



US012384842B2

(12) **United States Patent**
Loew et al.

(10) **Patent No.:** US 12,384,842 B2
(b5) **Date of Patent:** *Aug. 12, 2025

(54) **ANTIBODY MOLECULES THAT BIND TO NKP30 AND USES THEREOF**

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Related U.S. Application Data

(63) Continuation of application No. PCT/US2020/019329, filed on Feb. 21, 2020.

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(60) Provisional application No. 62/808,582, filed on Feb. 21, 2019.

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(51) **Int. Cl.**

<i>C07K 16/28</i>	(2006.01)
<i>A61K 39/395</i>	(2006.01)
<i>A61K 45/06</i>	(2006.01)

(52) **U.S. Cl.**

CPC	<i>C07K 16/2803</i> (2013.01); <i>A61K 39/3955</i> (2013.01); <i>C07K 2317/24</i> (2013.01); <i>C07K 2317/31</i> (2013.01); <i>C07K 2317/52</i> (2013.01); <i>C07K 2317/565</i> (2013.01)
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(58) **Field of Classification Search**

CPC	<i>C07K 16/2803; C07K 2317/24; C07K 2317/31; C07K 2317/52; C07K 2317/565; C07K 2317/74; A61K 39/3955; A61K 45/06; A61P 31/00; A61P 35/00; A61P 37/00</i>
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See application file for complete search history.

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Antibody molecules that specifically bind to NKp30 are disclosed. The anti-NKp30 antibody molecules can be used to treat, prevent and/or diagnose cancerous, autoimmune or infectious conditions and disorders.

23 Claims, 2 Drawing Sheets
Specification includes a Sequence Listing.

ABSTRACT

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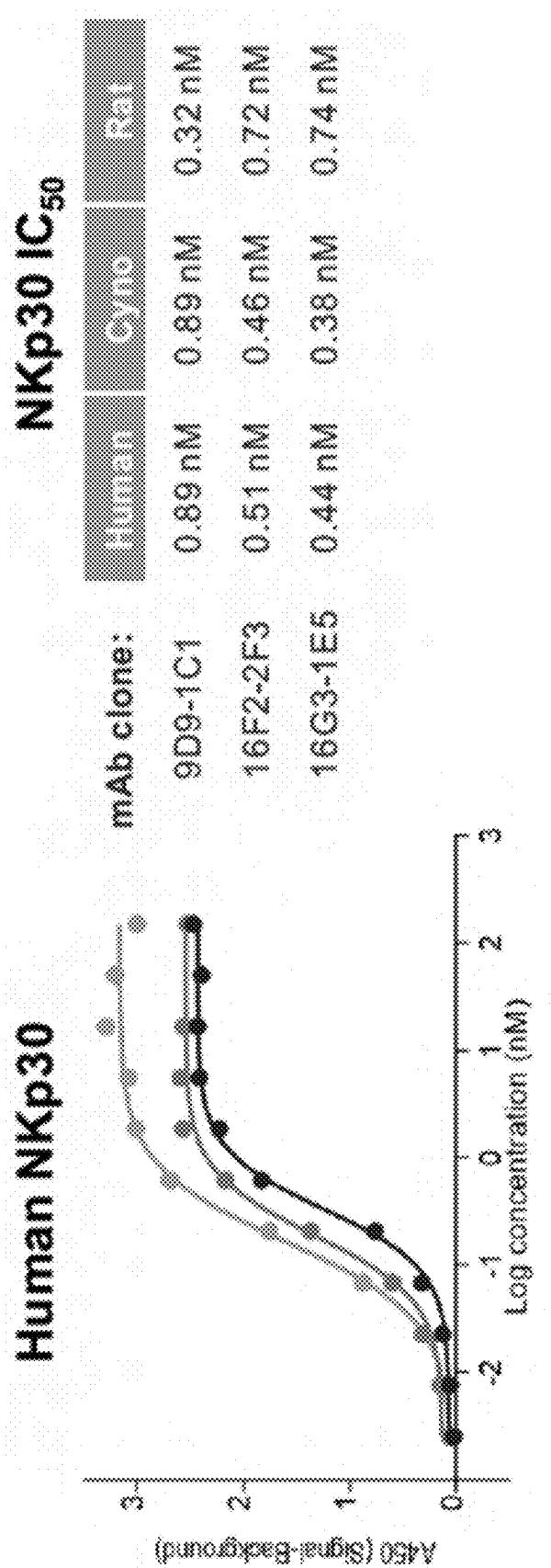
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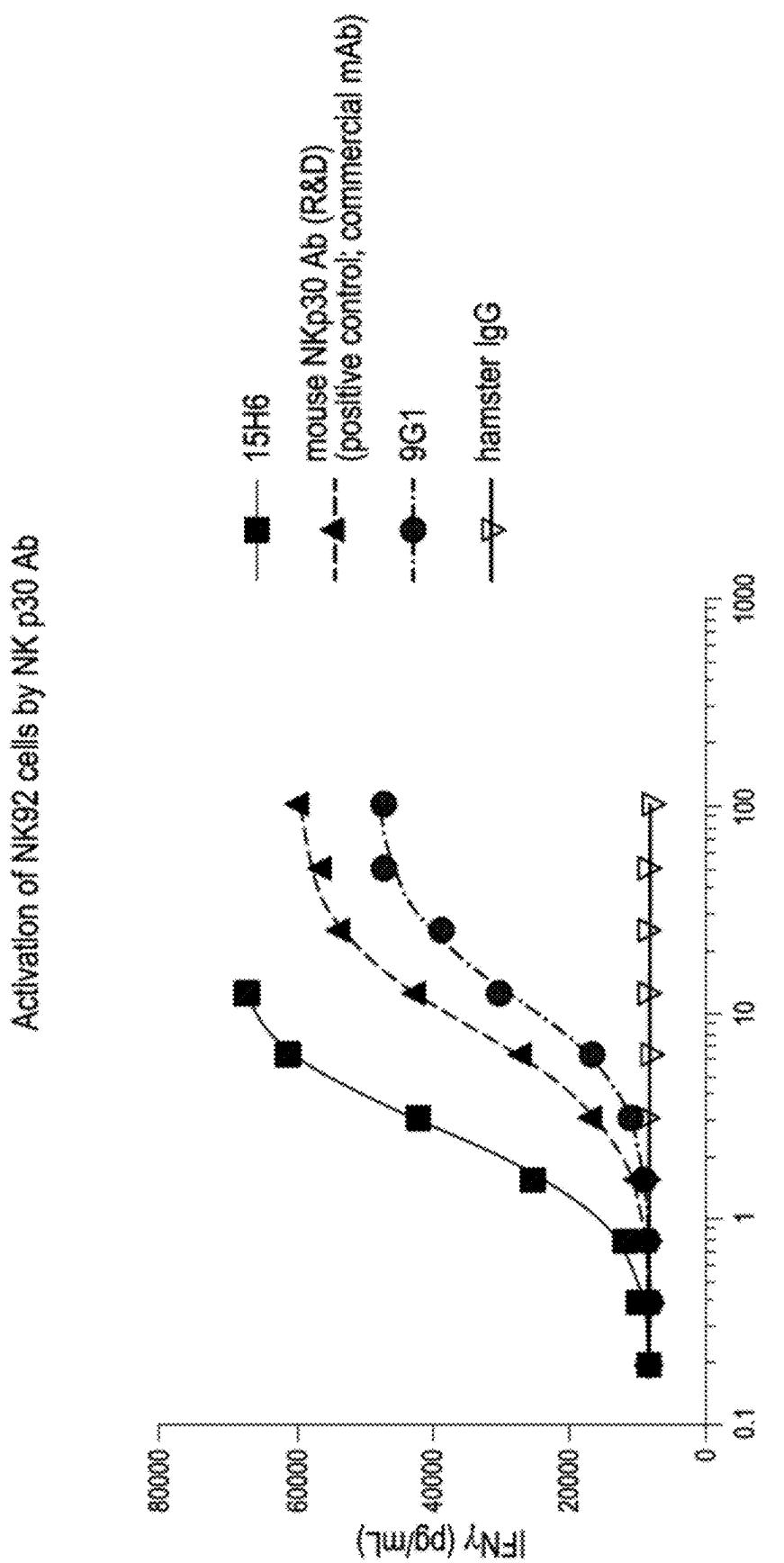


FIG. 2

1

**ANTIBODY MOLECULES THAT BIND TO
NKP30 AND USES THEREOF**

RELATED APPLICATIONS

This application is a continuation of International Application No. PCT/US2020/019329, filed on Feb. 21, 2020, which claims the benefit of U.S. Provisional Application 62/808,582 filed Feb. 21, 2019, the entire contents of each of which are hereby incorporated by reference.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Feb. 20, 2020, is named 53676-735.301_SL.txt and is 517,567 bytes in size.

BACKGROUND

Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKP30, NKP44 and NKP46.

Given the importance of immune checkpoint pathways in regulating an immune response, the need exists for developing novel agents that modulate the activity of immunoinhibitory proteins, such as PD-1, thus leading to activation of the immune system. Such agents can be used, e.g., for cancer immunotherapy and treatment of other conditions, such as chronic infection.

SUMMARY OF THE INVENTION

Disclosed herein are antibody molecules (e.g., humanized antibody molecules) that bind to NKP30 with high affinity and specificity. Nucleic acid molecules encoding the antibody molecules, expression vectors, host cells and methods for making the antibody molecules are also provided. Multi- or bispecific or multifunctional antibody molecules and pharmaceutical compositions comprising the antibody molecules are also provided. The anti-NKP30 antibody molecules disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent and/or diagnose disorders, such as cancerous disorders (e.g., solid and soft-tissue tumors), as well as autoimmune and infectious diseases. Thus, compositions and methods for detecting NKP30, as well as methods for treating various disorders including cancer, autoimmune and/or infectious diseases, using the anti-NKP30 antibody molecules are disclosed herein.

Accordingly, in one aspect, the invention features an antibody molecule (e.g., an isolated or recombinant antibody molecule), comprising one or more sequences according to the following enumerated embodiments. Additional features of any of the disclosed antibody molecules, multifunctional molecules, nucleic acids, vectors, host cells, or methods include one or more of the following enumerated embodiments.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention

2

described herein. Such equivalents are intended to be encompassed by the following enumerated embodiments.

ENUMERATED EMBODIMENTS

- 5 1. An isolated antibody molecule that binds to NKP30, comprising:
 - (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 7315 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or
 - (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 7327 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7329 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).
- 10 2. The antibody molecule of embodiment 1, wherein the antigen binding domain comprises:
 - (i) a VH comprising the amino acid sequence of any of SEQ ID NOs: 7298 or 7300-7304 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to any of SEQ ID NOs: 7298 or 7300-7304), and/or
 - (ii) a VL comprising the amino acid sequence of any of SEQ ID NOs: 7299 or 7305-7309 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to any of SEQ ID NOs: 7299 or 7305-7309).
- 15 3. The antibody molecule of embodiment 2, wherein the antigen binding domain comprises:
 - (i) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7305 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7305); or
 - (ii) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7309 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7309).
- 20 4. The antibody molecule of any of embodiments 1-3, wherein the antigen binding domain comprises:
 - (i) an amino acid sequence of SEQ ID NO: 7310 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7310); or
 - (ii) an amino acid sequence of SEQ ID NO: 7311 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7311).
- 25 5. An isolated antibody molecule that binds to NKP30, comprising:

- (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and
- (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

6. The antibody molecule of embodiment 5, wherein the antigen binding domain comprises:

- (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and
- (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

7. The antibody molecule of embodiment 5 or 6, wherein the antigen binding domain comprises:

- (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6006 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or
- (2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ

ID NO: 6069 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

8. The antibody molecule of embodiment 7, wherein the antigen binding domain comprises:

- (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and

- (3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

9. The antibody molecule of any one of embodiments 5-8, wherein the antigen binding domain comprises:

- (i) a VH comprising the amino acid sequence of SEQ ID NO: 6121 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6121), and/or

- (ii) a VL comprising the amino acid sequence of SEQ ID NO: 7294 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 7294).

10. The antibody molecule of any one of embodiments 5-9, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOS: 6148 or 6149 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOS: 6148 or 6149).

11. The antibody molecule of either of embodiments 5-10, wherein the antigen binding domain comprises a light chain comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6150).

12. The antibody molecule of either of embodiments 5-11, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOS: 6148 or 6149 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOS: 6148 or 6149), and a light chain comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6150).

13. The antibody molecule of any of embodiments 5-12, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6015 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6016 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6017 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

14. The antibody molecule of embodiment 13, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework

NO: 6036 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6037 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6038 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

29. The antibody molecule of embodiment 28, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6035, a VHFWR2 amino acid sequence of SEQ ID NO: 6036, a VHFWR3 amino acid sequence of SEQ ID NO: 6037, or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.

