 410 415

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr
420 425 430

Gln Lys Ser Leu Ser Leu Ser Leu His His His His His His His His
435 440 445

<210> 55
<211> 455
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 55

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
195 200 205

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

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Arg Leu Thr Val Asp Lys
405 410 415

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

Ala Leu His Asn His Tyr Thr Gln Glu Ser Leu Ser Leu Ser Leu Asp
435 440 445

Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 56
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 56

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

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

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 57
<211> 336
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 57

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Cys Glu
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
325 330 335

<210> 58
<211> 338
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 58

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
1 5 10 15

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
20 25 30

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
35 40 45

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
50 55 60

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
65 70 75 80

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
85 90 95

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
100 105 110

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
115 120 125

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
130 135 140

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
145 150 155 160

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
165 170 175

Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr
180 185 190

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
195 200 205

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
210 215 220

Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg
225 230 235 240

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
245 250 255

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
260 265 270

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
275 280 285

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
290 295 300

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
305 310 315 320

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro His His His His His His
325 330 335

His His

<210> 59
<211> 230
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 59

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

```
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                85                  90                  95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
            100                 105                 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
        115                 120                 125

Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
    130                 135                 140

Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser
145                 150                 155                 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
                165                 170                 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
            180                 185                 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
        195                 200                 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys
    210                 215                 220
```

Ser Leu Ser Leu Ser Pro
225 230

<210> 60
<211> 325
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 60

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

```
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
            100                 105                 110

Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145                 150                 155                 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175

Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Lys Glu Met Thr Lys
225                 230                 235                 240
```

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Pro
325

<210> 61
<211> 325
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 61

```
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1               5                  10                  15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
            100                 105                 110

Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140
```

```
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145                 150                 155                 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175

Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225                 230                 235                 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                245                 250                 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            260                 265                 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        275                 280                 285
```

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Glu Ser
305 310 315 320

Leu Ser Leu Ser Pro
325

<210> 62
<211> 325
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 62

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110

Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Lys Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Pro
325

<210> 63
<211> 107

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 63

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 64
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 64

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 65
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 65

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Gln Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 66
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 66

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Gln Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 67
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 67

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Gln Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 68
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 68

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 69
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 69

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

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

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

Ala Gln Ile Lys Ala Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 70
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 70

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

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

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

Ala Gln Ile Lys Ser Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 71
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 71

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 72
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 72

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Pro
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 73
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 73

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 74
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 74

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 75
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 75

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 76
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 76

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 77
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 77

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Pro
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 78
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 78

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 79
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 79

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Tyr Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 80
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 80

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 81
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 81

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 82
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 82

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 83
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 83

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Pro
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 84
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 84

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 85
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 85

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Pro
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 86
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 86

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 87
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 87

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 88
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 88

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

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

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

Ala Gln Ile Lys Ser Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 89
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 89

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

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

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

Ala Gln Ile Lys Ser Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

```
Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 90
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 90

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

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

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

Ala Gln Ile Lys Ser Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60
```

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 91
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 91

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

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

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

Ala Gln Ile Lys Ser Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 92
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 92

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 93
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 93

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 94
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 94

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110
```

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 95
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 95

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

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

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

Ala Gln Ile Lys Ser Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 96
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 96

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

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

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

Ala Gln Ile Lys Ser Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 97
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 97

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 98
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 98

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

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

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

Ala Gln Ile Lys Gly Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 99
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 99

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 100
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 100

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

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

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

Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110
```

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 101
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 101

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 102
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 102

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 103
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 103

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 104
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 104

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 105
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 105

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 106
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 106

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

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

<220>
<223> An artificially generated sequence

<400> 107

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 108
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 108

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 109
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 109

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 110
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 110

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 111
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 111

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 112
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 112

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 113
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 113

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 114
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 114

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 115
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 115

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 116
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 116

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 117
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 117

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 118
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 118

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 119
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 119

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 120
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 120

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 121
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 121

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

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

<220>
<223> An artificially generated sequence

<400> 122

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 123
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 123

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 124
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 124

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 125
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 125

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 126
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 126

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 127
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 127

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 128
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 128

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 129
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 129

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 130
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 130

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 131
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 131

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 132
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 132

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 133
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 133

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 134
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 134

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 135
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 135

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 136
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 136

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 137
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 137

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 138
<211> 124
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 138

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ala Glu Met Val Arg Asp Asp
100 105 110

Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 139
<211> 128
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 139

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ala Glu Met Val Arg Asp Ser
100 105 110

