Anti-VASA antibodies (mAbs), particularly humanized mAbs that specifically bind to VASA with high affinity, are disclosed. The amino acid sequences of the CDRs of the light chains and the heavy chains, as well as consensus sequences for these CDRs, of these anti-VASA mAbs are provided. The disclosure also provides nucleic acid molecules encoding the anti-VASA mAbs, expression vectors, host cells, methods for making the anti-VASA mAbs, and methods for expressing the anti-VASA mAbs. Finally, methods of using the anti-VASA mAbs to isolate and/or purify cells expressing VASA are disclosed.
Human VASA Amino Acid Sequence

(Accession: NP_077726; SEQ ID NO: 1)

FIG. 1

Mouse VASA Homolog Amino Acid Sequence

(Accession: NP_001139357, SEQ ID NO: 2)

FIG. 2
Human ...nvfasvdtrkgkstlnitagfissqqapnvpvddeswd
(SEQ ID NO: 1 residues 690-724)
Mouse ...avfasvdtrknyggkhtlnitagfissqqapnvpvddeswd
(SEQ ID NO: 2 residues 694-728)

FIG. 3

CTERM HUMAN MOUSE
REGION Overlapping between two tests: PNPVDDDE

FIG. 4A

ELISA analysis of control antibody AB13840

FIG. 4B
**FIG. 5A**

Dose response binding of 1A12

Dose response binding of 1E9

**Best-fit values**

- **BOTTOM**: 0.02413
- **TOP**: 0.4334
- **LOGEC50**: -0.6664
- **HILLSLOPE**: 1.275
- **EC50**: 0.2156

**Goodness of Fit**

- Degrees of Freedom: 6
- **R2**: 0.9669

**FIG. 5B**

ELISA analysis of 1A12

ELISA analysis of 1E9

**Best-fit values**

- **BOTTOM**: 0.1137
- **TOP**: 0.4941
- **LOGEC50**: -1.556
- **HILLSLOPE**: 1.020
- **EC50**: 0.02779

**Goodness of Fit**

- Degrees of Freedom: 14
- **R2**: 0.9282
Dose response binding of 1E9 IgG

Dose response binding of 1E9 scFv-Fc

Best-fit values

<p>| | |</p>
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Best-fit values

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FIG. 6A

ELISA analysis of 1E9

VASA peptide sequence: GKSTLNTAGFSSSQAPNPVDDESWD
VASA-1 peptide sequence: SQAPNPVDDE
VASA-2 peptide sequence: GKSTLNTAGF

FIG. 6B
Specificity analysis

FIG. 7A

Dose response curve of VASA antibodies

FIG. 7B
Dose response binding of VASA antibodies

**FIG. 7C**

Hybridoma subtype determination

**FIG. 8**
FIG. 9A Cont.
### Light Chain Variable Region Sequence Alignments (continued)

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<th>SEQ ID NO.</th>
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<td>MQHLEYP - LGAG TKLIEK- 112</td>
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**FIG. 9B**
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<th>SEQ ID NO.</th>
<th>CLONE NAME</th>
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<th>CDR2</th>
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<td>1K3VH6-7</td>
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<td>40</td>
<td>1K3VH6-8</td>
<td>0816</td>
<td>LVQLIQSGAILRPGASVKLSCASGYTFTSWMQVVRFRQGQGLEWIGAIYFG--NGDT 58</td>
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<tr>
<td>41</td>
<td>1K3VH3-8</td>
<td>0816</td>
<td>LVQLQKSGAILRPGASVKLSCASGYTFTSWMQVVRFRQGQGLEWIGAIYFG--NGDT 58</td>
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<tr>
<td>42</td>
<td>2K4VH3-8</td>
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<td>43</td>
<td>1K3VH3-4</td>
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<td>1K3VH3-3</td>
<td>0816</td>
<td>SVQLQKSGAILRPGASVKLSCASGYTFTSWMQVVRFRQGQGLEWIGAIYFG--NGDT 58</td>
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<td>45</td>
<td>2K4VH2-8</td>
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<td>SVQLKQSGAILRPGASVKLSCASGYTFTSWMQVVRFRQGQGLEWIGAIYFG--NGDT 58</td>
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<td>46</td>
<td>2K4VH1-1</td>
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<td>2K4VH1-4</td>
<td>SVQLKQSGAILRPGASVKLSCASGYTFTSWMQVVRFRQGQGLEWIGAIYFG--NGDT 58</td>
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<tr>
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<td>1C9 VH404-8</td>
<td>1024</td>
<td>QVQLIQSGAILRPGASVKLSCASGYTFTSWMQVVRFRQGQGLEWIGAIYFG--NGET 58</td>
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<td>1C9 VH405-12</td>
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FIG. 10A
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<th>SEQ NO.</th>
<th>CDR3</th>
<th>Heavy Chain Variable Region Sequence Alignments (continued)</th>
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<tbody>
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<td>RYTKFKGKATLADKSSSTAYQMSSLASEDASAVYCAARG---GIAFWAYWGQGTLTVSA 117</td>
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<td>RYTKFKGKATLADKSSSTAYQMSSLASEDASAVYCAARG---GIAFWAYWGQGTLTVSA 117</td>
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<td>41</td>
<td>1K3VH3-3</td>
<td>RYTKFKGKATLADKSSSTAYQMSSLASEDASAVYCAARG---GIAFWAYWGQGTLTVSA 117</td>
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<td>43</td>
<td>1K3VH3-4</td>
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<td>RYTKFKGKATLADKSSSTAYQMSSLASEDASAVYCAARG---GIAFWAYWGQGTLTVSA 117</td>
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<td>45</td>
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<td>46</td>
<td>2K4VH1-1</td>
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**FIG. 10B**
FIG. 10B Cont.
### Unique Light Chain CDR Sequence Alignments

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<td>HNS</td>
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**FIG. 11**

### Unique Heavy Chain CDR Sequence Alignments

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<td>IYPG--NGDT</td>
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<td>GFTFTNYW</td>
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<td>IYPG--NGET</td>
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<td>ASGYP------YFAY</td>
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<td>GYSPTSYW</td>
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<td>IYPG--DEGT</td>
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<td>AKG----D--GNPFAY</td>
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<td>109</td>
<td>GFTPYNMA</td>
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<td>IYPG--DAAT</td>
<td>126</td>
<td>VRS---------GDF</td>
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<td>IRSKTRNYAI</td>
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<td>ISYS---GNT</td>
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<td>ARYNS-LLRLGAMDY</td>
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<td>GFTPNSYG</td>
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<td>IKRD--GSEK</td>
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<td>ARGGN-S----YYG</td>
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<td>AKRED-----G-NDV</td>
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**FIG. 12**
ANTI-VASA ANTIBODIES, AND METHODS OF PRODUCTION AND USE THEREOF

[0001] This application is a continuation of U.S. application Ser. No. 15/203,040, filed Jul. 6, 2016, which is a continuation of U.S. application Ser. No. 14/856,380, filed Sep. 16, 2015 (now U.S. Pat. No. 9,403,913), which claims the benefit of priority of U.S. Provisional Application No. 62/089,054, filed Dec. 8, 2014, and U.S. Provisional Application No. 62/051,130, filed Sep. 16, 2014, the entire contents of which are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

[0002] The present disclosure relates generally to antibodies, their production and use. Specifically, the present disclosure pertains to antibodies which specifically bind to the human VASA protein, methods of producing such antibodies, and diagnostic, therapeutic and clinical methods of using such antibodies.

BACKGROUND

[0003] The VASA protein was identified in Drosophila as a component of the germplasm that encodes a DEAD-family ATP-dependent RNA helicase (Liang et al. (1994), Development, 120:1201-11; Lasko et al. (1988), Nature 335:611-17). The molecular function of VASA is directed to binding target mRNAs involved in germ cell establishment, oogenesis, and translation onset (Gavis et al. (1996), Development 110:521-28). VASA is required for pole cell formation and is exclusively restricted to the germ cell lineage throughout development.

[0004] Vasa homolog genes have been isolated in various animal species, and VASA can be used as a molecular marker for the germ cell lineage in most animal species (Noce et al. (2001), Cell Structure and Function 26:131-36). Castrillon et al. (2000), Proc. Natl. Acad. Sci. (USA) 97(17):958590-9590, for example, demonstrated that the human Vasa gene is expressed in ovary and testis but is undetectable in somatic tissues.

[0005] The existence of mammalian female germline stem cells, also known as oogonal stem cells or ovarian stem cells (OSCs) or egg precursor cells, in the somatic tissue of mammalian ovaries was first described in Johnson et al. (2004), Nature 428:145-50, and has now been confirmed by other research groups (e.g., Zou et al. (2009), Nature Cell Biology, published online DOI: 10.1038/ncb1869; Telfer & Albertini (2012), Nature Medicine 18(3):353-4). The potential use of OSCs to produce oocytes for use in artificial reproduction technologies (ART), including in vitro fertilization (IVF), or as sources of highly functional mitochondria for mitochondrial transfer to oocytes, as well as the use of OSCs to treat various symptoms of menopause, have been described in the scientific and patent literature (e.g., Tilly & Telfer (2009), Mol. Hum. Repro. 15(7):393-8; Zou et al. (2009), supra; Telfer & Albertini (2012), supra; White et al. (2012), Nature Medicine 18(3):413-21; WO 2005/121321; U.S. Pat. No. 7,955,846; U.S. Pat. No. 8,652,840; WO2012/142500; U.S. Pat. No. 8,642,329 and U.S. Pat. No. 8,647,869).

[0006] When OSCs were first characterized by Johnson et al. (2004), supra, it was demonstrated that the cells expressed the VASA protein, and antibodies against the VASA protein have been used to isolate OSCs from ovarian tissue homogenates (e.g., Zou et al. (2009), supra; White et al. (2012), supra). Moreover, White et al. (2012), supra, demonstrated that antibodies to an N-terminal domain of VASA could not be used to isolate viable VASA-expressing OSCs whereas antibodies to a C-terminal domain could effectively isolate the cells, suggesting that the C-terminal domain, but not the N-terminal domain, was extracellular and thus accessible to the antibodies.

[0007] The production of anti-VASA polyclonal antibodies was first described in Castrillon et al. (2000), supra, and WO01/36445. Polyclonal antibodies directed to the C-terminal portion of human VASA protein are commercially available from Abcam plc (Cambridge, UK; Product Code AB13840), and R&D Systems, Inc. (Minneapolis, Minn.; Catalog No. AF2030), and a monoclonal antibody directed against the N-terminal portion of human VASA is also commercially available from R&D Systems, Inc. (Minneapolis, Minn.; Catalog No. AF2030).

[0008] There remains, however, a need for high affinity antibodies directed to the C-terminal extracellular domain of VASA for identifying (e.g., by immunohistochecmistry or labeled antibodies) and isolating (e.g., by magnetic or fluorescence activated cell sorting) cells, including but not limited to OSCs, expressing VASA.

SUMMARY

[0009] Anti-VASA antibodies (mAbs), particularly humanized mAbs that specifically bind to VASA with high affinity, are disclosed. The amino acid sequences of the CDRs of the light chains and the heavy chains, as well as consensus sequences for these CDRs, of these anti-VASA mAbs are provided. The disclosure also provides nucleic acid molecules encoding the anti-VASA mAbs, expression vectors, host cells, methods for making the anti-VASA mAbs, and methods for expressing the anti-VASA mAbs. Finally, methods of using the anti-VASA mAbs to isolate and/or purify cells expressing VASA are disclosed.

[0010] These and other aspects and embodiments of the disclosure are illustrated and described below. Other systems, processes, and features will become apparent to one with skill in the art upon examination of the following drawings and detailed description. It is intended that all such additional systems, processes, and features be included within this description, be within the scope of the present invention, and be protected by the accompanying claims.

BRIEF DESCRIPTION OF THE FIGURES

[0011] FIG. 1 provides the amino acid sequence of the human VASA protein isoform 1 from GenBank Accession from NP_077726 (SEQ ID NO: 1).