30. The antibody molecule of embodiment 29, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6128 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6128).

31. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6078 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6079 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6080 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

32. The antibody molecule of embodiment 31, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077, a VLFWR2 amino acid sequence of SEQ ID NO: 6078, a VLFWR3 amino acid sequence of SEQ ID NO: 6079, or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

33. The antibody molecule of embodiment 32, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6137 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6137).

34. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6082 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6083 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6084 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

35. The antibody molecule of embodiment 34, wherein
the antigen binding domain comprises a light chain variable
region (VL) comprising a light chain framework region 1
(VLFWR1) amino acid sequence of SEQ ID NO: 6081, a
5 VLFWR2 amino acid sequence of SEQ ID NO: 6082, a
VLFWR3 amino acid sequence of SEQ ID NO: 6083, or a
VLFWR4 amino acid sequence of SEQ ID NO: 6084.

36. The antibody molecule of embodiment 35, wherein
the antigen binding domain comprises a VL comprising the
amino acid sequence of SEQ ID NO: 6138 (or an amino acid
sequence having at least about 93%, 95%, or 99% sequence
identity to SEQ ID NO: 6138).

15 37. The antibody molecule of any of embodiments 5, 6, or
13-30, wherein the antigen binding domain comprises a light
chain variable region (VL) comprising a light chain frame-
work region 1 (VLFWR1) amino acid sequence of SEQ ID
NO: 6085 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VLFWR2 amino acid sequence of SEQ ID
NO: 6086 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VLFWR3 amino acid sequence of SEQ ID
NO: 6087 (or a sequence with no more than 1, 2, 3, 4, 5, or
20 6 mutations, e.g., substitutions, additions, or deletions,
therefrom), or a VLFWR4 amino acid sequence of SEQ ID
NO: 6088 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom),
25

30 38. The antibody molecule of embodiment 37, wherein
the antigen binding domain comprises a light chain variable
region (VL) comprising a light chain framework region 1
(VLFWR1) amino acid sequence of SEQ ID NO: 6085, a
VLFWR2 amino acid sequence of SEQ ID NO: 6086, a
35 VLFWR3 amino acid sequence of SEQ ID NO: 6087, or a
VLFWR4 amino acid sequence of SEQ ID NO: 6088.

39. The antibody molecule of embodiment 38, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6139 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6139).

40. The antibody molecule of any of embodiments 5, 6, or
13-30, wherein the antigen binding domain comprises a light
chain variable region (VL) comprising a light chain frame-
45 work region 1 (VLFWR1) amino acid sequence of SEQ ID
NO: 6089 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VLFWR2 amino acid sequence of SEQ ID
NO: 6090 (or a sequence with no more than 1, 2, 3, 4, 5, or
50 6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VLFWR3 amino acid sequence of SEQ ID
NO: 6091 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), or a VLFWR4 amino acid sequence of SEQ ID
55 NO: 6092 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom).

41. The antibody molecule of embodiment 40, wherein
the antigen binding domain comprises a light chain variable
region (VL) comprising a light chain framework region 1
(VLFWR1) amino acid sequence of SEQ ID NO: 6089, a
VLFWR2 amino acid sequence of SEQ ID NO: 6090, a
VLFWR3 amino acid sequence of SEQ ID NO: 6091, or a
VLFWR4 amino acid sequence of SEQ ID NO: 6092.

65 42. The antibody molecule of embodiment 41, wherein
the antigen binding domain comprises a VL comprising the
amino acid sequence of SEQ ID NO: 6140 (or an amino acid

sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6140).

43. The antibody molecule of any of embodiments 5, 6, or 13-30, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6094 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6095 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6096 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

44. The antibody molecule of embodiment 43, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093, a VLFWR2 amino acid sequence of SEQ ID NO: 6094, a VLFWR3 amino acid sequence of SEQ ID NO: 6095, or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.

45. The antibody molecule of embodiment 44, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6141 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6141).

46. An isolated antibody molecule that binds to NKp30, comprising:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

47. The antibody molecule of embodiment 46, wherein the antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070,

a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

48. The antibody molecule of embodiments 46 or 47, wherein the antigen binding domain comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6013 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or

(2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6076 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

49. The antibody molecule of embodiment 48, wherein the antigen binding domain comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and

(3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

50. The antibody molecule of any one of embodiments 46-49, wherein the antigen binding domain comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 6122 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6122), and/or

(ii) a VL comprising the amino acid sequence of SEQ ID NO: 6136 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6136).

51. The antibody molecule of any of embodiments 46-50, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOS: 6151 or 6152 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOS: 6151 or 6152).

52. The antibody molecule of any of embodiments 46-51, wherein the antigen binding domain comprises a light chain

11

comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6153).

53. The antibody molecule of any of embodiments 46-51, wherein the antigen binding domain comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6151 or 6152 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6151 or 6152), and a light chain comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6153).

54. The antibody molecule of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6040 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6041 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6042 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

55. The antibody molecule of embodiment 54, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039, a VHFWR2 amino acid sequence of SEQ ID NO: 6040, a VHFWR3 amino acid sequence of SEQ ID NO: 6041, or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

56. The antibody molecule of embodiment 55, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6129 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6129).

57. The antibody molecule of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6044 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6045 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6046 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

58. The antibody molecule of embodiment 57, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043, a VHFWR2 amino acid sequence of SEQ ID NO: 6044, a VHFWR3 amino acid sequence of SEQ ID NO: 6045, or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.

12

59. The antibody molecule of embodiment 58, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6130 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6130).

60. The antibody molecule of any of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6048 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6049 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6050 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

61. The antibody molecule of embodiment 60, wherein
the antigen binding domain comprises a heavy chain vari-
able region (VH) comprising a heavy chain framework
region 1 (VHFWR1) amino acid sequence of SEQ ID NO:
25 6047, a VHFWR2 amino acid sequence of SEQ ID NO:
6048, a VHFWR3 amino acid sequence of SEQ ID NO:
6049, or a VHFWR4 amino acid sequence of SEQ ID NO:
6050.

30 62. The antibody molecule of embodiment 61, wherein
the antigen binding domain comprises a VH comprising the
amino acid sequence of SEQ ID NO: 6131 (or an amino acid
sequence having at least about 75%, 80%, 85%, 90%, 95%,
or 99% sequence identity to SEQ ID NO: 6131).

35 63. The antibody molecule of any of embodiments 46 or
47, wherein the antigen binding domain comprises a heavy
chain variable region (VH) comprising a heavy chain frame-
work region 1 (VHFWR1) amino acid sequence of SEQ ID
NO: 6051 (or a sequence with no more than 1, 2, 3, 4, 5, or
40 6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VHFWR2 amino acid sequence of SEQ ID
NO: 6052 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VHFWR3 amino acid sequence of SEQ ID
45 NO: 6053 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), or a VHFWR4 amino acid sequence of SEQ ID
NO: 6054 (or a sequence with no more than 1, 2, 3, 4, 5, or
50 6 mutations, e.g., substitutions, additions, or deletions,
therefrom).

50 thereof).
54 64. The antibody molecule of embodiment 63, wherein
the antigen binding domain comprises a heavy chain vari-
able region (VH) comprising a heavy chain framework
region 1 (VHFWR1) amino acid sequence of SEQ ID NO:
55 6051, a VHFWR2 amino acid sequence of SEQ ID NO:
6052, a VHFWR3 amino acid sequence of SEQ ID NO:
6053, or a VHFWR4 amino acid sequence of SEQ ID NO:
6054.

65. The antibody molecule of embodiment 64, wherein
60 the antigen binding domain comprises a VH comprising the
amino acid sequence of SEQ ID NO: 6132 (or an amino acid
sequence having at least about 75%, 80%, 85%, 90%, 95%,
or 99% sequence identity to SEQ ID NO: 6132).

66. The antibody molecule of any of embodiments 46 or
67, wherein the antigen binding domain comprises a heavy
chain variable region (VH) comprising a heavy chain frame-
work region 1 (VHFWR1) amino acid sequence of SEQ ID

13

NO: 6055 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6058 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

67. The antibody molecule of embodiment 66, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055, a VHFWR2 amino acid sequence of SEQ ID NO: 6056, a VHFWR3 amino acid sequence of SEQ ID NO: 6057, or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.

68. The antibody molecule of embodiment 67, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6133 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6133).

69. The antibody molecule of any of embodiments 46 or 47, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6062 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

70. The antibody molecule of embodiment 69, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

71. The antibody molecule of embodiment 70, wherein the antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6134 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6134).

72. The antibody molecule of any of embodiments 46, 47, or 54-71, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6098 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6099 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID

14

NO: 6100 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

73. The antibody molecule of embodiment 72, wherein
5 the antigen binding domain comprises a light chain variable
region (VL) comprising a light chain framework region 1
(VLFWR1) amino acid sequence of SEQ ID NO: 6097, a
VLFWR2 amino acid sequence of SEQ ID NO: 6098, a
VLFWR3 amino acid sequence of SEQ ID NO: 6099, or a
10 VLFWR4 amino acid sequence of SEQ ID NO: 6100.

74. The antibody molecule of embodiment 73, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6142 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6142).

75. The antibody molecule of any of embodiments 46, 47, or 54-74, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain

20 framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6102 (or a sequence with no more than 1, 2, 3, 4, 5, 25 or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6103 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID 30 NO: 6104 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom)

76. The antibody molecule of embodiment 75, wherein
the antigen binding domain comprises a light chain variable
region (VL) comprising a light chain framework region 1
35 (VLFWR1) amino acid sequence of SEQ ID NO: 6101, a
VLFWR2 amino acid sequence of SEQ ID NO: 6102, a
VLFWR3 amino acid sequence of SEQ ID NO: 6103, or a
VLFWR4 amino acid sequence of SEQ ID NO: 6104.

40 77. The antibody molecule of embodiment 76, wherein
the antigen binding domain comprises a VL comprising the
amino acid sequence of SEQ ID NO: 6143 (or an amino acid
sequence having at least about 93%, 95%, or 99% sequence
identity to SEQ ID NO: 6143).

45 78. The antibody molecule of any of embodiments 46, 47,
or 54-77, wherein the antigen binding domain comprises a
light chain variable region (VL) comprising a light chain
framework region 1 (VLFWR1) amino acid sequence of
SEQ ID NO: 6105 (or a sequence with no more than 1, 2, 3,
50 4, 5, or 6 mutations, e.g., substitutions, additions, or dele-
tions, therefrom), a VLFWR2 amino acid sequence of SEQ
ID NO: 6106 (or a sequence with no more than 1, 2, 3, 4, 5,
or 6 mutations, e.g., substitutions, additions, or deletions,
therefrom), a VLFWR3 amino acid sequence of SEQ ID
55 NO: 6107 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
therefrom), or a VLFWR4 amino acid sequence of SEQ ID
NO: 6108 (or a sequence with no more than 1, 2, 3, 4, 5, or
6 mutations, e.g., substitutions, additions, or deletions,
60 therefrom)

60 thereof).

79. The antibody molecule of embodiment 78, wherein
the antigen binding domain comprises a light chain variable
region (VL) comprising a light chain framework region 1
(VLFWR1) amino acid sequence of SEQ ID NO: 6105, a
65 VLFWR2 amino acid sequence of SEQ ID NO: 6106, a
VLFWR3 amino acid sequence of SEQ ID NO: 6107, or a
VLFWR4 amino acid sequence of SEQ ID NO: 6108.

15

80. The antibody molecule of embodiment 79, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6144 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6144).

81. The antibody molecule of any of embodiments 46, 47, or 54-80, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6110 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6111 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6112 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

82. The antibody molecule of embodiment 81, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109, a VLFWR2 amino acid sequence of SEQ ID NO: 6110, a VLFWR3 amino acid sequence of SEQ ID NO: 6111, or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

83. The antibody molecule of embodiment 78, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6145 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6145).

84. The antibody molecule of any of embodiments 46, 47, or 54-83, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6116 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

85. The antibody molecule of embodiment 84, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

86. The antibody molecule of embodiment 85, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6146 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6146).

87. The antibody molecule of any of embodiments 46, 47, or 54-86, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or dele-

16

tions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6120 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

88. The antibody molecule of embodiment 87, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID NO: 6119, or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

89. The antibody molecule of embodiment 88, wherein the antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6147 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6147).

90. The antibody molecule of any one of the preceding embodiments, wherein the antigen binding domain comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 6122 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6122), and/or

(ii) a VL comprising the amino acid sequence of SEQ ID NO: 6136 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6136).

91. A multispecific molecule comprising the antibody molecule of any of embodiments 1-90.

92. The multispecific molecule of embodiment 91, further comprising one, two, three, four or more of:

a. a tumor targeting moiety, e.g., as described herein;

b. a cytokine molecule, e.g., as described herein;

c. a T cell engager, e.g., as described herein; or

d. a stromal modifying moiety, e.g., as described herein.