Tyr Gly Val Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 140
<211> 128
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 140

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Val Arg Arg Arg Leu Ser Ser
100 105 110

Tyr Gly Val Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 141
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 141

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 142
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 142

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 143
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 143

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

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

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

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 144
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 144

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 145
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 145

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 146
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 146

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 147
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 147

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Ala Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 148
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 148

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Gln Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 149
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 149

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Ser Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 150
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 150

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Phe Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 151
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 151

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Gly Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 152
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 152

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Leu Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 153
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 153

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Pro Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 154
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 154

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Gln Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 155
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 155

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Ser Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 156
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 156

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Val Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 157
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 157

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Phe Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 158
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 158

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Gly Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 159
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 159

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Ile Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 160
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 160

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Leu Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 161
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 161

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Pro Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 162
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 162

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Gln Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 163
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 163

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Thr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 164
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 164

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Val Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 165
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 165

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 166
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 166

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 167
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 167

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Gln Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 168
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 168

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Val Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 169
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 169

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

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

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

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Ser Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 170
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 170

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Asp Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 171
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 171

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Glu Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 172
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 172

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110
```

Val Ser Ser
115

<210> 173
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 173

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Asp Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 174
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 174

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 175
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 175

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Asp Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 176
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 176

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Glu Glu Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 177
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 177

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 178
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 178

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 179
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 179

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Glu Glu Ser Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 180
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 180

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
50 55 60

Gln Asp Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 181
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 181

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 182
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 182

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 183
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 183

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 184
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 184

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110
```

Val Ser Ser
115

<210> 185
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 185

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Glu Ser Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 186
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 186

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 187
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 187

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 188
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 188

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 189
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 189

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Glu Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 190
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 190

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Glu Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 191
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 191

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 192
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 192

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 193
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 193

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 194
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 194

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 195
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 195

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115
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<210> 196
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 196

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Glu Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 197
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 197

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 198
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 198

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Asp Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 199
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 199

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Glu Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 200
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 200

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Glu Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 201
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 201

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Glu Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 202
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 202

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Glu Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 203
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 203

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

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

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

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 204
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 204

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 205
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 205

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 206
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 206

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Pro Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 207
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 207

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Trp Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 208
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 208

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Tyr Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 209
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 209

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 210
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 210

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Pro Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Glu Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 211
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 211

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

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

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

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 212
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 212

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

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

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

Gly Ala Ile Asp Gly Pro Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 213
<211> 115
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 213

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

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

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

Gly Ala Ile Asp Gly Trp Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115
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<210> 214
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 214

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

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

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

Gly Ala Ile Asp Gly Tyr Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 215
<211> 115
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 215

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 216
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 216

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 Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
65 70 75 80

Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 217
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 217

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

Glu Pro Ala Ser Ile Ser Cys Arg Ala Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 218
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 218

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

Glu Pro Ala Ser Ile Ser Cys Arg Ile Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 219
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 219

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 220
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 220

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

Glu Pro Ala Ser Ile Ser Cys Arg Thr Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 221
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 221

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

Glu Pro Ala Ser Ile Ser Cys Arg Val Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 222
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 222

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Pro Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 223
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 223

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 224
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 224

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Phe Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 225
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 225

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 226
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 226

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Met Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 227
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 227

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 228
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 228

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Val Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 229
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 229

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Arg Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 230
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 230

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Phe
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 231
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 231

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His His
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 232
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 232

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Leu
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 233
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 233

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Met
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 234
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 234

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Asn
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 235
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 235

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Pro
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 236
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 236

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Gln
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 237
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 237

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Val
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 238
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 238

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Trp
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 239
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 239

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asp Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 240
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 240

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Glu Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 241
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 241

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Arg Phe Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 242
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 242

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Gly Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 243
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 243

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg His Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 244
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 244

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Met Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 245
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 245

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Trp Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 246
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 246

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 247
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 247

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 248
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 248

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu Glu Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 249
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 249

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 250
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 250

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu Met Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 251
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 251

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 252
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 252

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 253
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 253

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Phe Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 254
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 254

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser His Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 255
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 255

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Ile Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 256
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 256

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Met Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 257
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 257

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Thr Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 258
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 258

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Trp Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 259
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 259

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 260
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 260

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Gly Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 261
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 261

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 262
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 262

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Lys Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 263
<211> 112

<212> PRT
<213> Artificial

<220>
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<400> 263

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Leu Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 264
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<212> PRT
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<220>
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<400> 264

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Met Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 265
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<212> PRT
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<220>
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<400> 265

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Asn Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 266
<211> 112
<212> PRT
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<220>
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<400> 266

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Pro Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 267
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 267

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Arg Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 268
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 268