[0012] FIG. 2 provides the amino acid sequence of the mouse VASA homolog protein isoform 1 from GenBank Accession from NP_001139357 (SEQ ID NO: 2).

[0013] FIG. 3 provides an amino acid alignment between the C-terminal portion of the human VASA protein (residues 690-724 of SEQ ID NO: 1) and the mouse VASA homolog (residues 691-728 of SEQ ID NO: 2).

[0014] FIG. 4A shows the region of the C-terminal domains of the VASA/DDX4 polypeptide that is reactive with an antibody of the invention and the control antibody (AB13840, Abcam plc, Cambridge, UK) and FIG. 4B shows binding of the control antibody to the VASA protein and the V1 and V2 polypeptides.
FIG. 5A shows dose response binding curves of the affinity for VASA of 1E9 and 1A12; and FIG. 5B shows the results of ELISA assays with the VASA, V1 and V2 peptides that suggest that 1E9 binds the same epitope as the commercially available rabbit polyclonal antibody (AB13840, Abcam plc, Cambridge, UK). NC=negative control; VASA=SEQ ID NO: 1 residues 700-724; VASA-1=V1 or SEQ ID NO: 1 residues 712-721; VASA-2=V2 or SEQ ID NO: 1 residues 700-709.

FIG. 6A shows dose response binding curves of the affinity for VASA of the IgG and scFv-Fc forms of 1E9; and FIG. 6B shows the results of ELISA assays of the binding of the IgG and scFv-Fc forms of 1E9 with the VASA, V1 and V2 peptides. NC=negative control; VASA=SEQ ID NO: 1 residues 700-724; VASA-1=V1 or SEQ ID NO: 1 residues 712-721; VASA-2=V2 or SEQ ID NO: 1 residues 700-709.

FIG. 7A shows the results of binding experiments with three anti-VASA hybridoma antibodies (2M1/IK3, 2M1/IK23 and 2M1/1L5) and two negative controls (2M1/1F5 and 2M1/1H5) which are not VASA-specific; FIG. 7B shows dose response curves of four VASA-specific hybridoma antibodies (2M1/IK3, 2M1/IK23 and 2M1/1L5) compared to 1E9-lambda; and FIG. 7C shows dose response curves of the VASA-specific hybridoma antibody 2M1/2K4 compared to 1E9-lambda.

FIG. 8 shows the result of subtyping analysis for anti-VASA antibodies from eight hybridomas (2M1/1L20, 2M1/1L20, 1M1/1C9, 2M1/1N3, 2M1/1K23, 1M1/1L5 and 2M1/2K4).

FIGS. 9A-9B show alignments of some of the VL sequences of the anti-VASA invention. The figure indicates the approximate locations of the three CDR regions (bold, underscore) and the SEQ ID NO corresponding to each sequence.

FIGS. 10A-10B show alignments of some of the VH sequences of the anti-VASA invention. The figure indicates the approximate locations of the three CDR regions (bold, underscore) and the SEQ ID NO corresponding to each sequence.

FIG. 11 shows alignments of the unique CDR sequences of the VL regions of FIG. 9.

FIG. 12 shows alignments of the unique CDR sequences of the VH regions of FIG. 10.

DETAILED DESCRIPTION

The present disclosure relates to isolated antibodies (Abs), particularly Abs that bind specifically to VASA with high affinity. In certain embodiments, the anti-VASA Abs are derived from particular heavy and light chain sequences and/or comprise particular structural features, such as CDR regions comprising particular amino acid sequences. This disclosure provides isolated anti-VASA Abs, methods of making such anti-VASA Abs, immunonjugates and bispecific molecules comprising such anti-VASA Abs, and methods of expressing such anti-VASA Abs. This disclosure also relates to methods of using the anti-VASA Abs to isolate and/or purify cells expressing VASA, including mammalian female germline stem cells or oogonial stem cells (OSCs) or egg precursor cells and their progenitor cells.

In order that the present disclosure may be more readily understood, certain terms are defined. Additional definitions are set forth throughout the detailed description.

DEFINITIONS

The term “antibody” or abbreviation “Ab,” as used herein, includes whole antibodies and any antigen binding fragment (i.e., “antigen-binding portion”) or single chains thereof, with or without native glycosylation. A complete “antibody” refers to a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds or an antigen binding portion thereof. Each heavy chain includes a heavy chain variable region (VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH₁, CH₂, and CH₃. Each light chain includes a light chain variable region (VL) and a light chain constant region with one domain, CL. The VH and VL regions can be further subdivided into complementarity determining regions (CDR) and framework regions (FR). The VH and VL regions each include three CDRs, designated CDR1, CDR2 and CDR3, that interact with an antigen (e.g., VASA).

The term “antigen-binding portion” of an antibody, as used herein, refers to one or more fragments of an antibody that retain the ability to specifically bind to an antigen (e.g., VASA). Examples of binding fragments encompassed within the term “antigen-binding portion” of an antibody include a Fab fragment, F(ab')₂ fragment, Fab' fragment, Fd fragment, Fv fragment, scFv fragment, dAb fragment, and an isolated CDR.

The term “monoclonal antibody” or “monoclonal antibody preparation,” as used herein, refers to a preparation of antibody molecules consisting essentially of antibodies having a single heavy chain amino acid sequence and a single light chain amino acid sequence (but which may have heterogeneous glycosylation).

The term “humanized antibody,” as used herein, includes antibodies having constant region and variable region framework regions (FRs) but not CDRs derived from human germline immunoglobulin sequences.

The term “recombinant antibody,” as used herein, includes all antibodies prepared, expressed, created, or isolated by recombinant means. In certain embodiments, recombinant antibodies are isolated from a host cell transformed to express the antibody (e.g., from a transfectoma). In other embodiments, recombinant antibodies are isolated from a recombinant, combinatorial antibody library, such as a phage display library. Recombinant antibodies may also be prepared, expressed, created, or isolated by any other means that involve splicing of human immunoglobulin gene sequences to other DNA sequences.

The term “isotype,” as used herein, refers to the heavy chain class (e.g., IgA, IgD, IgE, IgG, and IgM for human antibodies) or light chain class (e.g., kappa or lambda in humans) encoded by the constant region genes. The term
“subtype” refers to subclasses within the subtype (e.g., IgA1, IgA2, IgG1, IgG2, IgG3, IgG4 in humans).

[0031] The phrase “an antibody specific for” a specified antigen is used interchangeably herein with the phrase “an antibody which specifically binds to” a specified antigen. As used herein, the term “Kd,” refers to the association rate and the term “Kd,” to the dissociation rate of a particular antibody-antigen complex. The term “Kd,” refers to the dissociation constant, which is obtained from the ratio of Ka to Kd and expressed as a molar concentration (M). According to some embodiments, an antibody that “specifically binds to human VASA” is intended to refer to an antibody that binds to human VASA with a Kd of 5x10^{-8} M or less, more preferably 5x10^{-8} M or less.

[0032] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Anti-VASA Antibodies

[0033] The invention provides a variety of new antibodies with high affinity against the human VASA protein, particularly the C-terminal region. The antibodies may comprise the complete VH and VL regions disclosed herein, or may comprise only the CDR sequences disclosed herein. In addition, based upon CDR sequences disclosed herein, sequence motifs for CDR sequences are provided, and the antibodies may comprise CDR sequences defined by the motifs.

[0034] The CDR sequences of the invention (including both the CDRs disclosed in FIGS. 11 and 12 and the CDRs defined by the sequence motifs disclosed herein) can be combined with other immunoglobulin sequences according to methods well known in the art to produce immunoglobulin molecules with antigen-binding specificity determined by the CDRs of the invention.

[0035] In some embodiments, the CDRs of the invention are combined with framework region (FR) and constant domain (CH or CL) sequences from other antibodies. For example, although some of the CDRs disclosed herein are derived from murine hybridomas and have murine FR and constant domain sequences, they can be recombined with human or other mammalian FR and constant domain sequences to produce humanized or other recombinant antibodies. The production of such recombinant antibodies is well known to those of skill in the art and requires only routine experimentation.

[0036] The type of constant regions included in such recombinant antibodies can be chosen according to their intended use. For example, if the antibodies are intended for therapeutic use to target VASA-expressing cells for destruction, heavy chain constant domains (i.e., Fe regions) of IgG subtypes can be used. If the antibodies are intended only as reagents for labeling cells (e.g., for fluorescence-activated cell sorting (FACS)), a complete antibody, antigen binding fragment (Fab), single-chain variable fragment (scFv), single domain antibody (sdAb) or even non-antibody immunoglobulin molecule (e.g., an MHC receptor extracellular domain) can be used with the CDRs of the invention.

[0037] The CDRs of the invention can be selected independently such that the CDR1, CDR2 and CDR3 sequences of a given variable light (VL) chain or variable heavy (VH) chain can be chosen from different original VL and VH chains, from different VL and VH CDR motifs, or from a combination of the disclosed CDRs and motifs. However, sequences for light chain CDRs should be selected from the disclosed VL CDRs or VL CDR motifs, and sequences for heavy chain CDRs should be selected from the disclosed VH CDRs or VH CDR motifs. Similarly, the sequences for CDR1 regions should be selected from the disclosed CDR1 or CDR1 motif sequences, the sequences for CDR2 regions should be selected from the disclosed CDR2 or CDR2 motif sequences, and the sequences for CDR3 regions should be selected from the disclosed CDR3 or CDR3 motif sequences, for VL or VH chains as appropriate.

Methods of Using Anti-VASA Antibodies to Detect or Isolate Cells

[0038] The anti-VASA antibodies of the invention can be used in standard methods of immunoaffinity purification, immunohistochemistry and immunotherapy, but with specific application to cells and tissue expressing the VASA protein.

[0039] For example, the anti-VASA antibodies of the invention can be used to isolate cells expressing VASA from a mixed population of cells including only a fraction of cells that express VASA. For example, female germ line stem cells or oogonial stem cells or their precursors have been discovered to be present in ovarian tissue at very low proportions. Ovarian tissue (e.g., ovarian surface epithelial and/or cortex) can be excised, dissociated into individual cells, and subjected to techniques such as FACs using fluorescently-labeled anti-VASA antibodies or immunoaffinity purification using immobilized anti-VASA antibodies. The isolated VASA-expressing cells have various utilities in assisted reproductive technologies, as described above.

[0040] Alternatively, immunohistochemistry may be performed using the anti-VASA antibodies of the invention to identify cells or tissues expressing VASA and/or to quantify VASA expression in such cells.

[0041] In addition, the anti-VASA antibodies of the invention can be used therapeutically to target VASA-expressing cells for destruction either by antibody-dependent cell-mediated cytotoxicity (ADCC) or immunotoxins comprising anti-VASA antibodies of the invention conjugated to radio- or chemo-toxic moieties. Antibody-drug conjugates of the anti-VASA antibodies of the invention could also be used to deliver therapeutic drugs to VASA-expressing cells.
Nucleic Acid Molecules Encoding Anti-VASA Antibodies

The invention also provides nucleic acid molecules encoding the anti-VASA antibodies of the invention. Such nucleic acids can be designed using standard tables for the universal genetic code to choose codons which will encode the desired amino acid sequence, or specialized codon tables can be used that reflect codon biases characteristic of different organisms. Thus, for example, to optimize expression of the anti-VASA antibodies of the invention in CHO cells, a nucleic acid encoding the desired antibody can be designed using a codon table optimized for CHO cells.

The nucleic acids encoding the anti-VASA antibodies of the invention can be included in a wide variety of vectors known in the art, including cloning vectors (e.g., bacterial or mammalian cloning vectors), transformation vectors (e.g., homologous recombination, viral integration or autonomously replicating vectors) and expression vectors (e.g., high copy number, inducible or constitutive mammalian expression vectors).