93. The multispecific molecule of embodiment 91, further comprising a binding specificity that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.

94. The multispecific molecule of embodiment 91, further comprising a binding specificity that binds to an infected cell, e.g., a viral or bacterial infected cell.

95. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which is a monospecific antibody molecule, a bispecific antibody molecule, or a trispecific antibody molecule.

96. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which is a monovalent antibody molecule, a bivalent antibody molecule, or a trivalent antibody molecule.

97. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which is a full antibody (e.g., an antibody that includes at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains), or an antigen-binding fragment (e.g., a Fab, F(ab')₂, Fv, a single chain Fv, a single domain antibody, a diabody (dAb), a bivalent antibody, or a bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

98. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which comprises a

17

heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, or a fragment thereof.

99. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, which comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof.

100. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, wherein the immunoglobulin chain constant region (e.g., Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.

101. The antibody molecule, or the multispecific molecule of any of the preceding embodiments, wherein an interface of a first and second immunoglobulin chain constant regions (e.g., Fc region) is altered, e.g., mutated, to increase or decrease dimerization, e.g., relative to a non-engineered interface.

102. The antibody molecule or the multispecific molecule of embodiment 101, wherein the dimerization of the immunoglobulin chain constant region (e.g., Fc region) is enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired cavity-protuberance ("knob-in-a hole"), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer:homomultimer forms, e.g., relative to a non-engineered interface.

103. The antibody molecule or the multispecific molecule of embodiment 101 or 102, wherein the immunoglobulin chain constant region (e.g., Fc region) comprises an amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1.

104. The antibody molecule or the multispecific molecule of embodiment 103, wherein the immunoglobulin chain constant region (e.g., Fc region) comprises an amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), or T366W (e.g., corresponding to a protuberance or knob), or a combination thereof.

105. The antibody molecule or the multispecific molecule of any of embodiments 1-104, further comprising a linker, e.g., a linker between one or more of: the targeting moiety and the cytokine molecule or the stromal modifying moiety, the targeting moiety and the immune cell engager, the cytokine molecule or the stromal modifying moiety, and the immune cell engager, the cytokine molecule or the stromal modifying moiety and the immunoglobulin chain constant region (e.g., the Fc region), the targeting moiety and the immunoglobulin chain constant region, or the immune cell engager and the immunoglobulin chain constant region.

106. The antibody molecule or the multispecific molecule of embodiment 105, wherein the linker is selected from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker.

107. The antibody molecule or the multispecific molecule of embodiment 106, wherein the linker is a peptide linker.

108. The antibody molecule or the multispecific molecule of embodiment 107, wherein the peptide linker comprises Gly and Ser.

109. An isolated nucleic acid molecule, which comprises the nucleotide sequence encoding any of the antibody molecules or multispecific or multifunctional molecules described herein, or a nucleotide sequence substantially homologous thereto (e.g., at least 95% to 99.9% identical thereto).

18

110. An isolated nucleic acid encoding the antibody molecule or the multispecific molecule of any of embodiments 1-108.

111. A vector, e.g., an expression vector, comprising one or more of the nucleic acid molecules of any of embodiments 109 or 110.

112. A host cell comprising the nucleic acid molecule or the vector of embodiment 111.

113. A method of making, e.g., producing, the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of embodiments 1-108, comprising culturing the host cell of embodiment 112, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

114. A pharmaceutical composition comprising the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of embodiments 1-108 and a pharmaceutically acceptable carrier, excipient, or stabilizer.

115. A method of treating a cancer, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the cancer.

116. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating cancer.

117. The method of embodiment 115 or the use of embodiment 116, wherein the cancer is a solid tumor cancer, or a metastatic lesion.

118. The method of embodiment 117 or the use of embodiment 117, wherein the solid tumor cancer is one or more of pancreatic (e.g., pancreatic adenocarcinoma), breast, colorectal, lung (e.g., small or non-small cell lung cancer), skin, ovarian, or liver cancer.

119. The method of embodiment 115 or the use of embodiment 116, wherein the cancer is a hematological cancer.

120. The method of any of embodiments 115 or 116-119 or the use of any of embodiments 116-119, further comprising administering a second therapeutic treatment.

121. The method of embodiment 120 or the use of embodiment 120, wherein the second therapeutic treatment comprises a therapeutic agent (e.g., a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery.

122. The method of embodiment 121 or the use of embodiment 121, wherein the therapeutic agent is selected from: a chemotherapeutic agent, or a biologic agent.

123. A method of treating an autoimmune or an inflammatory disorder, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the autoimmune or the inflammatory disorder.

124. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating an autoimmune or an inflammatory disorder.

125. A method of treating an infectious disorder, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the infectious disorder.

126. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating an infectious disorder.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a graph showing binding of NKp30 antibodies to NK92 cells. Data was calculated as the percent-AF747 positive population.

FIG. 2 is a graph showing activation of NK92 cells by NKp30 antibodies. Data were generated using hamster anti-NKp30 mAbs.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

Certain terms are defined below.

As used herein, the articles “a” and “an” refer to one or more than one, e.g., to at least one, of the grammatical object of the article. The use of the words “a” or “an” when used in conjunction with the term “comprising” herein may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.”

As used herein, “about” and “approximately” generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given range of values.

As used herein, the term “molecule” as used in, e.g., antibody molecule, cytokine molecule, receptor molecule, includes full-length, naturally-occurring molecules, as well as variants, e.g., functional variants (e.g., truncations, fragments, mutated (e.g., substantially similar sequences) or derivatized form thereof), so long as at least one function and/or activity of the unmodified (e.g., naturally-occurring) molecule remains.

“Antibody molecule” as used herein refers to a protein, e.g., an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. An antibody molecule encompasses antibodies (e.g., full-length antibodies) and antibody fragments. In an embodiment, an antibody molecule comprises an antigen binding or functional fragment of a full-length antibody, or a full-length immunoglobulin chain. For example, a full-length antibody is an immunoglobulin (Ig) molecule (e.g., an IgG antibody) that is naturally occurring or formed by normal immunoglobulin gene fragment recombinatorial processes). In embodiments, an antibody molecule refers to an immunologically active, antigen-binding portion of an immunoglobulin molecule, such as an antibody fragment. An antibody fragment, e.g., functional fragment, is a portion of an antibody, e.g., Fab, Fab', F(ab')₂, F(ab)₂, variable fragment (Fv), domain antibody (dAb), or single chain variable fragment (scFv). A functional antibody fragment binds to the same antigen as that recognized by the intact (e.g., full-length) antibody. The terms “antibody fragment” or “functional fragment” also include isolated fragments consisting of the variable regions, such as the “Fv” fragments consisting of the variable regions of the heavy and light chains or recombinant single chain polypeptide molecules in which light and heavy variable regions are connected by a peptide linker (“scFv proteins”). In some embodiments, an antibody fragment does not include portions of antibodies without antigen binding activity, such as

Fc fragments or single amino acid residues. Exemplary antibody molecules include full length antibodies and antibody fragments, e.g., dAb (domain antibody), single chain, Fab, Fab', and F(ab')₂ fragments, and single chain variable fragments (scFvs).

As used herein, an “immunoglobulin variable domain sequence” refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids, or may include other alterations that are compatible with formation of the protein structure.

15 In embodiments, an antibody molecule is monospecific, e.g., it comprises binding specificity for a single epitope. In some embodiments, an antibody molecule is multispecific, e.g., it comprises a plurality of immunoglobulin variable domain sequences, where a first immunoglobulin variable domain sequence has binding specificity for a first epitope and a second immunoglobulin variable domain sequence has binding specificity for a second epitope. In some embodiments, an antibody molecule is a bispecific antibody molecule. “Bispecific antibody molecule” as used herein refers to an antibody molecule that has specificity for more than one (e.g., two, three, four, or more) epitope and/or antigen.

“Antigen” (Ag) as used herein refers to a molecule that can provoke an immune response, e.g., involving activation of certain immune cells and/or antibody generation. Any 30 macromolecule, including almost all proteins or peptides, can be an antigen. Antigens can also be derived from genomic recombinant or DNA. For example, any DNA comprising a nucleotide sequence or a partial nucleotide sequence that encodes a protein capable of eliciting an immune response encodes an “antigen.” In embodiments, an antigen does not need to be encoded solely by a full-length nucleotide sequence of a gene, nor does an antigen need to be encoded by a gene at all. In embodiments, an antigen can be synthesized or can be derived from a biological sample, e.g., a tissue sample, a tumor sample, a cell, or a fluid with other biological components. As used, herein a “tumor antigen” or interchangeably, a “cancer antigen” includes any molecule present on, or associated with, a cancer, e.g., a cancer cell or a tumor microenvironment that can provoke an immune response. As used, herein an “immune cell antigen” includes any molecule present on, or associated with, an immune cell that can provoke an immune response.

The “antigen-binding site,” or “binding portion” of an antibody molecule refers to the part of an antibody molecule, e.g., an immunoglobulin (Ig) molecule, that participates in antigen binding. In embodiments, the antigen binding site is formed by amino acid residues of the variable (V) regions of the heavy (H) and light (L) chains. Three highly divergent stretches within the variable regions of the heavy and light chains, referred to as hypervariable regions, are disposed between more conserved flanking stretches called “framework regions,” (FRs). FRs are amino acid sequences that are naturally found between, and adjacent to, hypervariable regions in immunoglobulins. In embodiments, in an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface, which is complementary to the three-dimensional surface of a bound antigen. 55 The three hypervariable regions of each of the heavy and light chains are referred to as “complementarity-determining regions,” or “CDRs.” The framework region and CDRs have

been defined and described, e.g., in Kabat, E. A., et al. (1991) *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242, and Chothia, C. et al. (1987) *J. Mol. Biol.* 196:901-917. Each variable chain (e.g., variable heavy chain and variable light chain) is typically made up of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the amino acid order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

"Cancer" as used herein can encompass all types of oncogenic processes and/or cancerous growths. In embodiments, cancer includes primary tumors as well as metastatic tissues or malignantly transformed cells, tissues, or organs.

In embodiments, cancer encompasses all histopathologies and stages, e.g., stages of invasiveness/severity, of a cancer. In embodiments, cancer includes relapsed and/or resistant cancer. The terms "cancer" and "tumor" can be used interchangeably. For example, both terms encompass solid and liquid tumors. As used herein, the term "cancer" or "tumor" includes premalignant, as well as malignant cancers and tumors.

As used herein, an "immune cell" refers to any of various cells that function in the immune system, e.g., to protect against agents of infection and foreign matter. In embodiments, this term includes leukocytes, e.g., neutrophils, eosinophils, basophils, lymphocytes, and monocytes. Innate leukocytes include phagocytes (e.g., macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. Innate leukocytes identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms, and are mediators in the activation of an adaptive immune response. The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are important types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response. The term "immune cell" includes immune effector cells.

"Immune effector cell," as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include, but are not limited to, T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NK T) cells, and mast cells.

The term "effector function" or "effector response" refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

The compositions and methods of the present invention encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, e.g., sequences at least 80%, 85%, 90%, 95% identical or higher to the sequence specified. In the context of an amino acid sequence, the term "substantially identical" is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, e.g., a sequence provided herein.

In the context of nucleotide sequence, the term "substantially identical" is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For example, nucleotide sequences having at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, e.g., a sequence provided herein.

The term "variant" refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence. In some embodiments, the variant is a functional variant.

The term "functional variant" refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence, and is capable of having one or more activities of the reference amino acid sequence.

Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.

To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared.

When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology").

The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are

a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) CABIOS, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences described herein can be used as a “query sequence” to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (1990) *J Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to a nucleic acid molecule of the invention. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See ncbi.nlm.nih.gov.

It is understood that the molecules of the present invention may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

The term “amino acid” is intended to embrace all molecules, whether natural or synthetic, which include both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term “amino acid” includes both the D- or L-optical isomers and peptidomimetics.

A “conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

The terms “polypeptide”, “peptide” and “protein” (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The terms “nucleic acid,” “nucleic acid sequence,” “nucleotide sequence,” or “polynucleotide sequence,” and “polynucleotide” are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

The term “isolated,” as used herein, refers to material that is removed from its original or native environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of the environment in which it is found in nature.

Various aspects of the invention are described in further detail below. Additional definitions are set out throughout the specification.