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Val Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 269
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 269

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Tyr Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 270
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 270

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Phe Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 271
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 271

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Gly Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 272
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 272

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe His Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 273
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 273

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ile Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 274
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 274

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Leu Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 275
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 275

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Met Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 276
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 276

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Pro Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 277
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 277

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Gln Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 278
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 278

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 279
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 279

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Val Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 280
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 280

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Trp Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 281
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 281

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 282
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 282

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Glu Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 283
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 283

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 284
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 284

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ile Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 285
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 285

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 286
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 286

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Asn Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 287
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 287

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 288
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 288

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Val Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 289
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 289

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 290
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 290

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Ser
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 291
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 291

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Thr
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 292
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 292

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 293
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 293

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln His Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 294
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 294

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Asn Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 295
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 295

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Pro Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 296
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 296

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 297
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 297

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 298
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 298

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 299
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 299

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 300
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 300

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Trp Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 301
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 301

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 302
<211> 112
<212> PRT
<213> Artificial

<220>
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<400> 302

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 303
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 303

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Trp Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 304
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 304

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 305
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 305

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 306
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 306

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Trp Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 307
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 307

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 308
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 308

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Trp Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 309
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 309

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 310
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 310

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 311
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 311

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 312
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 312

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 313
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 313

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 314
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 314

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 315
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 315

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 316
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 316

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 317
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 317

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 318
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 318

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 319
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 319

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 320
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 320

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Leu Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 321
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 321

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Pro Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 322
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 322

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ile Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 323
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 323

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

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Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 324
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 324

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60
```

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Val Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 325
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 325

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Ser
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 326
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 326

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Thr
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 327
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 327

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 328
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 328

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 329
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 329

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Glu Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 330
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 330

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Glu Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 331
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 331

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Glu Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 332
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 332

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Glu Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Trp Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 333
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 333

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Glu Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 334
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 334

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 335
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 335

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 336
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 336

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 337
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 337

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Trp Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 338
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 338

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 339
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 339

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Glu Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 340
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 340

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 341
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 341

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ile Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 342
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 342

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
            20                  25                  30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60
```

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 343
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 343

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 344
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 344

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ile Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 345
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 345

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 346
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 346

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 347
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 347

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 348
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 348

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 349
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 349

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 350
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 350

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 351
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 351

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 352
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 352

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 353
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 353

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Val Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 354
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 354

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

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Val Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 355
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 355

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Val Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 356
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 356

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

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

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 357
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 357

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Gln Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 358
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 358

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
20 25 30

Asn Arg Gln Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 359
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 359

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Leu Val His Ser
20 25 30

Asn Arg Gln Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 360
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 360

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60
```

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 361
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 361

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 362
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 362

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 363
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 363

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 364
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 364

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 365
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 365

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 366
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 366

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 367
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 367

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 368
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 368

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 369
<211> 112
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 369

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 370
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 370

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 371
<211> 112

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 371

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 372
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 372

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu
100 105 110

<210> 373
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 373

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 374
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 374

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 375
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 375

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile Gln Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 376
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 376

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 377
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 377

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 378
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 378

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Ile Gln Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60
```

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 379
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 379

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 380
<211> 112
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 380

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

Glu Pro Ala Ser Ile Ser Cys Gln Ala Ser Glu Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Thr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 381
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 381

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

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

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

Ala Asn Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

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

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

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

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 382
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 382

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Ala Tyr Tyr Gly Val Gln Ala Trp
100 105 110

```
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

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

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
```

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

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

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

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

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 383
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 383

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

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

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

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

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 384
<211> 440
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 384

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

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

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

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

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

Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
210 215 220

Pro Ala Pro Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro
225 230 235 240

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

```
Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
            260                 265                 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        275                 280                 285

Glu Gln Phe Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
    290                 295                 300

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

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                325                 330                 335

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
            340                 345                 350

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
        355                 360                 365

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
    370                 375                 380

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
385                 390                 395                 400
```

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
405 410 415

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
420 425 430

Gln Glu Ser Leu Ser Leu Ser Pro
435 440

<210> 385
<211> 440
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 385

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

```
Gly Ala Ile Asp Gly Pro Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

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

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
    130                 135                 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145                 150                 155                 160

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

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

```
Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
    210                 215                 220

Pro Ala Pro Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro
225                 230                 235                 240

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

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
            260                 265                 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        275                 280                 285

Glu Gln Phe Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
    290                 295                 300