Cells Expressing Anti-VASA Antibodies

Also provided are host cells expressing heterologous sequences encoding the anti-VASA antibodies of the invention. Such host cells can be useful for commercial production of the anti-VASA antibodies of the invention, and can be produced by transforming appropriate host cells with expression vectors described above.

In some embodiments the invention provides mammalian cells, including CHO cells, expressing the anti-VASA antibodies of the invention. However, those of skill in the art can express the antibodies in a variety of host cells, including bacterial, yeast, insect and mammalian systems. See, e.g., Verma et al. (1998), J. Immunol. Methods 216(1-2):165-81, incorporated by reference in its entirety herein.

Examples

Immunogenic Peptides

The following peptides were used as immunogens to generate antibodies against the C-terminal domain of human VASA and to screen for antibodies with high affinity binding to VASA:

VASA-1 (V1) immunogen: (SEQ ID NO: 1 residues 712-721) SQAPNPHVDE
VASA-2 (V2) immunogen: (SEQ ID NO: 1 residues 700-709) GKSLLMTAGF

As shown in FIG. 3, these immunogens comprise amino acid sequences from the C-terminal domain of VASA that are highly conserved between the human VASA protein and the mouse VASA homolog.

Hybridoma Generation

Hybridomas were formed in separate experiments with the VASA peptide immunogens V1 and V2 (above).

Peptides were conjugated to carrier proteins by standard methods. Conjugated peptides were used to immunize mice, and to increase the immune response through boosting with the conjugated peptide. Following a period of increased antibody titer in the sera, animals were sacrificed and spleens removed. Splenic B cells were fused to mouse fusion partner cell lines (SP2-0) for isolation and cloning. Hybridomas were formed by outgrowth at limiting dilution, and clones were developed by cloning titration experiments. The presence of VASA-reactive antibodies was examined by ELISA assays. Hybridomas were derived by outgrowth and stabilization of cells plated at limiting dilution cell cloning.

The binding of the VASA-reactive antibodies in the region of the C-terminal domains of the VASA/DDX4 polypeptide was compared with the binding control antibodies (AB13840, Abcam plc, Cambridge, UK) to delineate the similarity of the binding epitopes. Exemplary results are shown in FIG. 4.

Analysis of Hybridomas

Hybridomas were injected intraperitoneally into mice and, after allowing for a period of growth, ascites fluid was collected and purified, all using standard procedures, and then analyzed by ELISA.

Binding of the ascites-derived antibodies to the VASA, VASA-1 and VASA-2 polypeptides was used to select antibodies for further analysis. For example, as shown in FIG. 7, the binding of four anti-VASA hybridoma antibodies (2M1/1K3, 2M1/1K3, 2M1/1L5 and 2M1/2K4) were compared to two negative controls (2M1/1F5 and 2M1/1H5) which are not VASA-specific and/or to the 1E9-lambda antibody (described below).

Recombinant Library Panning

As an alternative to hybridoma technology, the generation of antibodies against amino acid residues 700-724 of human VASA/DDX4 was conducted using phage display technology. The phage display library was formed from a pool of normal B cells from ~40 blood donors. Phage were used to display the scFv chain of an antibody

The results of panning the human naive scFv library against the VASA/DDX4 700-724 peptide were as shown in Table 1 below:

<table>
<thead>
<tr>
<th>Peptide</th>
<th>Round</th>
<th>Titer of output phage (pfu/ml)</th>
<th>Titer of rescued phage (pfu/ml)</th>
<th>ELISA results</th>
</tr>
</thead>
<tbody>
<tr>
<td>VASA</td>
<td>1st</td>
<td>10^7</td>
<td>10^13</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>2nd</td>
<td>10^7</td>
<td>10^13</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>3rd</td>
<td>10^7</td>
<td>10^12</td>
<td>No positive clones</td>
</tr>
<tr>
<td></td>
<td>4th</td>
<td>10^7</td>
<td>10^13</td>
<td>Two positive clones</td>
</tr>
<tr>
<td></td>
<td>5th</td>
<td>10^7</td>
<td>10^13</td>
<td>Several positive clones</td>
</tr>
<tr>
<td></td>
<td>6th</td>
<td>10^7</td>
<td>/</td>
<td>/</td>
</tr>
</tbody>
</table>

ELISA results of single colonies identified after 3 and 4 rounds of selection are shown in Tables 2-4 below. Two clones were of note: “1A12” (plate 1, row A, column 12) and “1E9” (plate 1, row E, column 9).
### TABLE 2

<table>
<thead>
<tr>
<th>plate 1</th>
<th>3 rounds</th>
<th>4 rounds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VASA peptide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>A</td>
<td>0.062</td>
<td>0.061</td>
</tr>
<tr>
<td>B</td>
<td>0.055</td>
<td>0.058</td>
</tr>
<tr>
<td>C</td>
<td>0.059</td>
<td>0.058</td>
</tr>
<tr>
<td>D</td>
<td>0.072</td>
<td>0.064</td>
</tr>
<tr>
<td>E</td>
<td>0.778</td>
<td>0.058</td>
</tr>
<tr>
<td>F</td>
<td>0.057</td>
<td>0.099</td>
</tr>
<tr>
<td>G</td>
<td>0.058</td>
<td>0.055</td>
</tr>
<tr>
<td>H</td>
<td>0.044</td>
<td>0.058</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>A</td>
<td>0.085</td>
<td>0.062</td>
</tr>
<tr>
<td>B</td>
<td>0.062</td>
<td>0.035</td>
</tr>
<tr>
<td>C</td>
<td>0.064</td>
<td>0.063</td>
</tr>
<tr>
<td>D</td>
<td>0.094</td>
<td>0.063</td>
</tr>
<tr>
<td>E</td>
<td>0.078</td>
<td>0.058</td>
</tr>
<tr>
<td>F</td>
<td>0.062</td>
<td>0.056</td>
</tr>
<tr>
<td>G</td>
<td>0.057</td>
<td>0.060</td>
</tr>
<tr>
<td>H</td>
<td>0.061</td>
<td>0.066</td>
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### TABLE 3

<table>
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<th>plate 2-after 4 round of selection</th>
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<tbody>
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<tr>
<td>VASA peptide</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>B</td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>D</td>
</tr>
<tr>
<td>E</td>
</tr>
<tr>
<td>F</td>
</tr>
<tr>
<td>G</td>
</tr>
<tr>
<td>H</td>
</tr>
</tbody>
</table>

### TABLE 4

<table>
<thead>
<tr>
<th>plate 3-after 4 rounds of selection</th>
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</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>VASA peptide</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>B</td>
</tr>
<tr>
<td>C</td>
</tr>
</tbody>
</table>
ELISA results of single colonies identified after 5 rounds of selection are shown in Tables 5-7 below. Clones of note included 1A11, 1B4, 1B7, 1D4, 1D5, 1E2, 1E3, 1F7, 1G3, 1G12, 2B8, 2C7, 2E11, 2F1, 2G8, 2G10, 2H9, 3B2, 3B5, 3B7, 3D11, 3E5, 3E12, 3F6 and 3H11.

### Table 5

<table>
<thead>
<tr>
<th>VASA peptide</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clones</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>non-relevant peptide</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. 0.050 0.056 0.055 0.049 0.053 0.055 0.051 0.059 0.051 0.044 0.047 0.054</td>
</tr>
<tr>
<td>B. 0.058 0.075 0.061 0.064 0.073 0.061 0.053 0.054 0.059 0.056 0.059 0.063</td>
</tr>
<tr>
<td>C. 0.076 0.056 0.053 0.054 0.056 0.053 0.053 0.057 0.063 0.040 0.061</td>
</tr>
<tr>
<td>D. 0.069 0.052 0.052 0.058 0.056 0.048 0.059 0.059 0.056 0.052 0.051 0.056</td>
</tr>
<tr>
<td>E. 0.047 0.056 0.050 0.118 0.063 0.067 0.052 0.053 0.054 0.053 0.056 0.054</td>
</tr>
<tr>
<td>F. 0.053 0.054 0.054 0.052 0.054 0.054 0.053 0.043 0.056 0.046 0.056</td>
</tr>
<tr>
<td>G. 0.063 0.056 0.054 0.045 0.045 0.049 0.050 0.053 0.053 0.052 0.053 0.053</td>
</tr>
<tr>
<td>H. 0.058 0.055 0.054 0.047 0.053 0.048 0.050 0.051 0.054 0.053 0.053 0.058</td>
</tr>
</tbody>
</table>

Apr. 20, 2017
### TABLE 6

<table>
<thead>
<tr>
<th>VASA peptide</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
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Non-relevant peptide

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</table>

- **Clones shown in bold were PCR amplified.**
- Conversion to scFv-Fc fusion and expression in mammalian cells after 5 rounds of selection for conversion to scFv-Fc fusions for expression in mammalian cells and for ELISA and FACS analysis. FIG. 5A shows dose...
response binding curves that indicated that 1E9 had an EC50 of 0.02779 nM and 1A12 had an EC50 of 0.2156 nM. In addition, FIG. 5B shows the results of ELISA assays with the V1 and V2 VASA peptides which suggest that 1E9 binds the same epitope as the commercially available rabbit polyclonal antibody (AB13840, Abcam plc, Cambridge, UK).

[0059] Two different forms of the 1E9 antibody were compared: IgG and scFv-Fc. As shown in FIG. 6A, 1E9 IgG had an EC50 of 0.08919 nM and the 1E9 scFv-Fc had an EC50 of 0.3072 nM. In addition, as shown in FIG. 6B, both forms were specific towards the VASA-1 epitope.

Synthetic Antibody Gene Production

[0060] The following steps were employed to produce synthetic antibody genes:

[0061] (1) Subtype Determination of Hybridoma Antibodies

[0062] The IgG subtypes of the hybridoma antibodies were determined using commercially available kits according to manufacturer’s protocols (e.g., Mouse Monoclonal Antibody Isotyping Kit, Catalog No. AbDSerotech, Kidlington, UK). FIG. 8 shows the result of subtyping analysis for anti-VASA antibodies from eight hybridomas (2M1/1L20, 2M1/1L20, 1M1/1C9, 2M1/1N3, 2M1/1K23, 1M1/1L5 and 2M1/2K4). All of the antibodies were IgG1, IgG2a or IgG2b.

[0063] (2) Degenerate Primer Synthesis

[0064] Based on the subtype information for the eight hybridoma antibodies tested, degenerate primers for mouse IgV GH and VL were designed using sequence information from a mouse IgG database (i.e., the International Immunogenetics Information System® or MGT database; see Lefranc et al. (2003), Leukemia 17:260-266, and Alamy et al. (2012), Methods Mol. Biol. 2012; 882:569-604). Ten degenerate forward primers were designed and synthesized for the VH chain and ten for the VL chain (9 for kappa and one for lambda chains). In addition, two degenerate reverse primers for the VH chain (one for the IgG1 and IgG2b subtypes, and one for the IgG2a subtype) and five for the VL chain (four for kappa and one for lambda chains) were designed and synthesized.

[0065] (3) RNA Extraction, Amplification, Cloning and Sequencing.

[0066] RNA was extracted from hybridoma cells by standard techniques, first strand cDNA synthesis was performed by standard techniques using gene-specific and oligo(dT) primers, and the cDNA was amplified using gene-specific primers. The amplified DNA was then ligated into a commercially available bacterial cloning vector (pMD18-T, Sino Biological, Inc., Beijing, China). Standard methodologies were conducted to transform the ligation products into E. coli DH5α, and to sequence positive clones.

Antibody Sequence Analyses

[0067] Clones producing potentially useful anti-Vasa antibodies were DNA sequenced and the corresponding amino acid sequences were deduced. Sequences are disclosed for eight antibodies derived from the hybridomas described above (i.e., 1N23, 1K23, 2K4, 1C9, 1J20, 1L20, 1K3, 1L5). Four additional antibodies derived from hybridomas produced under contract (i.e., CTA4/5, CTB4/11, CTC2/6, CTD2/6) and two antibodies derived from phage display (i.e., IA12 and IE9).