Natural Killer Cell Engagers

Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKp30, NKp44 and NKp46. The NCRs initiate tumor targeting by recognition of heparan sulfate on cancer cells. NKG2D is a receptor that provides both stimulatory and costimulatory innate immune responses on activated killer (NK) cells, leading to cytotoxic activity. DNAM1 is a receptor involved in intercellular adhesion, lymphocyte signaling, cytotoxicity and lymphokine secretion mediated by cytotoxic T-lymphocyte (CTL) and NK cell. DAP10 (also known as HCST) is a transmembrane adapter protein which associates with KLRK1 to form an activation receptor KLRK1-HCST in lymphoid and myeloid cells; this receptor plays a major role in triggering cytotoxicity against target cells expressing cell surface ligands such as MHC class I chain-related MICA and MICB, and U (optionally L1)6-binding proteins (ULBPs); it KLRK1-HCST receptor plays a role in immune surveillance against tumors and is required for cytolysis of tumors cells; indeed, melanoma cells that do not express KLRK1 ligands escape from immune surveillance mediated by NK cells. CD16 is a receptor for the Fc region of IgG, which binds complexed or aggregated IgG and also monomeric IgG and thereby mediates antibody-dependent cellular cytotoxicity (ADCC) and other antibody-dependent responses, such as phagocytosis.

The present disclosure provides, inter alia, antibody molecules, e.g., multispecific (e.g., bi-, tri-, quad-specific) or multifunctional molecules, that are engineered to contain one or more NK cell engagers that mediate binding to and/or activation of an NK cell. Accordingly, in some embodi-

ments, the NK cell engager is selected from an antigen binding domain or ligand that binds to (e.g., activates): NKp30, NKp40, NKp44, NKp46, NKG2D, DNAM1, DAP10, CD16 (e.g., CD16a, CD16b, or both), CRTAM, CD27, PSGL1, CD96, CD100 (SEMA4D), NKp80, CD244 (also known as SLAMF4 or 2B4), SLAMF6, SLAMF7, KIR2DS2, KIR2DS4, KIR3DS1, KIR2DS3, KIR2DS5, KIR2DS1, CD94, NKG2C, NKG2E, or CD160.

In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Tables 7-10. In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in U.S. Pat. Nos. 6,979,546, 9,447,185, PCT Application No. WO2015121383A1, PCT Application No. WO2016110468A1, PCT Application No. WO2004056392A1, or U.S. Application Publication No. US20070231322A1, the sequences of which are hereby incorporated by reference. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp30, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKp30, the NK cell, or both.

In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more CDRs (e.g., VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and/or VLCDR3) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more framework regions (e.g., VFWR1, VFWR2, VFWR3, VFWR4, VLFWR1, VLFWR2, VLFWR3, and/or VLFWR4) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH and/or a VL disclosed in Table 9, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, any of the VH domains disclosed in Table 9 may be paired with any of the VL domains disclosed in Table 9 to form the antigen binding domain that binds to NKp30. In some embodiments, the antigen binding domain that binds to NKp30 comprises an amino acid sequence disclosed in Table 10, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto.

In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1), a VHCDR2, and a VHCDR3, and a VL comprising a light chain complementarity determining region 1 (VLCDR1), a VLCDR2, and a VLCDR3.

In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 6002, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID

NOS: 7313, 6008, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7326, 7327, and 7329, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 7315, 7326, 7327, and 7329, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 6002, 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6008, 6009, 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, 7315, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, 6009, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7298 or 7300-7304 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7299 or 7305-7309 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7302 and 7305, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7302 and 7309, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID

and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a

VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

- 5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a

10 VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or

15 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions),

20 a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a

25 VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ

30 ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ

35 ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

40 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID

45 NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO:

50 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence

55 with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a

60 VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.

65 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence

substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID NO: 6119, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid

sequence of SEQ ID NO: 6148 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6148). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6149). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6150). In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148, and a VL comprising the amino acid sequence of SEQ ID NO: 6150. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149, and a VL comprising the amino acid sequence of SEQ ID NO: 6150.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6151). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6152). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6153). In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151, and a VL comprising the amino acid sequence of SEQ ID NO: 6153. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152, and a VL comprising the amino acid sequence of SEQ ID NO: 6153.

In some embodiments, the antigen binding domain that targets NKp30 comprises an scFv. In some embodiments, the scFv comprises an amino acid sequence selected from SEQ ID NOS: 6187-6190, or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto.

TABLE 7

Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains							
Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
9G1-HC	QIQLQESG PGLVKPSQ SLSLTCSV TGF\$IN (SEQ ID NO: 6003)	TGGYHW N (SEQ ID NO: TGF\$IN (SEQ ID NO: 6000)	WIRQFP GKKLEW KS (SEQ (SEQ ID NO: 6003)	YIYSSGS TSYNPSL SKNQFFLQ ID NO: 6004)	RISITRDT LNSVITED (SEQ ID NO: 6005)	GNWHYF DF (SEQ ID NO: 6006)	WGQGTM VTVSS (SEQ ID NO: 6006)
15H6-HC	QIQLQESG PGLVKPSQ SLSLTCSV TGF\$IN (SEQ ID NO: 6010)	TGGYHW N (SEQ ID NO: TGF\$IN (SEQ ID NO: 6007)	WIRQFP GKKLEW KS (SEQ (SEQ ID NO: 6010)	YIYSSGT TRYNPSL SKNQFFLQ ID NO: 6011)	RISITRDT LNSVTPED (SEQ ID NO: 6012)	GNWHYF DY (SEQ ID NO: 6013)	WGQGTL VAVSS (SEQ ID NO: 6013)
9G1-HC_1	QIQLQESG PGLVKPSE TLSLTCTV SGFSIN (SEQ ID NO: 6014)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6000)	WIRQPA GKGLEW IG (SEQ ID NO: 6014)	YIYSSGS TSYNPSL SKNQFSLK KS (SEQ (SEQ ID NO: 6015)	RVTMSRDT SKNQFSLK LSSVTAAD (SEQ ID NO: 6016)	GNWHYF DF (SEQ ID NO: 6017)	WGQGTM VTVSS (SEQ ID NO: 6017)
9G1-HC_2	QIQLQESG PGLVKPSQ TLSLTCTV SGFSIN (SEQ ID NO: 6018)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6000)	WIRQHP GKGLEW IG (SEQ ID NO: 6018)	YIYSSGS TSYNPSL SKNQFSLK KS (SEQ (SEQ ID NO: 6019)	LVTISRDT SKNQFSLK LSSVTAAD (SEQ ID NO: 6020)	GNWHYF DF (SEQ ID NO: 6021)	WGQGTM VTVSS (SEQ ID NO: 6021)
9G1-HC_3	EIQLLESQ GGLVQPGG SLRLSCAV SGFSIN (SEQ ID NO: 6022)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6000)	WVRQAP GKGLEW VG (SEQ ID NO: 6022)	YIYSSGS TSYNPSL SKNTFYLQ KS (SEQ (SEQ ID NO: 6023)	RFTISRDT SKNTFYLQ MNSLRAED (SEQ ID NO: 6024)	GNWHYF DF (SEQ ID NO: 6025)	WGQGTM VTVSS (SEQ ID NO: 6025)
9G1-HC_4	QIQLVQSG AEVKKPGS SVKVSKV SGFSIN (SEQ ID NO: 6026)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6000)	WVRQAP GKGLEW MG (SEQ ID NO: 6026)	YIYSSGS TSYNPSL STNTFYME KS (SEQ (SEQ ID NO: 6027)	RVTITRDT STNTFYME LSSLRSED (SEQ ID NO: 6028)	GNWHYF DF (SEQ ID NO: 6029)	WGQGTM VTVSS (SEQ ID NO: 6029)
9G1-HC_5	EIQLVESQ GGLVQPGG SLRLSCAV SGFSIN (SEQ ID NO: 6030)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6000)	WVRQAP GKGLEW VG (SEQ ID NO: 6030)	YIYSSGS TSYNPSL AKNSFYLQ KS (SEQ (SEQ ID NO: 6032)	RFTISRDT AKNSFYLQ MNSLRAED (SEQ ID NO: 6033)	GNWHYF DF (SEQ ID NO: 6034)	WGQGTM VTVSS (SEQ ID NO: 6034)
9G1-HC_6	QIQLVQSG AEVKKPGA SVKVSKV SGFSIN (SEQ ID NO: 6035)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6000)	WVRQAP GKGLEW MG (SEQ ID NO: 6035)	YIYSSGS TSYNPSL STNTFYME KS (SEQ (SEQ ID NO: 6036)	RVTMTRDT STNTFYME LSSLRSED (SEQ ID NO: 6037)	GNWHYF DF (SEQ ID NO: 6038)	WGQGTM VTVSS (SEQ ID NO: 6038)
15H6-HC_1	QIQLQESG PGLVKPSQ TLSLTCTV SGFSIN (SEQ ID NO: 6039)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6007)	WIRQHP GKGLEW IG (SEQ ID NO: 6039)	YIYSSGT TRYNPSL SKNQFSLK KS (SEQ (SEQ ID NO: 6040)	LVTISRDT SKNQFSLK LSSVTAAD (SEQ ID NO: 6041)	GNWHYF DY (SEQ ID NO: 6042)	WGQGTL VTVSS (SEQ ID NO: 6042)
15H6-HC_2	QIQLQESG PGLVKPSE TLSLTCTV SGFSIN (SEQ ID NO: 6043)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6007)	WIRQPA GKGLEW IG (SEQ ID NO: 6043)	YIYSSGT TRYNPSL SKNQFSLK KS (SEQ (SEQ ID NO: 6044)	RVTMSRDT SKNQFSLK LSSVTAAD (SEQ ID NO: 6045)	GNWHYF DY (SEQ ID NO: 6046)	WGQGTL VTVSS (SEQ ID NO: 6046)
15H6-HC_3	EIQLLESQ GGLVQPGG SLRLSCAV SGFSIN (SEQ ID NO: 6007)	TGGYHW N (SEQ ID NO: SGFSIN (SEQ ID NO: 6007)	WVRQAP GKGLEW VG (SEQ ID NO: 6007)	YIYSSGT TRYNPSL SKNTFYLQ KS (SEQ (SEQ ID NO: 6008)	RFTISRDT SKNTFYLQ MNSLRAED (SEQ ID NO: 6009)	GNWHYF DY (SEQ ID NO: 6009)	WGQGTL VTVSS (SEQ ID NO: 6009)

TABLE 7-continued

Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains							
Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
	(SEQ ID NO: 6047)		ID NO: 6048)	6008)	(SEQ ID NO: 6049)	6009)	6050)
15H6-HC_4	QIQLVESG TGGYHW	WIRQAP	YIYSSGT RFTISRDT	GNWHYF	WGQGTL		
	GGLVKPGG N (SEQ	GKGLEW	TRYNPSL AKNSFYLQ	DY	VTVSS		
	SLRLSCAV ID NO:	VG	KS (SEQ MNSLRAED	(SEQ	(SEQ		
	SGFSIN 6007)	(SEQ	ID NO: TAVYYCAR	ID NO:	ID NO:		
	(SEQ ID NO: 6051)	ID NO: 6052)	6008)	(SEQ ID NO: 6053)	6009)	6054)	
15H6-HC_5	QIQLVQSG TGGYHW	WVRQAP	YIYSSGT RVTMTRDT	GNWHYF	WGQGTL		
	AEVKKPGN N (SEQ	GKGLEW	TRYNPSL STNTFYME	DY	VTVSS		
	SVKVSKV ID NO:	MG	KS (SEQ LSSLRSED	(SEQ	(SEQ		
	SGFSIN 6007)	(SEQ	ID NO: TAVYYCAR	ID NO:	ID NO:		
	(SEQ ID NO: 6055)	ID NO: 6056)	6008)	(SEQ ID NO: 6057)	6009)	6058)	
15H6-HC_6	EIQLVQSG TGGYHW	WVQQAP	YIYSSGT RVTITRDT	GNWHYF	WGQGTL		
	AEVKKPGN N (SEQ	GKGLEW	TRYNPSL STNTFYME	DY	VTVSS		
	TVKISCKV ID NO:	MG	KS (SEQ LSSLRSED	(SEQ	(SEQ		
	SGFSIN 6007)	(SEQ	ID NO: TAVYYCAR	ID NO:	ID NO:		
	(SEQ ID NO: 6059)	ID NO: 6060)	6008)	(SEQ ID NO: 6061)	6009)	6062)	