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

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                325                 330                 335
```

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
340 345 350

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
355 360 365

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
370 375 380

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
385 390 395 400

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
405 410 415

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
420 425 430

Gln Glu Ser Leu Ser Leu Ser Pro
435 440

<210> 386
<211> 440
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 386

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

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

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

Gly Ala Ile Asp Gly Glu Thr Pro Asp Thr Ala Tyr Ser Glu Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

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

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
    130                 135                 140
```

```
Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145                 150                 155                 160

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

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

Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
    210                 215                 220

Pro Ala Pro Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro
225                 230                 235                 240

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

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
            260                 265                 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        275                 280                 285
```

```
Glu Gln Phe Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
    290                 295                 300

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

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                325                 330                 335

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
            340                 345                 350

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
        355                 360                 365

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
    370                 375                 380

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
385                 390                 395                 400

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
                405                 410                 415

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
            420                 425                 430
```

Gln Glu Ser Leu Ser Leu Ser Pro
435 440

<210> 387
<211> 440
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 387

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

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

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

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

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
    130                 135                 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145                 150                 155                 160

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

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

Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys
    210                 215                 220
```

```
Pro Ala Pro Glu Phe Arg Gly Gly Pro Lys Val Phe Leu Phe Pro Pro
225                 230                 235                 240

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

Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp
            260                 265                 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        275                 280                 285

Glu Gln Phe Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
    290                 295                 300

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

Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                325                 330                 335

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu
            340                 345                 350

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
        355                 360                 365
```

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
370 375 380

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
385 390 395 400

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn
405 410 415

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
420 425 430

Gln Glu Ser Leu Ser Leu Ser Pro
435 440

<210> 388
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 388

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

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

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

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

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 389
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 389

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

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

Trp Met His Trp Val Arg Gln Ser Pro Glu Lys Gln Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Asn
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Glu Glu Asp Thr Ala Val Tyr
85 90 95

```
Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

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

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225                 230                 235                 240
```

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

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

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

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

```
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
    450                 455
```

<210> 390
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 390

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

Ser Leu Lys Leu Thr Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30
```

```
Trp Met His Trp Val Arg Gln Ser Pro Glu Lys Gln Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Asn
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Glu Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
195 200 205

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

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

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

<210> 391
<211> 458

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 391

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

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

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

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Lys Lys Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Tyr Tyr Gly Val Gln Ala Trp
100 105 110

```
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

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

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

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

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

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

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
```

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr
290 295 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
340 345 350

Val Tyr Thr Leu Pro Pro Ser Arg Cys Glu Leu Thr Lys Asn Gln Val
355 360 365

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
370 375 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
405 410 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 392
<211> 458
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 392

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ala Gln Ile Lys Gly Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
```

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
210 215 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225 230 235 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
275 280 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr
290 295 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305 310 315 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
325 330 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
340 345 350

Val Tyr Thr Leu Pro Pro Ser Arg Cys Glu Leu Thr Lys Asn Gln Val
355 360 365

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
370 375 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
405 410 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Asp Tyr Lys Asp Asp Asp Asp Lys
450 455

<210> 393
<211> 447

<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 393

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ser Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

```
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
    210                 215                 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225                 230                 235                 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 394
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 394

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

```
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
```

```
His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
    210                 215                 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225                 230                 235                 240

Lys 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 Gln Glu Asp
            260                 265                 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 395
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 395

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
```

```
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
    210                 215                 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225                 230                 235                 240

Lys 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 Gln Glu Asp
            260                 265                 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285
```

```
Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
        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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430
```

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 396
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 396

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
115 120 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
130 135 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
210 215 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 397
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 397

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

```
Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Asp Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Ser Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
210 215 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 398
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 398

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
115 120 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
130 135 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
210 215 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

```
Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
        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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 399
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 399

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

```
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
```

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
210 215 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 400
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 400

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Val Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
```

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
195 200 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
210 215 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225 230 235 240

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

<210> 401
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 401

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Val Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65 70 75 80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

```
Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
    210                 215                 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225                 230                 235                 240
```

Lys 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 Gln Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430

Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445
```

<210> 402
<211> 447
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 402

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ala Gln Ile Lys Asp Lys Ser Gln Asn Tyr Ala Thr Tyr Val Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Ala Asp Ser Lys Asn Ser
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Ala Ala Gly Tyr Gly Val Asp Ile Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
```

```
Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
    210                 215                 220

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Arg Gly Gly Pro
225                 230                 235                 240

Lys 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 Gln Glu Asp
            260                 265                 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Ala 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 Gly Leu Pro Ser 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 Gln Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr
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 Glu 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
435 440 445

<210> 403
<211> 450
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 403

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1               5                  10                  15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Asn
                85                  90                  95

Thr His Val Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
        115                 120                 125
```