[0068] Variable Light Chain Sequences

[0069] VL of 1N23. Positive VL clones from the 1N23 hybridoma were sequenced and six were found to encode functional VL chains. These six clones were designated 1N23V1.5-5, 1N23V1.5-8-0816, 1N23V1.1-8, 1N23V1.1-2_0820, 1N23V1.1-4_0820 and 1N23V1.1-2.

[0070] VL of 1K23. Positive VL clones from the 1K23 hybridoma were sequenced and four were found to encode functional VL chains. These four clones were designated 1K23V1.2-5, 1K23V1.2-6, 1K23V1.2-8_0822 and 1K23V1.2-3_0829.

[0071] VL of 2K4. Positive VL clones from the 2K4 hybridoma were sequenced and eight were found to encode functional VL chains. These eight clones were designated 2K4V1.1-3_0820, 2K4V1.1-4, 2K4V1.1-1, 2K4V1.1-6_0820, 2K4V1.2-5_0816, 2K4V1.2-4, 2K4V1.2-6_0816 and 2K4V1.2-5.

[0072] VL of 1C9. Positive VL clones from the 1C9 hybridoma were sequenced and three were found to encode functional VL chains. These three clones were designated 1C9V1.2-4, 1C9V1.2-6 and 1C9V1.2-3_0816.

[0073] VL of 1J20. Positive VL clones from the 1J20 hybridoma were sequenced and three were found to encode functional VL chains. These three clones were designated 1J20V1.5-2_0907, 1J20V1.5-6_0907 and 1J20V1.4-3_0907.

[0074] VL of 1L20. Positive VL clones from the 1L20 hybridoma were sequenced and one was found to encode a functional VL chain. That clone was designated 1L20V1.5-0912_091.

[0075] VL of 1K3. Positive VL clones from the 1K3 hybridoma were sequenced and four were found to encode functional VL chains. These four clones were designated 1K3V1.2-5, 1K3V1.2-5, 1K3V1.2-3 and 1K3V1.2-4.

[0076] VL of 1L5. Positive VL clones from the 1L5 hybridoma were sequenced and two were found to encode functional VL chains. These two clones were designated 1L5V1.2-4 and 1L5V1.3-1.

[0077] Additional VLs. VL sequences were obtained for four additional hybridoma antibodies designated CTA4 VL, CTB4 VL, CTC6 VL, CTD6 VL.

[0078] VL Sequence Alignments. Alignments of all of the VL sequences described above are shown in FIG. 9. The figure indicates the approximate locations of the three CDR regions (bold, underscore) and the SEQ ID NO. corresponding to each sequence.

[0079] Unique VL CDR Sequences. Alignments of the unique CDR sequences of the VLs of FIG. 9 are shown in FIG. 11. Of the 34 VL sequences, there are only 5 unique CDR1 sequences, 6 unique CDR2 sequences and 8 unique CDR3 sequences, as shown in FIG. 11.

[0080] VL CDR Consensus Sequences. Based on the sequences disclosed in FIG. 11, as well as structure/function characteristics of the naturally occurring amino acids, consensus sequences for the VL CDRs can be determined.

[0081] One consensus sequence is VL CDR1 Motif 1:
K or S; and/or X₂ is limited to S or N; and/or X₃ is limited to I or L; and/or X₄ is limited to V, L or absent; and/or X₅ is limited to H or absent; and/or X₆ is limited to S or absent; and/or X₇ is limited to N or absent; and/or X₈ is limited to G or absent; and/or X₉ is limited to N; and/or X₁₀ is limited to T, S or N; and/or X₁₁ is limited to Y or F. In some embodiments, the subsequence X₁ X₂ X₃ is limited to Q N I; in some embodiments, the subsequence X₁ X₂ X₃ is limited to Q S L; and in some embodiments, the subsequence X₁ X₂ X₃ is limited to K S L. In addition, in some embodiments, when X₁ X₂ X₃ is Q S L or Q N I, then X₄ is V; whereas in other embodiments, when X₁ X₂ X₃ is K S L, then X₄ is L. In some embodiments, when X₉ X₁₀ is N T, then X₁₁ is Y.

[0082] Noting in particular that the VL CDR1 sequences of SEQ ID NOs: 86-88 are quite distinct from the others in FIG. 11, an alternative consensus sequence is VL CDR1 Motif 2:

\[
\begin{align*}
X₁ &\quad X₂ &\quad X₃ &\quad X₄ &\quad X₅ &\quad X₆ &\quad X₇ &\quad X₈ &\quad X₉ &\quad X₁₀ &\quad X₁₁ \\
\text{(SEQ ID NO: 133)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where X₁ is Q, N, K or R; X₂ is S, T, C, N or Q; X₃ is I, L, V, M or A; X₄ is V, L, I, M or A; X₅ is H, K or R; X₆ is S, T or C; X₇ is N or Q; X₈ is M or A; X₉ is S or N; X₁₀ is T, S or C; and X₁₁ is Y, F or W. In some embodiments, X₁ is limited to Q or K; and/or X₂ is limited to S or N; and/or X₃ is limited to I or L; and/or X₄ is limited to V or L; and/or X₅ is limited to H; and/or X₆ is limited to S; and/or X₇ is limited to N; and/or X₈ is limited to G; and/or X₉ is limited to N; and/or X₁₀ is limited to T; and/or X₁₁ is Y. In some embodiments, the subsequence X₁ X₂ X₃ is limited to Q N I; in some embodiments, the subsequence X₁ X₂ X₃ is limited to Q S L; and in some embodiments, the subsequence X₁ X₂ X₃ is limited to K S L. In addition, in some embodiments, when X₁ X₂ X₃ is Q S L or Q N I, then X₄ is V; whereas in other embodiments, when X₁ X₂ X₃ is K S L, then X₄ is L. In some embodiments, when X₉ X₁₀ is N T, then X₁₁ is Y.

[0083] For the VL CDR2, one consensus sequence is VL CDR2 Motif 1:

\[
\begin{align*}
Y₁ &\quad Y₂ &\quad Y₃ \\
\text{(SEQ ID NO: 134)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where Y₁ is K, R or H; Y₂ is V, I, L, M, A, T, S or C; and Y₃ is S, T, C, N or Q. In some embodiments, Y₂ is limited to V, I, M or T; and/or Y₃ is limited to S or N.

[0084] Noting in particular that the VL CDR2 sequences of SEQ ID NO: 94 is quite distinct from the others in FIG. 11, an alternative consensus sequence is VL CDR2 Motif 2:

\[
\begin{align*}
Y₁ &\quad Y₂ &\quad Y₃ \\
\text{(SEQ ID NO: 135)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where Y₁ is D or F; Y₂ is N or Q; and Y₃ is N or Q. In some embodiments, Y₂ is limited to D; and/or Y₃ is limited to N; and/or Y₃ is limited to N.

[0085] Similarly, noting that the VL CDR2 sequences of SEQ ID NO: 95 is quite distinct from the others in FIG. 11, an alternative consensus sequence is VL CDR2 Motif 3:

\[
\begin{align*}
Y₁ &\quad Y₂ &\quad Y₃ \\
\text{(SEQ ID NO: 136)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where Y₁ is Q or N; Y₂ is D or E; and Y₃ is S or K, R or H. In some embodiments, Y₁ is limited to Q; and/or Y₂ is limited to D; and/or Y₃ is limited to K.

[0086] For the VL CDR3, one consensus sequence is VL CDR3 Motif 1:

\[
\begin{align*}
Z₁ &\quad Z₂ &\quad Z₃ &\quad Z₄ &\quad Z₅ &\quad Z₆ &\quad Z₇ &\quad Z₈ &\quad Z₉ &\quad Z₁₀ \\
\text{(SEQ ID NO: 137)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where Z₁ is S, T, C, F, Y, M, L, V, I or A; Z₂ is Q, N, S, T or C; Z₃ is S, T, C, G, A, H, K, R, Q, N, Y, F or W; Z₄ is A, G, S, T, C, I, L, V, M, D or E; Z₅ is H, K, R, E, D, S, T or C; Z₆ is V, L, I, M, A, Y, F, W, S, T or C; Z₇ is P, S, T, C or absent; Z₈ is S, T, C or absent; Z₉ is W, P, L, I, M, A, F, Y; and Z₁₀ is T, S, C, V, L, I, M, A. In some embodiments, Z₁ is limited to S, F, M or L; and/or Z₂ is limited to Q or S; and/or Z₃ is limited to S, G, H, Q or Y; and/or Z₄ is limited to A, S, T, L, or D; and/or Z₅ is limited to H, E, D or S; and/or Z₆ is limited to V, Y, F, or S; and/or Z₇ is limited to P, S or absent; and/or Z₈ is limited to S or absent; and/or Z₉ is limited to W, P, L or F; and/or Z₁₀ is limited to T or V.

[0087] Noting in particular that the VL CDR3 sequences of SEQ ID NOs: 96-98 have a positive charge at position Z₃ whereas the others in FIG. 11 do not, an alternative consensus sequence is VL CDR3 Motif 2:

\[
\begin{align*}
Z₁ &\quad Z₂ &\quad Z₃ &\quad Z₄ &\quad Z₅ &\quad Z₆ &\quad Z₇ &\quad Z₈ &\quad Z₉ &\quad Z₁₀ \\
\text{(SEQ ID NO: 138)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where Z₁ is S, T, C, F or Y; Z₂ is Q or N; Z₃ is S, T, C, G or A; Z₄ is A, G, S, T or C; Z₅ is H, K or R; Z₆ is V, L, I, M, A or C; Z₇ is P or absent; Z₈ is absent; Z₉ is W, P, L, I, V, M, A, F or Y; and Z₁₀ is T, S or C. In some embodiments, Z₁ is limited to S or F; and/or Z₂ is limited to Q; and/or Z₃ is limited to S or G; and/or Z₄ is limited to A, S or T; and/or Z₅ is limited to H; and/or Z₆ is limited to V; and/or Z₇ is limited to P or absent; and/or Z₈ is limited to absent; and/or Z₉ is limited to W, P or F; and/or Z₁₀ is limited to T.

[0088] Noting in particular that the VL CDR3 sequences of SEQ ID NOs: 99-102 have a negative charge at position Z₃ whereas the others in FIG. 11 do not, an alternative consensus sequence is VL CDR3 Motif 3:

\[
\begin{align*}
Z₁ &\quad Z₂ &\quad Z₃ &\quad Z₄ &\quad Z₅ &\quad Z₆ &\quad Z₇ &\quad Z₈ &\quad Z₉ &\quad Z₁₀ \\
\text{(SEQ ID NO: 139)} &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad &\quad
\end{align*}
\]

where Z₁ is M, C, L, I, V, A; Z₂ is Q or N; Z₃ is H, K, R, Q, N, G, A, Y or F; Z₄ is L, I, V, M, A, D or E; Z₅ is E or D; Z₆ is Y or F; Z₇ is F; Z₈ is absent; Z₉ is W, P, L, I, V, M, A, F or Y; and Z₁₀ is T, S, C or G. In some embodiments, Z₁ is limited to M or L; and/or Z₂ is limited to Q; and/or Z₃ is limited to H, Q, G or Y; and/or Z₄ is limited to L or D; and/or Z₅ is limited to E or D; and/or Z₆ is limited to Y or F; and/or Z₇ is limited to P; and/or Z₈ is limited to absent; and/or Z₉ is limited to W, P, L or F; and/or Z₁₀ is limited to T.