TABLE 18

Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains (according to the Kabat numbering scheme)							
Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
9G1-HC	QIQLQES GYHWN	WIRQFP	YIYSSGS RISITRDT	GNWHY	WGQGTM		
	GPGLVKP (SEQ	GKKLEW	TSYNPSL SKNQFFLQ	FDF	VTVSS		
	SQSLSLT ID NO:	MG	KS (SEQ LNSVTTED	(SEQ	(SEQ		
	CSVTGFS 7313)	(SEQ	ID NO: TATYYCAR	ID NO:	ID NO:		
	INTG	ID NO: 6004)	6001)	(SEQ	6002)	6006)	
	(SEQ			ID NO:			
	ID NO: 7317)			6005)			
15H6-HC	QIQLQES GYHWN	WIRQFP	YIYSSGT RISITRDT	GNWHY	WGQGTL		
	GPGLVKP (SEQ	GKKLEW	TSYNPSL SKNQFFLQ	FDY	VAVSS		
	SQSLSLT ID NO:	MG	KS (SEQ LNSVTPED	(SEQ	(SEQ		
	CSVTGFS 7313)	(SEQ	ID NO: TATYYCTR	ID NO:	ID NO:		
	INTG	ID NO: 6011)	6008)	(SEQ	6009)	6013)	
	(SEQ			ID NO:			
	ID NO: 7317)			6012)			
9G1-HC_1	QIQLQES GYHWN	WIRQPA	YIYSSGS RVTMMSRDT	GNWHY	WGQGTM		
	GPGLVKP (SEQ	GKGLEW	TSYNPSL SKNQFSLK	FDF	VTVSS		
	SETLSLT ID NO:	IG	KS (SEQ LSSVTAAD	(SEQ	(SEQ		
	CTVSGFS 7313)	(SEQ	ID NO: TAVYYCAR	ID NO:	ID NO:		
	INTG	ID NO: 6015)	6001)	(SEQ	6002)	6017)	
	(SEQ			ID NO:			
	ID NO: 7371)			6016)			
9G1-HC_2	QIQLQES GYHWN	WIRQHP	YIYSSGS LVTISRDT	GNWHY	WGQGTM		
	GPGLVKP (SEQ	GKGLEW	TSYNPSL SKNQFSLK	FDF	VTVSS		
	SQTLSLT ID NO:	IG	KS (SEQ LSSVTAAD	(SEQ	(SEQ		
	CTVSGFS 7313)	(SEQ	ID NO: TAVYYCAR	ID NO:	ID NO:		
	INTG	ID NO: 6019)	6001)	(SEQ	6002)	6021)	
	(SEQ			ID NO:			
	ID NO: 7372)			6020)			
9G1-HC_3	EIQLLES GYHWN	WVRQAP	YIYSSGS RFTISRDT	GNWHY	WGQGTM		
	GGGLVQP (SEQ	GKGLEW	TSYNPSL SKNTFYLQ	FDF	VTVSS		
	GGSLRLS ID NO:	VG	KS (SEQ MNSLRAED	(SEQ	(SEQ		
	CAVSGFS 7313)	(SEQ	ID NO: TAVYYCAR	ID NO:	ID NO:		

TABLE 18-continued

Exemplary heavy chain CDRs and FWRs
of NKp30-targeting antigen binding domains
(according to the Kabat numbering scheme)

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
	INTG (SEQ ID NO: 7373)		ID NO: 6001) 6023)	(SEQ ID NO: 6024)	(SEQ ID NO: 6002)	(SEQ ID NO: 6025)	
9G1-HC_4	QIQLVQS GYHWN GAEVKKP (SEQ GSSVKVS ID NO: CKVSGFS 7313) INTG (SEQ ID NO: 7374)	WVRQAP GQGLEW MG KS (SEQ (SEQ ID NO: 6027)	YIYSSGS TSYNPSL KS (SEQ (SEQ ID NO: 6001)	RVTITRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6028)	GNWHY FDF (SEQ ID NO: 6002)	WGQGTM VTVSS (SEQ ID NO: 6029)	
9G1-HC_5	EIQLVES GYHWN GGGLVQP (SEQ GGSLRLS ID NO: CAVSGFS 7313) INTG (SEQ ID NO: 7375)	WVRQAP GKGLEW VG KS (SEQ (SEQ ID NO: 6032)	YIYSSGS TSYNPSL AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6033)	RFTISRDT FDTISRD (SEQ ID NO: 6002)	GNWHY FDF (SEQ ID NO: 6034)	WGQGTM VTVSS	
9G1-HC_6	QIQLVQS GYHWN GAEVKKP (SEQ GASVKVS ID NO: CKVSGFS 7313) INTG (SEQ ID NO: 7376)	WVRQAP GQGLEW MG KS (SEQ (SEQ ID NO: 6036)	YIYSSGS TSYNPSL STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6037)	RVTMTRDT FDY (SEQ ID NO: 6002)	GNWHY FDF (SEQ ID NO: 6038)	WGQGTM VTVSS	
15H6-HC_1	QIQLQES GYHWN GPGLVKP (SEQ SQTLSLT ID NO: CTVSGFS 7313) INTG (SEQ ID NO: 7372)	WIRQHP GKGLEW IG KS (SEQ (SEQ ID NO: 6040)	YIYSSGT TRYNPSL LSSVTAAD TAVYYCAR (SEQ ID NO: 6008)	LVTISRDT SKNQFSLK (SEQ ID NO: 6041)	GNWHY FDY (SEQ ID NO: 6009)	WGQGTL VTVSS (SEQ ID NO: 6042)	
15H6-HC_2	QIQLQES GYHWN GPGLVKP (SEQ SETLSLT ID NO: CTVSGFS 7313) INTG (SEQ ID NO: 7371)	WIRQPA GKGLEW IG KS (SEQ (SEQ ID NO: 6044)	YIYSSGT TRYNPSL SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6008)	RVTMSRDT (SEQ ID NO: 6045)	GNWHY FDY (SEQ ID NO: 6009)	WGQGTL VTVSS (SEQ ID NO: 6046)	
15H6-HC_3	EIQLLES GYHWN GGGLVQP (SEQ GGSLRLS ID NO: CAVSGFS 7313) INTG (SEQ ID NO: 7373)	WVRQAP GKGLEW VG KS (SEQ (SEQ ID NO: 6048)	YIYSSGT TRYNPSL AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6049)	RFTISRDT FDY (SEQ ID NO: 6009)	GNWHY FDY (SEQ ID NO: 6050)	WGQGTL VTVSS (SEQ ID NO: 6050)	
15H6-HC_4	QIQLVES GYHWN GGGLVQP (SEQ GGSLRLS ID NO: CAVSGFS 7313) INTG (SEQ ID NO: 7377)	WIRQAP GKGLEW VG KS (SEQ (SEQ ID NO: 6052)	YIYSSGT TRYNPSL AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6008)	RFTISRDT FDY (SEQ ID NO: 6053)	GNWHY FDY (SEQ ID NO: 6009)	WGQGTL VTVSS (SEQ ID NO: 6054)	
15H6-HC_5	QIQLVQS GYHWN GAEVKKP (SEQ GASVKVS ID NO: CKVSGFS 7313) INTG (SEQ ID NO: 6056)	WVRQAP GQGLEW MG LKS (SEQ (SEQ ID NO: 6008)	YIYSSGT TRYNPS STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6008)	RVTMTRDT FDY (SEQ ID NO: 6009)	GNWHY FDY (SEQ ID NO: 6058)	WGQGTL VTVSS (SEQ ID NO: 6058)	

TABLE 18-continued

Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains (according to the Kabat numbering scheme)									
Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4		
	ID NO: 7376)			6057)					
15H6-HC_6	EIQLVQS GYHWN GAEVKKP (SEQ GATVKIS ID NO: CKVSGFS 7313) INTG ID NO: 7378)	WVQQAP GKGLEW KS (SEQ (SEQ ID NO: 6060)	YIYSSGT TRYNPSL LSSLRSED (SEQ ID NO: 6008)	RVTITRDT STNTFYME (SEQ TAVYYCAR (SEQ ID NO: 6061)	GNWHY FDY (SEQ ID NO: 6009)	WGQGTL VTVSS (SEQ ID NO: 6062)			
9D9-HC	QIQLQES GYHWN GPGLVKP (SEQ SQSLSL S ID NO: CSVTFGS 7313) INTG ID NO: 7312)	WIRQFP GKKVEW KS (SEQ (SEQ ID NO: 7314)	YIYSSGT TKYNPSL SKNQFFLQ (SEQ ID NO: 7385)	RISITRDT LNSVTTED (SEQ TATYYCAR (SEQ ID NO: 7315)	GDWHY FDY (SEQ ID NO: 7316)	WGQGTM VAVSS (SEQ ID NO: 7316)			
3A12-HC	QIQLQES GYHWN GPGLVKP (SEQ SQSLSL T ID NO: CSVTFGS 7313) INTG ID NO: 7317)	WIRQFP GKKLEW KS (SEQ (SEQ ID NO: 6004)	YIYSSGS TRYNPSL SKNQFFLQ (SEQ ID NO: 7318)	RFSITRDT LNSVTTED (SEQ TATYYCTR (SEQ ID NO: 6009)	GNWHY FDY (SEQ ID NO: 6013)	WGQGTL VAVSS (SEQ ID NO: 6013)			
12D10-HC	QIQLQES GYHWN GPGLVKP (SEQ SQSLSL T ID NO: CSVTFGS 7313) INTG ID NO: 7317)	WIRQFP GKKLEW KS (SEQ (SEQ ID NO: 6004)	YIYSSGT TRYNPSL SKNQFFLQ (SEQ ID NO: 6008)	RISITRDT LNSVTPED (SEQ TATYYCTR (SEQ ID NO: 6012)	GDWHY FDY (SEQ ID NO: 6012)	WGQGTM VAVSS (SEQ ID NO: 6012)			
15E1-HC	QIQLQES GYHWN GPGLVKP (SEQ SQSLSL S ID NO: CSVTFGS 7313) ITTT (SEQ ID NO: 7322)	WIRQFP GKKLEW KS (SEQ (SEQ ID NO: 6004)	YIYSSGS TSYNPSL SKNQFFLQ (SEQ ID NO: 6001)	RFSITRDT LNSVTTED (SEQ TATYYCAR (SEQ ID NO: 7323)	GDWHY FDY (SEQ ID NO: 7324)	WGPGTM VAVSS (SEQ ID NO: 7324)			
15E1_Humanized variant_VH1	QIQLQES GYHWN GPGLVKP (SEQ SQFLSLT ID NO: CTVSGFS 7313) ITTT (SEQ ID NO: 7330)	WIRQHP GKGLEW KS (SEQ (SEQ ID NO: 6019)	YIYSSGS TSYNPSL SKNQFSLK (SEQ ID NO: 6001)	LVTISRDT SKNQFFLQ (SEQ TAVYYCAR (SEQ ID NO: 6020)	GDWHY FDY (SEQ ID NO: 6006)	WGQGTM VTVSS (SEQ ID NO: 6006)			
15E1_Humanized variant_VH2	QIQLVES GYHWN GGGLVVP (SEQ GGSLRLS ID NO: CAVSGFS 7313) ITTT (SEQ ID NO: 7331)	WIRQAP GKGLEW KS (SEQ (SEQ ID NO: 6052)	YIYSSGS TSYNPSL AKNSFYLQ (SEQ ID NO: 6001)	RFTISRDT SKNQFFLQ (SEQ MNSLRAED (SEQ TAVYYCAR (SEQ ID NO: 6033)	GDWHY FDY (SEQ ID NO: 6006)	WGQGTM VTVSS (SEQ ID NO: 6006)			
15E1_Humanized variant_VH3	EIQLLES GYHWN GGGLVQP (SEQ GGSLRLS ID NO: CAVSGFS 7313) ITTT (SEQ ID NO: 7332)	WVRQAP GKGLEW KS (SEQ (SEQ ID NO: 6023)	YIYSSGS TSYNPSL SKNQFFLQ (SEQ ID NO: 6001)	RFTISRDT SKNQFFLQ (SEQ MNSLRAED (SEQ TAVYYCAR (SEQ ID NO: 6024)	GDWHY FDY (SEQ ID NO: 6006)	WGQGTM VTVSS (SEQ ID NO: 6006)			

TABLE 18-continued

Exemplary heavy chain CDRs and FWRS
of NKp30-targeting antigen binding domains
(according to the Kabat numbering scheme)

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
15E1_Humanized variant_VH4	EIQLVES GYHWN GGGLVQP (SEQ GGSRLS ID NO: CAVSGFS 7313) ITTT (SEQ ID NO: 7333)	WVRQAP GKGLEW VG (SEQ ID NO: 6023) ID NO: 7333)	YIYSSGS TSYNPSL KS (SEQ (SEQ ID NO: 6001) ID NO: 6033)	RFTISRDT AKNSFYLQ MNSLRAED (SEQ (SEQ ID NO: 7315) (SEQ ID NO: 6006)	GDWHY FDY VTVSS (SEQ (SEQ (SEQ ID NO: 7315) (SEQ ID NO: 6006)	WGQGTM VTVSS (SEQ (SEQ (SEQ ID NO: 7315) (SEQ ID NO: 6006)	
15E1_Humanized variant_VH5	QIQLVQS GYHWN GAEVKKP (SEQ GASVKS ID NO: CKVSGFS 7313) ITTT (SEQ ID NO: 7334)	WVRQAP GQGLEW MG (SEQ ID NO: 6027) ID NO: 7334)	YIYSSGS TSYNPSL KS (SEQ (SEQ ID NO: 6001) ID NO: 6037)	RVTMTRDT STNTFYME LSSLRSED (SEQ (SEQ ID NO: 7315) (SEQ ID NO: 6006)	GDWHY FDY VTVSS (SEQ (SEQ (SEQ ID NO: 7315) (SEQ ID NO: 6006)	WGQGTM VTVSS (SEQ (SEQ (SEQ ID NO: 7315) (SEQ ID NO: 6006)	