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
130 135 140

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
145 150 155 160

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
165 170 175

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
180 185 190

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
195 200 205

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
210 215 220

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
225 230 235 240

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
245 250 255

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
260 265 270

```
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
        275                 280                 285

Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr
    290                 295                 300

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305                 310                 315                 320

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
                325                 330                 335

Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg
            340                 345                 350

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
        355                 360                 365

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
    370                 375                 380

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
385                 390                 395                 400

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
                405                 410                 415
```

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
420 425 430

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro His His His His His His
435 440 445

His His
450

<210> 404
<211> 450
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 404

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
115 120 125

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
130 135 140

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
145 150 155 160

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
165 170 175

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
180 185 190

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
195 200 205

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
210 215 220

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
225 230 235 240

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
245 250 255

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
260 265 270

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
275 280 285

Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr
290 295 300

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305 310 315 320

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
325 330 335

Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg
340 345 350

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
355 360 365

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
370 375 380

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
385 390 395 400

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
405 410 415

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
420 425 430

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro His His His His His His
435 440 445

His His
450

<210> 405
<211> 222
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 405

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Pro Lys Thr Gly Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
        115                 120                 125
```

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
130 135 140

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
145 150 155 160

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
165 170 175

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
180 185 190

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
195 200 205

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 406
<211> 222
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 406

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Glu Met His Trp Ile Arg Gln Pro Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Asp Gly Lys Thr Pro Asp Thr Ala Tyr Ser Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Leu Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Thr Arg Phe Tyr Ser Tyr Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
        115                 120                 125

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
    130                 135                 140

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
145                 150                 155                 160
```

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
165 170 175

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
180 185 190

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
195 200 205

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 407
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 407

Asp Val Val Met Thr Gln Thr Pro Val Ser Met Ser Val Ser Leu Gly
1 5 10 15

Gly Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Asn
20 25 30

```
Asn Gly Asn Thr Tyr Val Ser Trp Tyr Ile Gln Lys Pro Ser Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Ile Ser
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Pro Asp Asp Leu Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Asp Pro Tyr Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175
```

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 408
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 408

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205
```

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 409
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 409

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 410
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 410

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Leu Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 411
<211> 219
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 411

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1               5                  10                  15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125
```

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 412
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 412

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 413
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 413

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

```
Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Arg Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gly Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175
```

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 414
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 414

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205
```

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 415
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 415

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Trp Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 416
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 416

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 417
<211> 219
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 417

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1               5                  10                  15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Pro Pro Val His Ser
            20                  25                  30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125
```

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 418
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 418

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Pro Ser Gln Ser Pro Val His Ser
20 25 30

Asn Arg Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
85 90 95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 419
<211> 219
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 419

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Pro Val His Ser
20 25 30

```
Asn Arg Asn Thr Tyr Ile Gln Trp Tyr Gln Gln Lys Pro Gly Gln Ala
        35                  40                  45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Gly
                85                  90                  95

Thr Gln Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175
```

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 420
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 420

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Tyr Tyr Gly Val Gln Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 421
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 421

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Lys Lys Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Tyr Tyr Gly Val Gln Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 422
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 422

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Arg Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 423
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 423

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Arg Val His Tyr Tyr Tyr Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 424
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 424

```
Glu Val Gln Leu Val Glu Thr Gly Gly Ser Leu Val Gln Pro Gly Lys
1               5                  10                  15

Ser Leu Lys Leu Thr Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ser Pro Glu Lys Gln Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Asn
65                  70                  75                  80

Ile Tyr Leu Gln Met Asn Ser Leu Lys Glu Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110
```

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 425
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 425

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Leu Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 426
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 426

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 427
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 427

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Leu Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Gly Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 428
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 428

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Ala Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 429
<211> 122
<212> PRT
<213> Artificial

<220>

<223> An artificially generated sequence

<400> 429

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Tyr Ala Tyr Tyr Gly Val Gln Ala Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 430
<211> 122
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 430

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Glu
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65                  70                  75                  80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Tyr Tyr Gly Val Asp Ala Trp
            100                 105                 110
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Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 431
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<220>
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<400> 431

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Lys Ala Lys Ser Asn Asn Tyr Lys Lys Tyr Tyr Ala Glu
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Arg Tyr Val His Tyr Tyr Tyr Tyr Tyr Gly Val Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 432
<211> 107
<212> PRT
<213> Artificial

<220>
<223> An artificially generated sequence

<400> 432

Ala Ser Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105