[0089] Noting in particular that the VL CDR3 sequence of SEQ ID NO: 103 is quite distinct from the others in FIG. 11, an alternative consensus sequence is VL CDR3 Motif 4:
where $Z$ is S, T or C; $Z_2$ is S, T or C; $Z_3$ is Y or F; $Z_4$ is T, S, or C; $Z_5$ is S, T or C; $Z_6$ is S, T or C; $Z_7$ is W, P, F or Y; and $Z_{10}$ is V, L, I, M, A, T, S or C. In some embodiments, $Z_1$ is limited to S or T; and/or $Z_2$ is limited to S or T; and/or $Z_3$ is limited to S or T; and/or $Z_4$ is limited to S or T; and/or $Z_5$ is limited to S or T; and/or $Z_6$ is limited to S or T; and/or $Z_7$ is limited to W, P or F; and/or $Z_{10}$ is limited to V, L, I, M, A, T, S or C. In some embodiments, $Z_1$ is limited to S or T; and/or $Z_2$ is limited to S or T; and/or $Z_3$ is limited to S or T; and/or $Z_4$ is limited to S or T; and/or $Z_5$ is limited to S or T; and/or $Z_6$ is limited to S or T; and/or $Z_7$ is limited to W; and/or $Z_{10}$ is limited to V.

Finally, noting in particular that the VL CDR3 sequence of SEQ ID NO: 104 is quite distinct from the others in FIG. 11, an alternative consensus sequence is VL CDR3 Motif 5:

where $Z_1$ is Q or N; $Z_2$ is A or G; $Z_3$ is W, Y or F; $Z_4$ is D or E; $Z_5$ is S, T or C; $Z_6$ is R, K or H; $Z_7$ is I, L, M or A; $Z_8$ is V, I, L, M or A; and $Z_{10}$ is I, L, V, M or A. In some embodiments, $Z_1$ is limited to Q; and/or $Z_2$ is limited to A; and/or $Z_3$ is limited to S or T; and/or $Z_4$ is limited to D; $Z_5$ is limited to S; and/or $Z_6$ is limited to R; and/or $Z_7$ is limited to T; and/or $Z_8$ is limited to V; and/or $Z_{10}$ is limited to I.

Variable Heavy Chain Sequences

VH of IN23. Positive VH clones from the IN23 hybridoma were sequenced and all four were found to encode functional VH chains. These four clones were designated 1N23VH3-5, 1N23VH3-7, 1N23VH3-1 and 1N23VH1-5.

VH of 1K23. Positive VH clones from the 1K23 hybridoma were sequenced and six were found to encode functional VH chains. These six clones were designated 1K23VH2-1_0910, 1K23VH1-4_0907, 1K23VH1-10_0907, 1K23VH1-4_0907, 1K23VH8-5_0907 and 1K23VH8-9_0907.

VH of 2K4. Positive VH clones from the 2K4 hybridoma were sequenced and four were found to encode functional VH chains. These four clones were designated 2K4VH3-8, 2K4VH2-8, 2K4VH1-1 and 2K4VH1-4.

VH of 1C9. Positive VH clones from the 1C9 hybridoma were sequenced and eight were found to encode functional VH chains. These eight clones included four unique sequences which are designated 1C9VH2-405-12_1024, 1C9VH2-411-1_1024 and 1C9VH2-406-4_1024.

VH of JU20. Positive VH clones from the JU20 hybridoma were sequenced and two were found to encode functional VH chains. These two clones were designated JU20VH1-7_0910 and JU20VH1-1_0829.

VH of IL20. Positive VH clones from the IL20 hybridoma were sequenced and three were found to encode functional VH chains. These three clones were designated 1L20VH2-3_0903, 1L20VH1-1_0907 and 1L20VH2-3_0910.

VH of 1K3. Positive VH clones from the 1K3 hybridoma were sequenced and five were found to encode functional VH chains. These five clones were designated 1K3VH6-7, 1K3VH6-8_0816, 1K3VH3-4, 1K3VH3-4 and 1K3VH3-3_0816.

VH of 1L5. Positive VH clones from the 1L5 hybridoma were sequenced and nine were found to encode functional VH chains. These nine clones were designated 1L5VH003-5_0807, 1L5VH003-6_0907, 1L5VH001-7_0807, 1L5VH001-5_0807, 1L5VH001-6_0907, 1L5VH001-6_0907, 1L5VH001-6_0907, 1L5VH001-6_0907 and 1L5VH003-3_0807.

Additional VHs. VH sequences were obtained for four additional hybridoma antibodies designated CTA5_VH, CTB11_VH, CTB2_VH, CTD2_VH.

VH Sequence Alignments. Alignments of all of the VH sequences described above are shown in FIG. 10. The figure indicates the approximate locations of the three CDR regions (bold, underscore) and the SEQ ID NO corresponding to each sequence.

Unique VH CDR Sequences. Alignments of the unique CDR sequences of the VHs of FIG. 10 are shown in FIG. 12. Of the 43 VH sequences, there are only 8 unique CDR1 sequences, 9 unique CDR2 sequences and 10 unique CDR3 sequences, as shown in FIG. 12.

VH CDR Consensus Sequences. Based on the sequences disclosed in FIG. 12, as well as structure/function characteristics of the naturally occurring amino acids, consensus sequences for the VH CDRs can be determined.

For the VH CDR1, one consensus sequence is VH CDR1 Motif 1:

$$
\text{(SEQ ID NO: 142)}
$$

VH of 1K3. Positive VH clones from the 1K3 hybridoma were sequenced and five were found to encode functional VH chains. These five clones were designated 1K3VH6-7, 1K3VH6-8_0816, 1K3VH3-4, 1K3VH3-4 and 1K3VH3-3_0816.
embodiments, the subsequence X1 X2 X3 is limited to G F T. In addition, in some embodiments, the subsequence X1 X2 X3 is limited to S Y W.

[0106] For the VH CDR2, one consensus sequence is VH CDR2 Motif 1:

\[
\text{(SEQ ID NO: 144) }
\]

\[
Y_1 Y_2 Y_3 Y_4 Y_5 Y_6 Y_7 Y_8 Y_9 Y_{10}
\]

where Y1 is I, L, V, or M; Y2 is Y, F, H, R, K, S or T; Y3 is P, S, T, Y, F, R, K or H; Y4 is G, A, S, T, K, R, H, D or E; Y5 is T, S, or absent; Y6 is R, K, H or absent; Y7 is Y, N, Q, D, E, G, A or absent; Y8 is G, A, S, T, Y or F; Y9 is D, E, A, G, N or Q; and Y10 is T, S, I, L, V, M, A, K, R or H. In some embodiments, Y1 is limited to I; and/or Y2 is limited to Y, H, R, or S; and/or Y4 is limited to P, S, T, or Y; and/or Y5 is limited to G, S, or T; and/or Y7 is limited to T or absent; and/or Y8 is limited to P or absent; and/or Y9 is limited to D, E, A, G, N, or Q; and/or Y10 is limited to T, I, or K.

[0107] Noting in particular that the VH CDR2 sequence of SEQ ID NO: 120-121 are quite distinct from the others in FIG. 12, an alternative consensus sequence is VH CDR2 Motif 2:

\[
\text{(SEQ ID NO: 145) }
\]

\[
Y_1 Y_2 Y_3 Y_4 Y_5 Y_6 Y_7 Y_8 Y_9 Y_{10}
\]

where Y1 is I, L, V, or M; Y2 is Y, F, H, R, K, S or T; Y3 is P, S, T, Y or F; Y4 is G, A, S, T, K, R, H, or I; Y5 is T, S, or absent; Y6 is R, K, H or absent; Y7 is Y, N, Q, D, E or absent; Y8 is G, A, S, T, Y or F; Y9 is D, E, A, G, N or Q; and Y10 is T, S, I, L, V, M, A or M. In some embodiments, Y1 is limited to I; and/or Y2 is limited to Y, H, R, or S; and/or Y4 is limited to P, S, or T; and/or Y5 is limited to G, S, or T; and/or Y7 is limited to T or absent; and/or Y8 is limited to R or absent; and/or Y9 is limited to N, D or absent; and/or Y10 is limited to G, A, or S; and/or Y11 is limited to D, E, A, N, Y, or T; and/or Y12 is limited to T or I.

[0108] For the VH CDR3, one consensus sequence is VH CDR3 Motif 1:

\[
\text{(SEQ ID NO: 146) }
\]

\[
z_1 z_2 z_3 z_4 z_5 z_6 z_7 z_8 z_9 z_{10} z_{11} z_{12} z_{13} z_{14} z_{15}
\]

where Z1 is A, G, V, L, I or M; Z2 is R, K, H, C or M; Z3 is G, A, R, K, H, S, T, Y, F, W, D, E or absent; Z4 is Y, F, W, N, Q, G, A, R, K, H or absent; Z5 is S, T, N, Q, E, D or absent; Z6 is D, E or absent; Z7 is I, L, V, M, A, or S; and/or Z8 is L, I, V, M, A or absent; Z9 is G, A, R, K, H or absent; Z10 is I, I, V, M, A, N, Q, R, K, H or absent; Z11 is A, M, F, Y, W, S, T, G or absent; Z12 is W, Y, F, A, G or absent; Z13 is F, Y, W, G, A, M or C; Z14 is A, G, M, D, E, W, Y or F; and Z15 is Y, F, W, G, A or V. In some embodiments, Z1 is limited to A or V; and/or Z2 is limited to R, K or C; and/or Z3 is limited to G, R, S, Y, D or absent; and/or Z4 is limited to Y, N, G, R or absent; and/or Z5 is limited to S, N, E or absent; and/or Z6 is limited to D or absent; and/or Z7 is limited to L, S or absent; and/or Z8 is limited to L or absent; and/or Z9 is limited to G, R or absent; and/or Z10 is limited to N, R, L or absent; and/or Z11 is limited to A, F, S, G or absent; and/or Z12 is limited to W, Y, A or absent; and/or Z13 is limited to F, Y, G or M; and/or Z14 is limited to A, D, W or Y; and/or Z15 is limited to Y, F, W or G.