TABLE 8

Exemplary light chain CDRs and FWRS of
NKp30-targeting antigen binding domains

Ab ID	VLFWR1	VLCDR1	VLFWR2	VLCDR2	VLFWR3	VLCDR3	VLFWR4
9G1-LC	SYTLTQ SGERLS PPLLSV DKYVH ALGHKA (SEQ TITC ID NO: (SEQ 6063) ID NO: 6066)	WYQQKP GRAPVM VIY (SEQ 6064) ID NO: 6067)	ENDKRP S (SEQ ID NO: 6064)	GIPDQFSG SNSGNIAT LTISKAQA (SEQ (SEQ ID NO: 7293) NO: 7292)	QSWDST NSAV (SEQ (SEQ ID NO: 6069)	FGSGTQ LTVL (SEQ (SEQ ID NO: 6069)	
15H6-LC	SYTLTQ SGENLS PPSLSV DKYVH APGQKA (SEQ TIIC ID NO: (SEQ 6070) ID NO: 6073)	WYQQKP GRAPVM VIY (SEQ 6071) ID NO: 6074)	ENEKRP S (SEQ ID NO: 6071)	GIPDQFSG SNSGNIAT LTISKAQP (SEQ (SEQ ID NO: 6072) NO: 6075)	HYWESI NSVV (SEQ (SEQ ID NO: 6076)	FGSGTH LTVL (SEQ (SEQ ID NO: 6076)	
9G1-LC_1	QSVTTQ SGERLS PPSVSG DKYVH APGQRV (SEQ TISC ID NO: (SEQ 6063) ID NO: 6077)	WYQQLP GTAPKM LIY (SEQ 6064) ID NO: 6078)	ENDKRP S (SEQ ID NO: 6064)	GVPDRFSG SNSGNAS LAITGLQA (SEQ (SEQ ID NO: 7293) NO: 6079)	QSWDST NSAV (SEQ (SEQ ID NO: 6080)	FGGGTQ LTVL (SEQ (SEQ ID NO: 6080)	
9G1-LC_2	QSVTTQ SGERLS PPSASG DKYVH TPGORV (SEQ TISC ID NO: (SEQ 6063) ID NO: 6081)	WYQQLP GTAPKM LIY (SEQ 6064) ID NO: 6082)	ENDKRP S (SEQ ID NO: 6064)	GVPDRFSG SNSGNAS LAISGLQS (SEQ (SEQ ID NO: 7293) NO: 6083)	QSWDST NSAV (SEQ (SEQ ID NO: 6084)	FGGGTQ LTVL (SEQ (SEQ ID NO: 6084)	
9G1-LC_3	QSVTTQ SGERLS PPSASG DKYVH TPGORV (SEQ TISC ID NO: (SEQ 6063) ID NO: 6085)	WYQQLP GTAPKM LIY (SEQ 6064) ID NO: 6086)	ENDKRP S (SEQ ID NO: 6064)	GVPDRFSG SNSGNAS LAISGLRS (SEQ (SEQ ID NO: 7293) NO: 6087)	QSWDST NSAV (SEQ (SEQ ID NO: 6088)	FGGGTQ LTVL (SEQ (SEQ ID NO: 6088)	
9G1-LC_4	SSETTQ SGERLS PHSVSV DKYVH ATAQMA (SEQ RITC ID NO: (SEQ 6063) ID NO:	WYQQKP GQDPVM VIY (SEQ 6064) ID NO:	ENDKRP S (SEQ ID NO: 6064)	GIPERFSG SNPGNTAT LTISRIEA (SEQ (SEQ ID NO: 7293) (SEQ ID NO: 6092)	QSWDST NSAV (SEQ (SEQ ID NO: 6092)	FGGGTQ LTVL (SEQ (SEQ ID NO: 6092)	

TABLE 8-continued

Exemplary light chain CDRs and FWRs of NKp30-targeting antigen binding domains							
Ab ID	VLFWR1	VLCDR1	VLFWR2	VLCDR2	VLFWR3	VLCDR3	VLFWR4
	ID NO: 6089)	6090)		NO: 6091)			
9G1-LC_5	DIQMTQ SPSTLS ASVGDR VTITC ID NO:	SGERLS DKYVH (SEQ LIY (SEQ 6063) ID NO:	WYQQKP GKAPKM S (SEQ ID NO: (SEQ 6064) ID NO:	ENDKRP S (SEQ ID NO: (SEQ 6064) ID NO:	GVPSRFSG SNSGNEAT LTISSLQP DDFATYYC (SEQ ID 7293) NO: 6095)	QSWDST NSAV (SEQ (SEQ ID NO: ID NO: 6096)	FGGGTK VEIK (SEQ (SEQ ID NO: ID NO: 6093)
15H6-LC_1	QYVLTQ PPSASG TPGQRV TISC ID NO:	SGENLS DKYVH (SEQ LIY (SEQ 6070) ID NO:	WYQQLP GTAPKM S (SEQ ID NO: (SEQ 6071) ID NO:	ENEKRP S (SEQ ID NO: (SEQ 6071) ID NO:	GVPDRFSG SNSGNAS LAISGLQS EDEADYYC (SEQ ID 6072) NO: 6099)	HYWESI NSVV (SEQ (SEQ ID NO: ID NO: 6100)	FGEGETE LTVL
15H6-LC_2	QYVLTQ PPSASG TPGQRV TISC ID NO:	SGENLS DKYVH (SEQ LIY (SEQ 6070) ID NO:	WYQQLP GTAPKM S (SEQ ID NO: (SEQ 6071) ID NO:	ENEKRP S (SEQ ID NO: (SEQ 6071) ID NO:	GVPDRFSG SNSGNAS LAISGLRS EDEADYYC (SEQ ID 6072) NO: 6103)	HYWESI NSVV (SEQ (SEQ ID NO: ID NO: 6104)	FGEGETE LTVL
15H6-LC_3	SYELTQ PPVSVV SPGQTA SITC ID NO:	SGENLS DKYVH (SEQ VIY (SEQ 6070) ID NO:	WYQQKP GQSPVM S (SEQ VIY (SEQ 6071) ID NO:	ENEKRP S (SEQ ID NO: (SEQ 6071) ID NO:	GIPERFSG SNSGNTAT LTISGTQA MDEADYYC (SEQ ID 6072) NO: 6107)	HYWESI NSVV (SEQ (SEQ ID NO: ID NO: 6108)	FGEGETE LTVL
15H6-LC_4	DYVLTQ SPLSLP VTPGEP ASISC ID NO:	SGENLS DKYVH (SEQ LIY (SEQ 6070) ID NO:	WYLQKP GQSPQM S (SEQ LIY (SEQ 6071) ID NO:	ENEKRP S (SEQ ID NO: (SEQ 6071) ID NO:	GVPDRFSG SNSGNDAT LKIISRVEA EDVGVYYC (SEQ ID 6072) NO: 6111)	HYWESI NSVV (SEQ (SEQ ID NO: ID NO: 6112)	FGGGTK VEIK
15H6-LC_5	AYQLTQ SPSSL5 ASVGDR VTITC ID NO:	SGENLS DKYVH (SEQ LIY (SEQ 6070) ID NO:	WYQQKP GKAPKM S (SEQ LIY (SEQ 6071) ID NO:	ENEKRP S (SEQ ID NO: (SEQ 6071) ID NO:	GVPSRFSG SNSGNDAT LTISSLQP EDFATYYC (SEQ ID 6072) NO: 6115)	HYWESI NSVV (SEQ (SEQ ID NO: ID NO: 6116)	FGGGTK VEIK
15H6-LC_6	EYVLTQ SPATLS VSPGER ATLSC ID NO:	SGENLS DKYVH (SEQ LIY (SEQ 6070) ID NO:	WYQQKP GQAPRM S (SEQ LIY (SEQ 6071) ID NO:	ENEKRP S (SEQ ID NO: (SEQ 6071) ID NO:	GIPARFSG SNSGNEAT LTISSLQS EDFAVYYC (SEQ ID 6072) NO: 6119)	HYWESI NSVV (SEQ (SEQ ID NO: ID NO: 6120)	FGGGTK VEIK
9D9-LC	SYTLTQ PPLVSV ALGQKA TIIC ID NO:	SGENLS DKYVH (SEQ VIY (SEQ 6070) ID NO:	WYQQKP GRAPVM S (SEQ VIY (SEQ 6064) ID NO:	ENDKRP S (SEQ ID NO: (SEQ 6064) ID NO:	GIPDQFSG SNSGNIAT LTISKAQA GYEADYYC (SEQ ID 7321) NO: 7292)	HCWDST NSAV (SEQ (SEQ ID NO: ID NO: 6076)	FGSGTH LTVL
3A12-LC	SYTLTQ PPLVSV ALGQKA TIIC ID NO:	SGENLS DKYVH (SEQ VIY (SEQ 6070) ID NO:	WYQQKP GRAPVM S (SEQ VIY (SEQ 6064) ID NO:	ENDKRP S (SEQ ID NO: (SEQ 6064) ID NO:	GIPDQFSG SNSGNIAT LTISKAQA GYEADYYC (SEQ ID 7321) NO: 7292)	HCWDST NSAV (SEQ (SEQ ID NO: ID NO: 6076)	FGSGTH LTVL

TABLE 8-continued

Exemplary light chain CDRs and FWRs of NKp30-targeting antigen binding domains							
Ab ID	VLFWR1	VLCDR1	VLFWR2	VLCDR2	VLFWR3	VLCDR3	VLFWR4
12D10-LC	SYTLTQ SPPSLV APGOKA TIIC	SGENLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQKP GRAPVM VIY (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	ENEKRP S (SEQ ID NO: 6071) 6074)	GIPDQFSG SNSGNIAT LTISKAQP GSEADYYC (SEQ ID NO: (SEQ ID NO: NO: 6075)	HYWESI NSVV (SEQ ID NO: 6072) 6076)	FGSGTH LTVL (SEQ ID NO: 6076)
15E1-LC	SFTLTO PPLVSV AVGQVA TITC	SGEKLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQKP GRAPVM VIY (SEQ ID NO: 7327) ID NO:	ENDRRP S (SEQ ID NO: 7327) 6067)	GIPDQFSG SNSGNIAS LTISKAQA GDEADYFC (SEQ ID NO: (SEQ ID NO: NO: 7328)	QFWDST NSAV (SEQ ID NO: 7329) 6080)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL1	SSETTQ PPSVSV SPGQTA SITC	SGEKLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQKP GQSPVM VIY (SEQ ID NO: 7327) ID NO: 6106)	ENDRRP S (SEQ ID NO: 7327) 6067)	GIPERFSG SNSGNTAT LTISGTQA MDEADYFC (SEQ ID NO: (SEQ ID NO: NO: 7336)	QFWDST NSAV (SEQ ID NO: 7329) 6080)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL2	SSETTQ PHSVSV ATAQMA RITC	SGEKLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQKP GQDPVM VIY (SEQ ID NO: 7327) ID NO: 6090)	ENDRRP S (SEQ ID NO: 7327) 6069)	GIPERFSG SNPNTAT LTISRIEA GDEADYFC (SEQ ID NO: (SEQ ID NO: NO: 7337)	QFWDST NSAV (SEQ ID NO: 7329) 6080)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL3	QSVTTO PPSASG TPQGRV TISC	SGEKLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQLP GTAPKM LIY (SEQ ID NO: 7327) ID NO: 6078)	ENDRRP S (SEQ ID NO: 7327) 6078)	GVPDRFSG SNSGNSAS LAISGLRS EDEADYFC (SEQ ID NO: (SEQ ID NO: NO: 7338)	QFWDST NSAV (SEQ ID NO: 7329) 6080)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL4	QSVTTO PPSVSG APGQRV TISC	SGEKLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQLP GTAPKM LIY (SEQ ID NO: 7327) ID NO: 6078)	ENDRRP S (SEQ ID NO: 7327) 6078)	GVPDRFSG SNSGNSAS LAITGLQA EDEADYFC (SEQ ID NO: (SEQ ID NO: NO: 7339)	QFWDST NSAV (SEQ ID NO: 7329) 6080)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL5	DSVTTO SPLSLP VTLGQP ASISC	SGEKLS DKYVH (SEQ ID NO: (SEQ ID NO: (SEQ ID NO:	WYQQRP GQSPRM LIY (SEQ ID NO: 7327) ID NO: 7341)	ENDRRP S (SEQ ID NO: 7327) 7341)	GVPDRFSG SNSGNDAT LKISRVEA EDVGVYFC (SEQ ID NO: (SEQ ID NO: NO: 7342)	QFWDST NSAV (SEQ ID NO: 7329) 233)	FGGGTK VEIK (SEQ ID NO: 233)