[0109] Although the disclosed subject matter has been described and illustrated in the foregoing exemplary embodiments, it is understood that the present disclosure has been made only by way of example, and that numerous changes in the details of implementation of the disclosed subject matter may be made without departing from the spirit and scope of the disclosed subject matter, which is limited only by the claims which follow.
Ser Asn Ser Arg Phe Glu Asp Gly Asp Ser Ser Gly Phe Trp Arg Glu 100 105 110
Ser Ser Asn Asp Cys Glu Asp Asn Pro Thr Arg Asn Arg Gly Phe Ser 115 120 125
Lys Arg Gly Gly Tyr Arg Asp Gly Asn Ser Glu Ala Ser Gly Pro 130 135 140
Tyr Arg Arg Gly Gly Ser Phe Arg Gly Cys Arg Gly Gly Phe 145 150 155 160
Gly Leu Gly Ser Pro Asn Asn Ser Leu Asp Pro Asp Glu Cys Met Gln 165 170 175
Arg Thr Gly Leu Gly Ser Arg Arg Pro Val Leu Ser Gly Thr 180 185 190
Gly Asn Gly Asp Thr Ser Gin Ser Arg Ser Gly Ser Gly Ser Glu Arg 195 200 205
Gly Gly Tyr Lys Gly Leu Asn Glu Glu Val Ile Thr Gly Ser Gly Lys 210 215 220
Asn Ser Trp Lys Ser Gin Ala Glu Gly Gly Gin Ser Ser Asp Thr Gin 225 230 235 240
Gly Pro Lys Val Thr Tyr Ile Pro Pro Pro Pro Pro Pro Glu Asp 245 250 255
Ser Ile Phe Ala His Tyr Gin Thr Gly Ile Asn Phe Asp Lys Tyr Asp 260 265 270
Thr Ile Leu Val Glu Val Ser Gly His Asp Ala Pro Ala Ile Leu 275 280 285 290
Thr Phe Glu Glu Ala Asn Leu Cys Gin Thr Leu Asn Asn Asn Ile Ala 295 300
Lys Ala Gly Tyr Thr Lys Leu Thr Pro Val Gin Lys Tyr Ser Ile Pro 305 310 315 320
Ile Ile Leu Ala Gly Arg Asp Leu Met Ala Cys Ala Gin Thr Gly Ser 325 330 335
Gly Lys Thr Ala Ala Phe Leu Leu Pro Ile Leu Ala His Met Met His 340 345 350
Asp Gly Ile Thr Ala Ser Arg Phe Lys Glu Leu Gin Glu Pro Glu Cys 355 360 365
Ile Ile Val Ala Pro Thr Arg Glu Leu Val Asn Gin Ile Tyr Leu Glu 370 375 380
Ala Arg Lys Phe Ser Phe Gly Thr Cys Val Arg Ala Val Val Ile Tyr 385 390 395 400
Gly Gly Thr Gin Leu Gly His Ser Ile Arg Gin Ile Val Gin Gly Cys 405 410
Asn Ile Leu Cys Ala Thr Pro Gly Arg Leu Met Asp Ile Ile Gly Lys 420 425 430
Glu Lys Ile Gly Leu Lys Gin Ile Lys Tyr Leu Val Leu Asp Glu Ala 435 440 445
Asp Arg Met Leu Asp Met Gly Phe Gly Pro Glu Met Lys Leu Ile 450 455 460
Ser Cys Pro Gly Met Pro Ser Lys Glu Gin Arg Gin Thr Leu Met Phe 465 470 475 480
Ser Ala Thr Phe Pro Glu Ile Gin Arg Leu Ala Ala Glu Phe Leu 485 490 495
Lys Ser Asn Tyr Leu Phe Val Ala Val Gly Gin Val Gly Gly Ala Cys
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Val Phe Val Glu Thr Lys Lys Ala Asp Phe Ile Ala Thr Phe Leu
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Cys Gln Glu Lys Ile Ser Thr Ser Ile His Gly Asp Arg Glu Gln
565 570 575
Arg Glu Arg Glu Glu Ala Leu Gly Asp Phe Arg Phe Gly Lys Cys Pro
580 585 590
Val Leu Val Ala Thr Ser Val Ala Ala Arg Gly Leu Asp Ile Glu Asn
595 600 605
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610 615 620
Val His Arg Ile Gly Arg Thr Gly Arg Cys Gly Asn Thr Gly Arg Ala
625 630 635 640
Ile Ser Phe Phe Asp Leu Glu Ser Asp Asn His Leu Ala Gln Pro Leu
645 650 655
Val Lys Val Leu Thr Asp Ala Glu Gln Glu Val Pro Ala Thr Leu Glu
660 665 670
Glu Ile Ala Phe Ser Thr Tyr Ile Pro Gly Phe Ser Gly Ser Thr Arg
675 680 685
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35 40 45
Pro Ser Gly Arg Asp Phe Met Arg Ser Gly Phe Pro Ser Gly Arg
50 55 60
Ser Leu Gly Ser Arg Ile Gly Glu Ser Ser Lys Lys Glu Asn Thr
65 70 75 80
Ser Thr Thr Gly Phe Gly Arg Gly Lys Gly Phe Gly Asn Arg Gly
85 90 95
Phe Leu Asn Asn Lys Phe Glu Gly Asp Ser Ser Gly Phe Trp Lys
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Arg Glu Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40  45
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Phe Ser Gly Val Pro
50 55  60
Asp Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
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 35  40  45
Pro Lys 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
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 35  40  45
Pro Lys 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
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 85  90  95
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 20  25  30
Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35  40  45
-continued

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Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
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35 40 45
Pro Lys 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
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Pro Lys 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
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35  40
Pro Asn Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50  55  60
Asn Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65  70  75  80
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<210> SEQ ID NO 13
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 13

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**Other Information:** Description of Artificial Sequence: Synthetic Polypeptide
<212> TYPE: PRT
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20  25  30
Asn Gly Asn Thr Tyr Leu Gln Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35  40  45
Pro Lys 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 Leu Gly Val Tyr Tyr Cys Phe Glu Gly
85  90  95
Ser His Val Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> SEQ ID NO 17
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 17
Leu Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly
1  5  10  15
Glu Ser Val Ser Ile Ser Cys Arg Ser Thr Lys Ser Leu Leu His Ser
20  25  30
Asn Gly Asn Thr Tyr Leu Gln Thr Phe Leu Gln Arg Pro Gly Gln Ser
35  40  45
Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Ala Ala Ser Gly Val Pro
50  55  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
65  70  75  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Glu His
85  90  95
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100 105 110

<210> SEQ ID NO 18
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 18
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Asn Gly Asn Thr Tyr Leu Ser Trp Phe Leu Gln Arg Pro Gly Gln Ser
35 40
Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
Leu Glu Tyr Pro Leu Thr Phe Gly Ala Gly Thr Leu Glu Ile Lys
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<210> SEQ ID NO 19
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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35 40 45
Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
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<210> SEQ ID NO 20
<211> LENGTH: 112
<212> TYPE: PRT
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1 5 10 15
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20 25 30
Asn Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
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<210> SEQ ID NO 21
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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1  5  10  15
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35 40 45
Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gin His
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Leu Glu Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile Lys
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<210> SEQ ID NO 22
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1  5  10  15
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20 25 30
Asn Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
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<210> SEQ ID NO 23
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Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu AlaSer Gly Val Pro
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Amp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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

<210> SEQ ID NO: 30
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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

<210> SEQ ID NO 31
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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

<210> SEQ ID NO 32
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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

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

<210> SEQ ID NO 34
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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

<210> SEQ ID NO 35
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 35
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20 25 30
Asn Gly Asn Thr Tyr Leu Tyr Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45
Pro Gln Arg Leu Ile Tyr His Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Arg Gly Ser Gly Thr Asp Phe Thr Leu Arg Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95
Leu Glu Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Gly Leu Lys
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

<400> SEQUENCE: 36

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

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polypeptide

<400> SEQUENCE: 37

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<210> TYPE: PRT
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
polypeptide

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20   25   30
Leu Thr Trp Phe His Gln Lys Pro Gly Lys Ser Pro Thr Thr Leu Ile
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Tyr Arg Thr Asn Arg Leu Asp Gln Val Pro Ser Arg Phe Ser Gly
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Ser Gly Ser Gly Gln Asp Tyr Ser Thr Ile Asn Ser Leu Gln Phe
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Glu Asp Met Gln Ile Tyr Tyr Cys Leu Gln Tyr Asp Phe Pro Leu
85   90   95
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100  105
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Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
85 90 95

Ser Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly
100 105 110

SEQ ID NO 38 LENGTH: 107 TYPE: PRT ORGANISM: Artificial Sequence FEATURE: OTHER INFORMATION: Description of polypeptide

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

Gln Lys Lys Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Glu Ala Thr Met
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Ser Arg Thr Val
85 90 95

Ile Gly Arg Gly Thr Lys Leu Thr Val Leu Gly
100 105

SEQ ID NO 39 LENGTH: 117 TYPE: PRT ORGANISM: Artificial Sequence FEATURE: OTHER INFORMATION: Description of polypeptide

Leu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Gln Trp Val Lys Gln Arg Pro Gly Glu Gln Gln Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
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<210> SEQ ID NO 40
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 40

Leu Val Glu Leu Glu Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1   6   10   15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20  25  30
Trp Met Glu Trp Val Gly Glu Arg Pro Gly Glu Leu Glu Trp Ile
35  40  45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Glu Lys Phe
50  55  60
Lys Gly Lys Ala Thr Leu Thr Ala Asp Ser Ser Ser Thr Ala Tyr
65  70  75  80
Met Glu Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
95  90  95
Ala Arg Gly Gly Ile Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ala

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

Leu Val Gln Leu Lys Gln Ser Gly Ala Glu Ala Arg Pro Gly Ala
1  5  10  15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20  25  30
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35  40  45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe
50  55  60
Lys Gly Lys Ala Thr Leu Thr Ala Asp Ser Ser Ser Thr Ala Tyr
65  70  75  80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85  90  95
Ala Arg Gly Gln Ile Ala Trp Phe Ala Tyr Trp Gln Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ala
115
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

SEQUENCE: 44

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

SEQ ID NO 45
LENGTH: 117
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

SEQUENCE: 45

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

SEQ ID NO 46
LENGTH: 117
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE: OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

SEQUENCE: 46
Ser Val Lys Leu Gln Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe
50 55 60
Lys Gln Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Gly Ile Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ala
115

<210> SEQ ID NO 47
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide
<400> SEQUENCE: 47
Ser Val Lys Leu Gln Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe
50 55 60
Lys Gln Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Gly Ile Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ala
115

<210> SEQ ID NO 48
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide
<400> SEQUENCE: 48
Gln Val Gln Leu Gln Pro Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asn Tyr
20 25 30
-continued

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

<210> SEQ ID NO 49
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide
<400> SEQUENCE: 49
Gln Val Gln Leu Gln Pro Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asn Tyr 20 25 30
Trp Met Gln Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45
Gly Ala Ile Tyr Pro Gly Asp Gly Glu Thr Arg His Thr Gln Lys Phe 50 55 60
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95
Ala Ser Gly Tyr Pro Tyr Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val 100 105 110
Thr Val Ser Ala 115

<210> SEQ ID NO 50
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide
<400> SEQUENCE: 50
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Pro Val Lys Leu Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asn Tyr 20 25 30
Trp Met Gln Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45
Gly Ala Ile Tyr Pro Gly Asp Gly Glu Thr Arg His Thr Gln Lys Phe 50 55 60
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
45 70 75 80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Ser Gly Tyr Pro Tyr Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ala
115

<210> SEQ ID NO 51
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 51
Gln Val Gln Leu Gln Pro Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1   5   10   25
Ser Val Lys Leu Ser Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asn Tyr
20  25  30
Trp Met Gln Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35  40  45
Gly Ala Ile Tyr Pro Gly Asp Gly Glu Thr Arg His Thr Glu Lys Phe
50  55  60
Lys Gly Lys Ala Thr Leu Ser Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65  70  75  80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85  90  95
Ala Ser Gly Tyr Pro Tyr Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110
Thr Val Ser Ala
115

<210> SEQ ID NO 52
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 52
Gln Val Gln Leu Lys Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1   5   10   15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20  25  30
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35  40  45
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Glu Lys Phe
50  55  60
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Asn
65  70  75  80
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85  90  95

Apr. 20, 2017
Ala Lys Gly Asp Gly Asn Phe Trp Ala Tyr Trp Gly Gln Gly Thr  

Leu Val Thr Val Ser Ala  

100 105 110 115

<210> SEQ ID NO 53  
<211> LENGTH: 118  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide  
<400> SEQUENCE: 53  
Gln Val Gln Leu Lys Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala  
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr  
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe  
Lys Gly Lys Ala Thr Leu Thr Ala Asp Ser Ser Ser Thr Ala Asn  
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
Ala Lys Gly Asp Gly Asn Phe Trp Phe Ala Tyr Trp Gly Gln Gly Thr  

Leu Val Thr Val Ser Ala  

115

<210> SEQ ID NO 54  
<211> LENGTH: 118  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide  
<400> SEQUENCE: 54  
Gln Val Gln Leu Lys Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala  
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr  
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe  
Lys Gly Lys Ala Thr Leu Thr Ala Asp Ser Ser Ser Thr Ala Asn  
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
Ala Lys Gly Asp Gly Asn Phe Trp Phe Ala Tyr Trp Gly Gln Gly Thr  

Leu Val Thr Val Ser Ala  

115
<210> SEQ ID NO 55
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 55

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

<210> SEQ ID NO 56
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 56

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

<210> SEQ ID NO 57
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 57

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

<210> SEQ ID NO 58
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 58

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

<210> SEQ ID NO 59
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 59
Glu Val Gln Leu Gln Gln Ser Gly Ala Ala Leu Val Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Leu Gly Leu Glu Trp Ile
35 40 45
Gly Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe
50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Cys Arg Tyr Asp Arg Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110
Thr Leu Thr Val Ser Ser
115

<210> SEQ ID NO 60
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

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

<210> SEQ ID NO 61
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 61
Glu Val Gln Leu Gln Gln Ser Gly Ala Ala Leu Val Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Leu Gly Leu Glu Trp Ile 35 40 45
Gly Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe 50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80
Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95
Ala Cys Arg Tyr Asp Arg Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr 100 105 110
Thr Leu Thr Val Ser Ser 115