TABLE 9

Exemplary variable regions of NKp30-targeting antigen binding domains			
SEQ ID NO	Ab ID	Description	Sequence
SEQ ID NO: 6121	9G1-HC	9G1 heavy chain variable region	QIQLQESGPGLVKPSQSLSLTCSTGFSINTGGYHWN WIRQFPKGKLEWMGYIYSSGSTSYPNPSLKSRSISITRD TSKNQFFLQLNSVTTEDTATYYCARGNWHYDFWGQG TMVTVSS
SEQ ID NO: 15H6-HC	15H6-HC	15H6 heavy chain variable	QIQLQESGPGLVKPSQSLSLTCSTGFSINTGGYHWN WIRQFPKGKLEWMGYIYSSGTTTRYNPNSLKSRSISITRD

TABLE 9-continued

Exemplary variable regions of NKp30-targeting antigen binding domains			
SEQ ID NO	Ab ID	Description	Sequence
6122		region	TSKNQFFLQLNSVTPEDEATYYCTRGNWYHFDYWGQG TLVAVSS
SEQ 9G1-HC_1 ID NO: 6123	9G1 heavy chain variable region humanized variant 1	9G1 heavy chain variable region humanized variant 1	QIQLQESGPGLVKPSETLSLTCTVSGFSINTGGYHWN WIRQAPGKGLEWIGYIYSSGSTSYPNSLKSRTMSRD TSKNQFSLKLSSVTAADTAVYYCARGNWYHFDFWGQG TMVTVSS
SEQ 9G1-HC_2 ID NO: 6124	9G1 heavy chain variable region humanized variant 2	9G1 heavy chain variable region humanized variant 2	QIQLQESGPGLVKPSETLSLTCTVSGFSINTGGYHWN WIRQAPGKGLEWIGYIYSSGSTSYPNSLKSRTMSRD TSKNQFSLKLSSVTAADTAVYYCARGNWYHFDFWGQG TMVTVSS
SEQ 9G1-HC_3 ID NO: 6125	9G1 heavy chain variable region humanized variant 3	9G1 heavy chain variable region humanized variant 3	EIQLLESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN WVRQAPGKGLEWVGYIYSSGSTSYPNSLKSRTISRD TSKNTFYLQMNSLRAEDTAVYYCARGNWYHFDFWGQG TMVTVSS
SEQ 9G1-HC_4 ID NO: 6126	9G1 heavy chain variable region humanized variant 4	9G1 heavy chain variable region humanized variant 4	QIQLVQSGAEVKPGSSVKVSCKVSGFSINTGGYHWN WVRQAPGQGLEWMGYIYSSGSTSYPNSLKSRTITRD TSTNTFYMEPLLRSEDTAVYYCARGNWYHFDFWGQG TMVTVSS
SEQ 9G1-HC_5 ID NO: 6127	9G1 heavy chain variable region humanized variant 5	9G1 heavy chain variable region humanized variant 5	EIQLVESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN WVRQAPGKGLEWVGYIYSSGSTSYPNSLKSRTISRD TAKNSFYLQMNSLRAEDTAVYYCARGNWYHFDFWGQG TMVTVSS
SEQ 9G1-HC_6 ID NO: 6128	9G1 heavy chain variable region humanized variant 6	9G1 heavy chain variable region humanized variant 6	QIQLVQSGAEVKPGASVKVSCKVSGFSINTGGYHWN WVRQAPGQGLEWMGYIYSSGSTSYPNSLKSRTMTRD TSTNTFYMEPLLRSEDTAVYYCARGNWYHFDFWGQG TMVTVSS
SEQ 15H6-HC_1 ID NO: 6129	15H6 heavy chain variable region humanized variant 1	15H6 heavy chain variable region humanized variant 1	QIQLQESGPGLVKPSETLSLTCTVSGFSINTGGYHWN WIRQAPGKGLEWIGYIYSSGTRYNPNSLKSRTISRD TSKNQFSLKLSSVTAADTAVYYCARGNWYHFDY GQGTLTVSS
SEQ 15H6-HC_2 ID NO: 6130	15H6 heavy chain variable region humanized variant 2	15H6 heavy chain variable region humanized variant 2	QIQLQESGPGLVKPSETLSLTCTVSGFSINTGGYHWN WIRQAPGKGLEWIGYIYSSGTRYNPNSLKSRTMSRD TSKNQFSLKLSSVTAADTAVYYCARGNWYHFDYWGQG TLVTVSS
SEQ 15H6-HC_3 ID NO: 6131	15H6 heavy chain variable region humanized variant 3	15H6 heavy chain variable region humanized variant 3	EIQLLESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN WVRQAPGKGLEWVGYIYSSGTRYNPNSLKSRTISRD TSKNTFYLQMNSLRAEDTAVYYCARGNWYHFDYWGQG TLVTVSS
SEQ 15H6-HC_4 ID NO: 6132	15H6 heavy chain variable region humanized variant 4	15H6 heavy chain variable region humanized variant 4	QIQLVESGGGLVQPGGSLRLSCAVSGFSINTGGYHWN WIRQAPGKGLEWVGYIYSSGTRYNPNSLKSRTISRD TAKNSFYLQMNSLRAEDTAVYYCARGNWYHFDYWGQG TLVTVSS
SEQ 15H6-HC_5 ID NO: 6133	15H6 heavy chain variable region humanized variant 5	15H6 heavy chain variable region humanized variant 5	QIQLVQSGAEVKPGASVKVSCKVSGFSINTGGYHWN WVRQAPGQGLEWMGYIYSSGTRYNPNSLKSRTMTRD TSTNTFYMEPLLRSEDTAVYYCARGNWYHFDYWGQG TLVTVSS
SEQ 15H6-HC_6 ID NO: 6134	15H6 heavy chain variable region humanized variant 6	15H6 heavy chain variable region humanized variant 6	EIQLVQSGAEVKPGATVKISCKVSGFSINTGGYHWN WVQQAPGKGLEWMGYIYSSGTRYNPNSLKSRTITRD TSTNTFYMEPLLRSEDTAVYYCARGNWYHFDYWGQG TLVTVSS

TABLE 9-continued

Exemplary variable regions of NKp30-targeting antigen binding domains			
SEQ ID NO	Ab ID	Description	Sequence
SEQ 9G1-LC ID NO: 7294	9G1 light chain variable region	9G1 light chain variable region	SYLTQPPPLSVALGHKATITCSGERLSDKYVHWYQQ KPGRAPVMVIYENDKRPSGIPDQFSGNSGNIAATLTI SKAQAGYEADYYCQSNDSTNSAVFGSGTQLTVL
SEQ 15H6-LC ID NO: 6136	15H6 light chain variable region	15H6 light chain variable region	SYLTQPPSLSVAPGOKATIICSGENLSDKYVHWYQQ KPGRAPVMVIYENEKRPSGIPDQFSGNSGNIAATLTI SKAQPGSEADYYCHYWEINSVVFGSGTHLTVL
SEQ 9G1-LC_1 ID NO: 6137	9G1 light chain variable region humanized variant 1	9G1 light chain variable region humanized variant 1	QSVTTQPPSVSGAPGQRVTISCSGERLSDKYVHWYQQ LPGTAPKMLIYENDKRPSGVPDFSGNSGNASLAI TGLQAEDEADEADYYCQSNDSTNSAVFGGGTQLTVL
SEQ 9G1-LC_2 ID NO: 6138	9G1 light chain variable region humanized variant 2	9G1 light chain variable region humanized variant 2	QSVTTQPPSASGTPGQRVTISCSGERLSDKYVHWYQQ LPGTAPKMLIYENDKRPSGVPDFSGNSGNASLAI SGLQSEDEADYYCQSNDSTNSAVFGGGTQLTVL
SEQ 9G1-LC_3 ID NO: 6139	9G1 light chain variable region humanized variant 3	9G1 light chain variable region humanized variant 3	QSVTTQPPSASGTPGQRVTISCSGERLSDKYVHWYQQ LPGTAPKMLIYENDKRPSGVPDFSGNSGNASLAI SGLRSEDEADYYCQSNDSTNSAVFGGGTQLTVL
SEQ 9G1-LC_4 ID NO: 6140	9G1 light chain variable region humanized variant 4	9G1 light chain variable region humanized variant 4	SSETTQPHSVSVATAQMARIITCSGERLSDKYVHWYQQ KPGQDPVMVIYENDKRPSGIPERFSGSNPGNTATLTI SRIEAGDEADYYCQSNDSTNSAVFGGGTQLTVL
SEQ 9G1-LC_5 ID NO: 6141	9G1 light chain variable region humanized variant 5	9G1 light chain variable region humanized variant 5	DIQMTQSPSTLSASVGDRVITISCSGERLSDKYVHWYQQ QKPGKAPKMLIYENDKRPSGVPSRFSGNSNEATLT ISSLQPDDFATYYCQSNDSTNSAVFGQGTKVEIK
SEQ 15H6-LC_1 ID NO: 6142	15H6 light chain variable region humanized variant 1	15H6 light chain variable region humanized variant 1	QYVLTQPPSASGTPGQRVTISCSGENLSDKYVHWYQQ LPGTAPKMLIYENEKRPSGVPDFSGNSGNASLAI SGLQSEDEADYYCHYWEINSVVFGEGTELTVL
SEQ 15H6-LC_2 ID NO: 6143	15H6 light chain variable region humanized variant 2	15H6 light chain variable region humanized variant 2	QYVLTQPPSASGTPGQRVTISCSGENLSDKYVHWYQQ LPGTAPKMLIYENEKRPSGVPDFSGNSGNASLAI SGLRSEDEADYYCHYWEINSVVFGEGTELTVL
SEQ 15H6-LC_3 ID NO: 6144	15H6 light chain variable region humanized variant 3	15H6 light chain variable region humanized variant 3	SYELTQPPSVSPGQTASITCSGENLSDKYVHWYQQ KPGQSPVMVIYENEKRPSGIPERFSGNSGNATLTI SGTQAMDEADYYCHYWEINSVVFGEGTELTVL
SEQ 15H6-LC_4 ID NO: 6145	15H6 light chain variable region humanized variant 4	15H6 light chain variable region humanized variant 4	DYVLTQSPSLPVTPEGEPASISCSGENLSDKYVHWYL QKPGQSPQMLIYENEKRPSGVPDFSGNSGNATLK ISRVEAEDVGVYYCHYWEINSVVFGQGTKVEIK
SEQ 15H6-LC_5 ID NO: 6146	15H6 light chain variable region humanized variant 5	15H6 light chain variable region humanized variant 5	AYQLTQSPSSLSASVGDRVITISCSGENLSDKYVHWYQ QKPGKAPKMLIYENEKRPSGVPSRFSGNSGNATLT ISSLQPDEDATYYCHYWEINSVVFGQGTKVEIK
SEQ 15H6-LC_6 ID NO: 6147	15H6 light chain variable region humanized variant 6	15H6 light chain variable region humanized variant 6	EYVLTQSPATLSVSPGERATLSCSGENLSDKYVHWYQ QKPGQAPRMLIYENEKRPSGIPARFSGNSGNATLT ISSLQSEDFAVYYCHYWEINSVVFGQGTKVEIK