<210> SEQ ID NO 62
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 62
Glu Val Gln Leu Gln Gln Ser Gly Ala Ala Leu Val Arg Pro Gly Ala 1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr 20 25 30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Leu Gly Leu Glu Trp Ile 35 40 45
Gly Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe 50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80
Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95
Ala Cys Arg Tyr Asp Arg Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr 100 105 110
Thr Leu Thr Val Ser Ser 115

<210> SEQ ID NO 63
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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 63
Arg Val Gln Leu Gln Gln Ser Gly Ala Ala Leu Val Arg Pro Gly Ala 1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr 20 25 30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Leu Gly Leu Glu Trp Ile 35 40 45
Gly Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe 50 55 60
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Thr Leu Thr Val Ser Ser
115

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

Ser Val Arg Leu Ser Arg Ser Gly Tyr Thr Phe Thr Thr Phe
20  25  30

Trp Ile Asn Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35  40  45

Gly Asn Ile Tyr Pro Gly Asp Ala Ala Thr Arg Asn Glu Lys Phe
50  55  60

Lys Gly Lys Ala Thr Leu Ser Val Asp Thr Ser Ser Thr Ala Tyr
65  70  75  80

Met His Leu Phe Ser Leu Thr Ser Asp Ser Ala Val Tyr Cys
85  90  95

Val Arg Ser Gly Asp Phe Trp Gly Gln Gly Thr Thr Leu Thr Val Ser
100 105 110

Ser

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

Ser Val Arg Leu Ser Cys Lys Ser Ser Gly Tyr Thr Phe Thr Thr Phe
20  25  30

Trp Ile Asn Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35  40  45

Gly Asn Ile Tyr Pro Gly Asp Ala Ala Thr Arg Asn Glu Lys Phe
50  55  60

Lys Gly Lys Ala Thr Leu Ser Val Asp Thr Ser Ser Thr Ala Tyr
65  70  75  80

Met His Leu Phe Ser Leu Thr Ser Asp Ser Ala Val Tyr Cys
85  90  95

Val Arg Ser Gly Asp Phe Trp Gly Gln Gly Thr Thr Leu Thr Val Ser
100 105 110

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

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

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

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

<210> SEQ ID NO: 71
<211> LENGTH: 120
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 71
Leu Val Gln Leu Lys Gln Ser Gly Pro Ser Leu Val Lys Pro Ser Gln
1   5   10   15
Thr Leu Ser Leu Thr Cys Ser Val Thr Gly Asp Ser Val Thr Ser Gly
20  25  30
Tyr Trp Asn Trp Ile Arg Lys Phe Pro Gly Asn Lys Leu Glu Tyr Met
35  40
Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Tyr Asn Pro Ser Leu Lys
50  55  60
Ser Arg Ile Ser Ile Thr Arg Thr Ser Lys Asn Gln Tyr Leu
65  70  75  80
Gln Leu Asn Ser Val Thr Glu Asp Thr Ala Thr Tyr Cys Ala
85  90  95
Arg Tyr Asn Ser Leu Leu Arg Leu Gly Ala Met Asp Tyr Trp Gly Gln
100 105 110
Gly Thr Ser Val Thr Val Val Ser
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<210> SEQ ID NO: 72
<211> LENGTH: 120
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 72
Leu Val Gln Leu Lys Gln Ser Gly Pro Ser Leu Val Lys Pro Ser Gln
1   5   10   15
Thr Leu Ser Leu Thr Cys Ser Val Thr Gly Asp Ser Val Thr Ser Gly
20 25 30

Tyr Trp Asn Trp Ile Arg Lys Phe Pro Gly Asn Lys Leu Glu Tyr Met
35 40 45

Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Tyr Asn Pro Ser Leu Lys
50 55 60

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

Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Cys Ala
85 90 95

Arg Tyr Asn Ser Leu Leu Arg Leu Gly Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 73
<211> LENGTH: 120
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 73
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Thr Leu Ser Leu Thr Cys Ser Val Thr Gly Asp Ser Val Thr Ser Gly
20 25 30
Tyr Trp Asn Trp Ile Arg Lys Phe Pro Gly Asn Lys Leu Glu Tyr Met
35 40 45
Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Tyr Asn Pro Ser Leu Lys
50 55 60
Ser Arg Ile Ser Ile Thr Arg Ser Lys Asn Gln Tyr Tyr Leu
65 70 75 80
Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Cys Ala
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Arg Tyr Asn Ser Leu Leu Arg Leu Gly Ala Met Asp Tyr Trp Gly Gln
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Gly Thr Ser Val Thr Val Ser Ser
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 74
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Thr Leu Ser Leu Thr Cys Ser Val Thr Gly Asp Ser Val Thr Ser Gly
20 25 30
Tyr Trp Asn Trp Ile Arg Lys Phe Pro Gly Asn Lys Leu Glu Tyr Met
35 40 45
... Continued

- gly tyr ile ser tyr ser gly asn thr tyr tyr ser leu lys
  50 55 60

- ser arg ile ser ile thr arg asp thr ser lys asn gln tyr tyr leu
  65 70 75 80

- gln leu asn ser val thr thr gln asp thr ala thr tyr tyr cyr ala
  85 90 95

- arg tyr asn ser leu leu arg leu gly ala met asp tyr trp gln gln
  100 105 110

- gly thy ser val thr val ser ser
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<210> SEQ ID NO: 75
<211> LENGTH: 120
<212> TYPE: PRT
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 75

asp val lys leu gln gln ser gly pro ser leu val lys pro ser gln
  1 5 10 15

thr leu ser leu thr cys ser val thr gly asp ser val thr ser gly
  20 25 30

ty r trp asp trp ile arg lys phe pro gly asn leu gln tyr tyr met
  35 40 45

gly tyr ile ser tyr ser gly asn thr tyr tyr asp pro ser leu lys
  50 55 60

- ser arg ile ser ile thr arg asp thr ser lys asn gln tyr tyr leu
  65 70 75 80

- gln leu asn ser val thr thr gln asp thr ala thr tyr tyr cyr ala
  85 90 95

- arg tyr asn ser leu leu arg leu gly ala met asp tyr trp gln gln
  100 105 110

- gly thy ser val thr val ser ser
  115 120

<210> SEQ ID NO: 76
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 76

leu val lys leu gln gln ser gly pro ser leu val lys pro ser gln
  1 5 10 15

thr leu ser leu thr cys ser val thr gly asp ser val thr ser gly
  20 25 30

ty r trp asp trp ile arg lys phe pro gly asn leu gln tyr tyr met
  35 40 45

gly tyr ile ser tyr ser gly asn thr tyr tyr asp pro ser leu lys
  50 55 60

- ser arg ile ser ile thr arg asp thr ser lys asn gln tyr tyr leu
  65 70 75 80
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LENGTH: 120
TYPE: PRT
ORGANISM: Artificial Sequence
OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

**SEQUENCE: 79**

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ORGANISM: Artificial Sequence
OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

**SEQUENCE: 80**

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

<210> SEQ ID NO 82
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic polypeptide

<400> SEQUENCE: 82

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

<210> SEQ ID NO 83
<211> LENGTH: 11
<212> TYPE: PRT
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<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr
1 5 10

Gln Asn Ile Val His Ser Asn Gly Asn Thr Tyr
1 5 10

Lys Ser Leu Leu His Ser Asn Gly Asn Thr Tyr
1 5 10

Gln Asn Ile Asn Ser Phe
1 5

Gln Asn Ile Asn Ser Phe
1 5

Ser Asn Ile Gly Asn Tyr
1 5

Lys Leu Gly Asn Lys Tyr
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<210> SEQ ID NO 94
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<400> SEQUENCE: 98
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<400> SEQUENCE: 99
Arg Thr Asn
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peptide

<400> SEQUENCE: 94
Asp Asn Asn

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

<400> SEQUENCE: 95
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Ser Gln Ser Ala His Val Pro Trp Thr

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Phe Gln Gly Ser His Val Leu Thr

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**Description of Artificial Sequence:** Synthetic peptide

**Sequence:**

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2. Met Gln Gly Leu Glu Tyr Pro Leu Thr
3. Leu Gln Tyr Asp Asp Phe Pro Leu Thr
4. Ser Ser Tyr Thr Ser Ser Ser Ser Trp Val
5. Gln Ala Trp Asp Ser Arg Thr Val Val Ile
FEATURE: OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

SEQUENCE: 105

Gly Tyr Thr Phe Thr Ser Tyr Trp

SEQUENCE: 106

Gly Phe Thr Phe Thr Asn Tyr Trp

SEQUENCE: 107

Gly Tyr Ser Phe Thr Ser Tyr Trp

SEQUENCE: 108

Gly Tyr Thr Phe Thr Thr Phe Trp

SEQUENCE: 109

Gly Tyr Thr Phe Thr Thr Phe Trp

SEQUENCE: 110

Gly Phe Thr Phe Asn Ala Asn Ala
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Gly Asp Ser Val Thr Ser Gly Tyr
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<210> SEQ ID NO 113
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Ile Tyr Pro Gly Asn Gly Asp Thr
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

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Ala Arg Gly Gly Ile Ala Trp Phe Ala Tyr
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<210> SEQ ID NO 123
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 123
Ala Ser Gly Tyr Pro Tyr Phe Ala Tyr
1  5

<210> SEQ ID NO 124
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 124
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1  5  10

<210> SEQ ID NO 125
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<220> FEATURES:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 126
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<212> TYPE: PRT
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1  5

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Ala Arg Tyr Asn Ser Leu Leu Arg Leu Gly Ala Met Asp Tyr

1  5  10

<210> SEQ ID NO 129
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 129

Ala Arg Gly Asn Ser Tyr Tyr Gly

1  5

<210> SEQ ID NO 130
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 130

Ala Arg Gly Asn Ser Phe Arg Asp

1  5

<210> SEQ ID NO 131
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<400> SEQUENCE: 131

Ala Lys Asp Arg Glu Asp Gly Met Asp Val

1  5  10

<210> SEQ ID NO 132
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: Gln, Asn, Lys, Arg, Ser or Thr

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: Ser, Thr, Cys, Asn or Gln

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: Ile, Leu, Val, Met or Ala

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (4)...(4)
<223> OTHER INFORMATION: Val, Leu, Ile, Met, Ala or absent

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: His, Lys, Arg or absent

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: Ser, Thr, Cys or absent

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: Asn, Gln or absent

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: Gly, Ala or absent

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: Asn or Gln

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: Thr, Ser, Cys, Asn or Gln

FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (11)...(11)
<223> OTHER INFORMATION: Tyr, Phe or Trp

FEATURE:
<223> OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 132

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1  5 10
<222> LOCATION: (4)...(4)
<223> OTHER INFORMATION: Val, Leu, Ile, Met or Ala

<221> NAME/KEY: MOD_RES

<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: His, Lys or Arg

<221> NAME/KEY: MOD_RES

<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: Ser, Thr or Cys

<221> NAME/KEY: MOD_RES

<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: Asn or Gln

<221> NAME/KEY: MOD_RES

<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: Gly or Ala

<221> NAME/KEY: MOD_RES

<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: Asn or Gln

<221> NAME/KEY: MOD_RES

<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: Thr, Ser or Cys

<221> NAME/KEY: MOD_RES

<222> LOCATION: (11)...(11)
<223> OTHER INFORMATION: Tyr, Phe or Trp

<400> SEQUENCE: 133

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

1  5 10

<210> SEQ ID NO 134
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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

<221> NAME/KEY: MOD_RES

<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: Lys, Arg or His

<221> NAME/KEY: MOD_RES

<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: Val, Ile, Leu, Met, Ala, Thr, Ser or Cys

<221> NAME/KEY: MOD_RES

<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: Ser, Thr, Cys, Asn or Gln

<400> SEQUENCE: 134

Xaa Xaa Xaa

1

<210> SEQ ID NO 135
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [1]..[1]
<223> OTHER INFORMATION: Asp or Glu

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [2]..[2]
<223> OTHER INFORMATION: Asn or Gln

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [3]..[3]
<223> OTHER INFORMATION: Asn or Gln

<400> SEQUENCE: 135

Xaa Xaa Xaa

<210> SEQ ID NO 136
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [1]..[1]
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [2]..[2]
<223> OTHER INFORMATION: Gln or Asn

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [3]..[3]
<223> OTHER INFORMATION: Asp or Glu

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [4]..[4]
<223> OTHER INFORMATION: Lys, Arg or His

<400> SEQUENCE: 136

Xaa Xaa Xaa

<210> SEQ ID NO 137
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [1]..[1]
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
<223> OTHER INFORMATION: Ser, Thr, Cys, Phe, Tyr, Met, Leu, Val, Ile or Ala

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [2]..[2]
<223> OTHER INFORMATION: Gln, Asn, Ser, Thr or Cys

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [3]..[3]
<223> OTHER INFORMATION: Ser, Thr, Cys, Gly, Ala, His, Lys, Arg, Gln, Asn, Tyr, Phe or Trp

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: [4]..[4]
<223> OTHER INFORMATION: Ala, Gly, Ser, Thr, Cys, Leu, Ile, Val, Met, Asp or Glu

<220> FEATURE:
<221> NAME/KEY: MOD_RES
OTHER INFORMATION: His, Lys, Arg, Glu, Asp, Ser, Thr or Cys

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (5) (5)

OTHER INFORMATION: Val, Leu, Ile, Met, Ala, Tyr, Phe, Trp, Ser, Thr or Cys

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (6) (6)

OTHER INFORMATION: Pro, Ser, Thr, Cys or absent

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (7) (7)

OTHER INFORMATION: Ser, Thr, Cys or absent

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (8) (8)

OTHER INFORMATION: Thr, Ser, Cys, Val, Leu, Ile, Met or Ala

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (9) (9)

OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 137

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

1   5   10

OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (1) (1)

OTHER INFORMATION: Ser, Thr, Cys, Phe or Tyr

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (2) (2)

OTHER INFORMATION: Gln or Asn

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (3) (3)

OTHER INFORMATION: Ser, Thr, Cys, Gly or Ala

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (4) (4)

OTHER INFORMATION: Ala, Gly, Ser, Thr or Cys

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (5) (5)

OTHER INFORMATION: His, Lys or Arg

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (6) (6)

OTHER INFORMATION: Val, Leu, Ile, Met or Ala

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (7) (7)

OTHER INFORMATION: Pro or absent

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (8) (8)

OTHER INFORMATION: Trp, Pro, Leu, Ile, Val, Met, Ala, Phe or Tyr

FEATURE:
- NAME/KEY: MOD_RES
- LOCATION: (9) (9)

OTHER INFORMATION: Thr, Ser or Cys
FEATURE: OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 138

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

1 5

SEQ ID NO 139
LENGTH: 9
TYPE: PRT
ORGANISM: Artificial Sequence

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (1) (1)
OTHER INFORMATION: Met, Cys, Leu, Ile, Val or Ala

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (2) (2)
OTHER INFORMATION: Gln or Asn

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (3) (3)
OTHER INFORMATION: His, Lys, Arg, Gln, Asn, Gly, Ala, Tyr or Phe

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (4) (4)
OTHER INFORMATION: Leu, Ile, Val, Met, Ala, Asp or Glu

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (5) (5)
OTHER INFORMATION: Glu or Asp

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (6) (6)
OTHER INFORMATION: Tyr or Phe

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (8) (8)
OTHER INFORMATION: Trp, Pro, Leu, Ile, Val, Met, Ala, Phe or Tyr

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (9) (9)
OTHER INFORMATION: Thr, Ser or Cys

FEATURE:
OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 139

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Pro Xaa Xaa

1 5

SEQ ID NO 140
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (1) (1)
OTHER INFORMATION: Ser, Thr or Cys

FEATURE:
NAME/KEY: MOD_RES
LOCATION: (2) (2)
OTHER INFORMATION: Ser, Thr or Cys
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: Tyr or Phe
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (4)...(4)
<223> OTHER INFORMATION: Thr, Ser or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: Ser, Thr or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: Ser, Thr or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: Ser, Thr or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: Ser, Thr or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: Trp, Pro, Phe or Tyr
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: Val, Leu, Ile, Met, Ala, Thr, Ser or Cys
<220> FEATURE:
<223> OTHER INFORMATION: see specification as filed for detailed
description of substitutions and preferred embodiments

SEQUENCE: 140
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

<210> SEQ ID NO 141
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: Gln or Asn
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: Ala or Gly
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: Trp, Tyr or Phe
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (4)...(4)
<223> OTHER INFORMATION: Asp or Glu
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: Ser, Thr or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: Arg, Lys or His
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: Thr, Ser or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (8) . . (8)
<223> OTHER INFORMATION: Val, Ile, Leu, Met or Ala

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (9) . . (9)
<223> OTHER INFORMATION: Val, Ile, Leu, Met or Ala

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (10) . . (10)
<223> OTHER INFORMATION: Ile, Leu, Val, Met or Ala

<220> FEATURE:
<223> OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

<400> SEQUENCE: 141
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1  5  10

<210> SEQ ID NO 142
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (1) . . (1)
<223> OTHER INFORMATION: Gly or Ala

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (2) . . (2)
<223> OTHER INFORMATION: Tyr, Phe, Trp, Asp or Glu

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (3) . . (3)
<223> OTHER INFORMATION: Thr, Ser, Cys or Met

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (4) . . (4)
<223> OTHER INFORMATION: Phe, Tyr, Trp, Val, Leu, Ile, Met or Ala

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (5) . . (5)
<223> OTHER INFORMATION: Thr, Ser, Cys, Asn or Gln

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (6) . . (6)
<223> OTHER INFORMATION: Ser, Thr, Cys, Ala or Gly

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (7) . . (7)
<223> OTHER INFORMATION: Tyr, Phe, Trp, Asn, Gln, Gly or Ala

<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (8) . . (8)
<223> OTHER INFORMATION: Trp, Ala, Gly, Tyr or Phe

<220> FEATURE:
<223> OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

<400> SEQUENCE: 142
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1  5

<210> SEQ ID NO 143
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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

peptide

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (1) ... (1)
OTHER INFORMATION: Gly or Ala

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (2) ... (2)
OTHER INFORMATION: Tyr, Phe or Trp

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (3) ... (3)
OTHER INFORMATION: Thr, Ser, Cys or Met

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (4) ... (4)
OTHER INFORMATION: Phe, Tyr or Trp

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (5) ... (5)
OTHER INFORMATION: Thr, Ser or Cys

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (6) ... (6)
OTHER INFORMATION: Ser, Thr or Cys

FEATURE:

NAME/KEY: MOD_RES
LOCATION: (7) ... (7)
OTHER INFORMATION: Tyr, Phe or Trp

FEATURE:

OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 143
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp
1  5

SEQ ID NO 144
LENGTH: 10
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:

OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (1) ... (1)
OTHER INFORMATION: Ile, Leu, Val, Met or Ala
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (2) ... (2)
OTHER INFORMATION: Tyr, Phe, His, Arg, Lys, Ser or Thr
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (3) ... (3)
OTHER INFORMATION: Pro, Ser, Thr, Tyr, Phe, Arg, Lys or His
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (4) ... (4)
OTHER INFORMATION: Gly, Ala, Ser, Thr, Lys, Arg, His, Asp or Glu
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (5) ... (5)
OTHER INFORMATION: Thr, Ser or absent
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (6) ... (6)
OTHER INFORMATION: Arg, Lys, His or absent
FEATURE:

NAME/KEY: MOD_RES
LOCATION: (7) ... (7)
OTHER INFORMATION: Asn, Gln, Asp, Glu, Gly, Ala or absent
FEATURE:

NAME/KEY: MOD_RES
OTHER INFORMATION: Gly, Ala, Ser, Thr, Tyr or Phe

FEATURE:

OTHER INFORMATION: Asp, Glu, Ala, Gly, Asn or Gln

FEATURE:

OTHER INFORMATION: Thr, Ser, Ile, Leu, Val, Met, Ala, Lys, Arg or His

FEATURE:

OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 144

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

SEQ ID NO 145

LENGTH: 10

TYPE: PRT

ORGANISM: Artificial Sequence

FEATURE: Description of Artificial Sequence: Synthetic peptide

FEATURE:

OTHER INFORMATION: Ile, Leu, Val, Met or Ala

FEATURE:

OTHER INFORMATION: Tyr, Phe, His, Arg, Lys, Ser or Thr

FEATURE:

OTHER INFORMATION: Pro, Ser, Thr, Tyr or Phe

FEATURE:

OTHER INFORMATION: Gly, Ala, Ser, Thr, Lys, Arg or His

FEATURE:

OTHER INFORMATION: Thr, Ser or absent

FEATURE:

OTHER INFORMATION: Arg, Lys, His or absent

FEATURE:

OTHER INFORMATION: Asn, Gln, Asp, Glu or absent

FEATURE:

OTHER INFORMATION: Gly, Ala, Ser, Thr, Tyr or Phe

FEATURE:

OTHER INFORMATION: Asp, Glu, Ala, Gly, Asn or Gln

FEATURE:

OTHER INFORMATION: Thr, Ser, Ile, Leu, Val, Met or Ala

FEATURE:

OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments

SEQUENCE: 145

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
<210> SEQ ID NO: 146
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
<221> NAME/KEY: MOD_RES
<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: Ala, Gly, Val, Leu, Ile or Met
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: Arg, Lys, His, Cys or Met
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: Gly, Ala, Arg, Lys, His, Ser, Thr, Tyr, Phe, Trp, Asp, Glu or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (4)...(4)
<223> OTHER INFORMATION: Tyr, Phe, Trp, Asn, Gln, Gly, Ala, Arg, Lys, His or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: Ser, Thr, Asn, Gln, Asp or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: Asp, Glu or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: Leu, Ile, Val, Met, Ala, Ser, Thr or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: Leu, Ile, Val, Met, Ala or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: Gly, Ala, Arg, Lys, His or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: Ile, Leu, Val, Met, Ala, Asn, Gln, Arg, Lys, His or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (11)...(11)
<223> OTHER INFORMATION: Ala, Met, Phe, Tyr, Trp, Ser, Thr, Gly or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (12)...(12)
<223> OTHER INFORMATION: Trp, Tyr, Phe, Ala, Gly or absent
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: Phe, Tyr, Trp, Gly, Ala, Met or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (14)...(14)
<223> OTHER INFORMATION: Ala, Gly, Met, Asp, Glu, Trp, Tyr or Phe
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (15)...(15)
<223> OTHER INFORMATION: Tyr, Phe, Trp, Gly, Ala or Val
<220> FEATURE:
<223> OTHER INFORMATION: see specification as filed for detailed description of substitutions and preferred embodiments
We claim:

1. A cell transformed with a nucleic acid molecule encoding a heavy chain or light chain of an antibody that specifically binds to a human VASA protein comprising an immunoglobulin heavy chain and an immunoglobulin light chain, wherein the variable region of said light chain comprises:
   a) wherein the variable region of said heavy chain comprises:
      i) a CDR1 region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 83-88;
      ii) a CDR2 region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 89-95; and
      iii) a CDR3 region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 96-104; and

b) wherein a CDR3 region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 105-112;

2. The cell of claim 1, wherein said nucleic acid molecule is selected from the group consisting of a cloning vector, an expression vector, a heterologous recombination vector, and a viral integration vector.

3. The cell of claim 1, wherein said cell is a mammalian cell.

4. The cell of claim 3, wherein said cell is a rodent cell.

5. The cell of claim 3, wherein said cell is a Chinese Hamster Ovary (CHO) cell.

6. The cell of claim 3, wherein said cell is a human cell.

* * * * *