TABLE 9-continued

 Exemplary variable regions of NKp30-targeting
 antigen binding domains

SEQ	ID NO	Ab ID	Description	Sequence
SEQ	9D9-HC	9D9	heavy chain variable region	QIQLQESGPGLVKPSQSLSLCSVTGFSINTGGYHWN WIRQFPGKVEWMGYIYSSGTTKYNPSLKSRSITRD TSKNQFFLQLNSVTTEDTATYYCARGDWHYFDYWGQQ TMVAVSS
SEQ	9D9-LC	9D9	light chain variable region	SYTLTQPPLVSVALGQKATIICSGENLSDKYVHWYQQ KPGRAPVMVIYENDKRPSGIPDQFSGNSGNIAATLTI SKAQAGYEADYYCHCWDSTNSAVFGSGTHLTVL
SEQ	3A12-HC	3A12	heavy chain variable region	QIQLQESGPGLVKPSQSLSLCSVTGFSINTGGYHWN WIRQFPGKLEWMGYIYSSGSTRYNPSLKSRSITRD TSKNQFFLQLNSVTTEDTATYYCTRGNWHDYWGQQ TLVAVSS
SEQ	3A12-LC	3A12	light chain variable region	SYTLTQPPLVSVALGQKATIICSGENLSDKYVHWYQQ KPGRAPVMVIYENDKRPSGIPDQFSGNSGNIAATLTI SKAQAGYEADYYCHCWDSTNSAVFGSGTHLTVL
SEQ	12D10-HC	12D10	heavy chain variable region	QIQLQESGPGLVKPSQSLSLCSVTGFSINTGGYHWN WIRQFPGKLEWMGYIYSSGSTRYNPSLKSRSITRD TSKNQFFLQLNSVTPEDTATYYCTRGNWHDYWGQQ TLVAVSS
SEQ	12D10-LC	12D 10	light chain variable region	SYTLTQPPLSVAPGQKATIICSGENLSDKYVHWYQQ KPGRAPVMVIYENEKRPMSGIPDQFSGNSGNIAATLTI SKAQPGSEADYYCHYWEINSVVFSGSGTHLTVL
SEQ	15E1-HC	15E1	heavy chain variable region	QIQLQESGPGLVKPSQSLSLCSVTGFSITTGYHWN WIRQFPGKLEWMGYIYSSGSTSYPNPSLKSRSITRD TSKNQFFLQLNSVTTEDTATYYCARGDWHYFDYWG PGTMVTVSS
SEQ	15E1-LC	15E1	light chain variable region	SFTLTQPPLVSVAVGQVATITCSGEKLSDKYVHWYQQ KPGRAPVMVIYENDRPSGIPDQFSGNSGNIASTLTI SKAQAGDEADYFCQFWDSTNSAVFGGGTQLTVL
SEQ	15E1_Humanized variant_VH1	15E1	heavy chain variable region	QIQLQESGPGLVKPSQSLSLCSVTGFSITTGYHWN WIRQHPGKLEWIGYIYSSGSTSYPNPSLKSLSVTISRD TSKNQFLKLSSVTAADTAVYYCARGDWHYFDYWGQQ TMVTVSS
SEQ	15E1_Humanized variant_VH2	15E1	heavy chain variable region	QIQLVESGGGLVKPGGSLRLSCAVSGFSITTGYHWN WIRQAPGKGLEWVGYIYSSGSTSYPNPSLKSRTFISRD TAKNSFYLQMNSLRAEDTAVYYCARGDWHYFDYWGQQ TMVTVSS
SEQ	15E1_Humanized variant_VH3	15E1	heavy chain variable region	EIQLLVESGGGLVQPGGSLRLSCAVSGFSITTGYHWN WVRQAPGKGLEWVGYIYSSGSTSYPNPSLKSRTFISRD TAKNSFYLQMNSLRAEDTAVYYCARGDWHYFDYWGQQ TMVTVSS
SEQ	15E1_Humanized variant_VH4	15E1	heavy chain variable region	EIQLVESGGGLVQPGGSLRLSCAVSGFSITTGYHWN WVRQAPGKGLEWVGYIYSSGSTSYPNPSLKSRTFISRD TAKNSFYLQMNSLRAEDTAVYYCARGDWHYFDYWGQQ TMVTVSS
SEQ	15E1_Humanized variant_VH5	15E1	heavy chain variable region	QIQLVQSGAEVKPGASVKVSCKVSGFSITTGYHWN WVRQAPGQGLEWMGYIYSSGSTSYPNPSLKSRTVMTRD TSTNTFYMLSSLRSEDTAVYYCARGDWHYFDYWGQQ TMVTVSS
SEQ	15E1_Humanized variant_VL1	15E1	light chain variable region	SSETTQPSSVSVPQTASITCSGEKLSDKYVHWYQQ KPGQSPVMVIYENDRPSGIPERFSGNSGNATLTI SGTQAMDEADYFCQFWDSTNSAVFGGGTQLTVL

TABLE 9-continued

Exemplary variable regions of NKp30-targeting antigen binding domains			
SEQ	ID NO	Ab ID	Description Sequence
SEQ	15E1_Humanized	15E1 light	SSETTQPHSVSVATAQMARITCSGEKLSDKYVHWYQQ
ID NO: variant_VL2		chain variable	KPGQDPVMVIYENDRPGSGIPERFSGSNPGNTATLTI
7306		region	SRIEAGDEADYFCQFWDSTNSAVFGGGTQLTVAL
		humanized	
		variant 2	
SEQ	15E1_Humanized	15E1 light	QSVTTOPPSASGTPGQRVTISCSGEKLSDKYVHWYQQ
ID NO: variant_VL3		chain variable	LPGTAPKMLIYENDRPGSGVPDRFSGSNSGNSASLAI
7307		region	SGLRSEDEADYFCQFWDSTNSAVFGGGTQLTVAL
		humanized	
		variant 3	
SEQ	15E1_Humanized	15E1 light	QSVTTOPPSASGTPGQRVTISCSGEKLSDKYVHWYQQ
ID NO: variant_VL4		chain variable	LPGTAPKMLIYENDRPGSGVPDRFSGSNSGNSASLAI
7308		region	TGLQAEDAEADYFCQFWDSTNSAVFGGGTQLTVAL
		humanized	
		variant 4	
SEQ	15E1_Humanized	15E1 light	DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVHWYQ
ID NO: variant_VL5		chain variable	QRPGQSPRMLIYENDRPGSGVPDRFSGSNSGNDATLK
7309	(BJM0411VL)	region	ISRVEAEDVGVYFCQFWDSTNSAVFGGGTKEIK
		humanized	
		variant 5	

TABLE 10

Exemplary NKp30-targeting antigen binding domains/antibody molecules			
SEQ	ID NO	Ab ID	Description Sequence
SEQ	Ch(anti- 9G1	heavy	QIQLQESGPGLVKPQSLSLTCSTGFSINTGGYHWNWIRO
ID NO: NKp30	chain		FPGKKLEWMGYIYSSGTSYNPSLKSRSISITRDTSKNQFFL
6148	9G1) HC		QLNSVTTEDTATYCARGNWHYFDWFNGQGTMTVSSASTKG
	N297A		PSVFP LAPSSKSTSGTAALGCLVKDYFPEPVTVSWNSGAL
			TSGVHTFPAPLVQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
			KPSNTKVDKRVEPKSCDKTHTCPCCPAPELLGGPSVFLFPP
			KPKDTLMISRTPEVTCVVVDVSHEDPEVFKFNWYVDGVEVHN
			AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
			LPAPIEKTIISKAKGQPREPVQVCTLPPSREEMTKNQVSLSCA
			VKGFYPSDIAVEWESNQCPENNYKTPVLDSDGSFFLVSK
			LTVDKSRWQQGNVFCSVHMHEALHNHYTQKSLSLSPGK
SEQ	Ch(anti- 9G1	heavy	QIQLQESGPGLVKPQSLSLTCSTGFSINTGGYHWNWIRO
ID NO: NKp30	chain		FPGKKLEWMGYIYSSGTSYNPSLKSRSISITRDTSKNQFFL
6149	9G1) HC		QLNSVTTEDTATYCARGNWHYFDWFNGQGTMTVSSASTKG
			PSVFP LAPSSKSTSGTAALGCLVKDYFPEPVTVSWNSGAL
			TSGVHTFPAPLVQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
			KPSNTKVDKRVEPKSCDKTHTCPCCPAPELLGGPSVFLFPP
			KPKDTLMISRTPEVTCVVVDVSHEDPEVFKFNWYVDGVEVHN
			AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
			LPAPIEKTIISKAKGQPREPVQVCTLPPSREEMTKNQVSLSCA
			VKGFYPSDIAVEWESNQCPENNYKTPVLDSDGSFFLVSK
			LTVDKSRWQQGNVFCSVHMHEALHNHYTQKSLSLSPGK
SEQ	Ch(anti- 9G1	light	SYTLTQPPLLSVALGHKATITCSGERLSDKYVHWYQQKGR
ID NO: NKp30	chain		APVMVIYENDKRPMSGIPDQFSGSNSGNIATLTISKQAGAYE
6150	9G1) LC		ADYYCQSWDSTNSAVFGSGTQLTVLGQPKANPTVTLFPPSS
			EELQANKATLVLCLISDFYPPGAVTVAWKADGSPVKAQGVETTK
			PSKQSNNKYAASSYSLTPEQWKSHRSYSQCQVTHEGSTVEK
			TVAPTECS
SEQ	Ch(anti- 15H6	heavy	QIQLQESGPGLVKPQSLSLTCSTGFSINTGGYHWNWIRO
ID NO: NKp30	chain		FPGKKLEWMGYIYSSGTRYNPNSLKSRSISITRDTSKNQFFL
6151	15H6) HC		QLNSVTPEDTATYCTRGNWHYFDWFNGQGTMTVAVSSASTKG
	N297A		PSVFP LAPSSKSTSGTAALGCLVKDYFPEPVTVSWNSGAL
			TSGVHTFPAPLVQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
			KPSNTKVDKRVEPKSCDKTHTCPCCPAPELLGGPSVFLFPP
			KPKDTLMISRTPEVTCVVVDVSHEDPEVFKFNWYVDGVEVHN

TABLE 10-continued

Exemplary NKp30-targeting antigen binding domains/antibody molecules			
SEQ ID NO	Ab ID	Description	Sequence
			AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTIASKAGKQPREPVCTLPPSREEMTKNQVSLSCA VKGFYPSDIAVEWESNGQPENNYKTPVPLSDGSFFLVSK LTVDKSRWQQGNVFCSVHEALHNHYTQKSLSLSPGK
SEQ ID NO: 6152	Ch(anti- 15H6 heavy chain 15H6) HC (hole)		QIQLQESGPGLVKPQSLSLTCSTGFSINTGGYHWNWIRO FPGKKLEWMGYIYSSGTTRYNPSLKSRSISITRDTSKNQFFL QLNSVTPEDTATYCTRGNWHYFDYWGQGTIVAVSSASTKG PSVFP LAPSSKSTSGGTAALGCLVKD YF PEP VTWSN GAL TSGVHTFP AVLQSSG LYSLSSV VTPS SLLG TQTY I C N V N H KPSNTKVDKRVEPKSCDKTHTCPCPAPELLGGPSVFLFPP KP KDTLMISRTPEVTCVVV DVS HEDP EVKFNWYV DGV E VHN AKTKPREEQYNS TYR VV SVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTIASKAGKQPREPVCTLPPSREEMTKNQVSLSCA VKGFYPSDIAVEWESNGQPENNYKTPVPLSDGSFFLVSK LTVDKSRWQQGNVFCSVHEALHNHYTQKSLSLSPGK
SEQ ID NO: 6153	Ch(anti- 15H6 light chain NKp30 15H6) LC		SYTLTQPPSLSVAPGQKATIIICSGENLSDKYVHWYQQKPG APVMVIIYENEKRPSGIPDQFSGNSGNIAITLISKQPGSE ADYYCHYWE SIN SVFGSGTHLTVLGQPKANPTVTLFPPSS EELQANKATLVCLISDFYPGAVTVANKADGSPVKA G VETTK PSKQSN NKY AASSYSLTPEQWKSHRSY SCQVTHEGSTVEK TVAPTECS
SEQ ID NO: 7310	BJM0859 lambda scFv		EIQ LLES GGG GLVQ PG G S LRL SCAV SG F S I T T G Y H W N W V R Q APG KGLEW V G Y I Y S S G S T S Y N P S L K S R F T I S R D T S K N T F Y L QM NSL R A E D T A V V Y C A R G D W H Y F D Y W G Q G T M V T V S S G G G S G G G S G G G S G G G S S E T T Q P P S V S V P G Q T A S I T C S G E K L S D K Y V H W Y Q Q K P G Q S P V M V I Y E N D R R P S G I P E R F S G S N S G N T A T L T I S G T Q A M D E A D Y F C Q F W D S T N S A V F G G G T Q L T V L
SEQ ID NO: 7311	BJM0860 kappa scFv		EIQ LLES GGG GLVQ PG G S LRL SCAV SG F S I T T G Y H W N W V R Q APG KGLEW V G Y I Y S S G S T S Y N P S L K S R F T I S R D T S K N T F Y L QM NSL R A E D T A V V Y C A R G D W H Y F D Y W G Q G T M V T V S S G G G S G G G S G G G S G G G S D V T T Q S P L S P V T L G Q P A S I S C S G E K L S D K Y V H W Y Q Q R P G Q S P R M L I Y E N D R R P S G V P D R F S G S N S G N D A T L K I S R V E A D V G V Y F C Q F W D S T N S A V F G G G T K V E I K

In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp46 (e.g., NKp46 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp46, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp46 (e.g., NKp46 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKp46, the NK cell, or both.

In some embodiments, the NK cell engager is an antigen binding domain that binds to NKG2D (e.g., NKG2D present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region

40 amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKG2D, to the NK cell activates the NK cell. An antigen binding domain that binds to NKG2D (e.g., NKG2D present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKG2D, the NK cell, or both.

45 In some embodiments, the NK cell engager is an antigen binding domain that binds to CD16 (e.g., CD16 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to CD16, to the NK cell activates the NK cell. An antigen binding domain that binds to CD16 (e.g., CD16 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target CD16, the NK cell, or both.

TABLE 15

Exemplary variable regions of NKp46, NKG2D, or CD16-targeting antigen binding domains			
SEQ ID NO	Ab ID	Description	Sequence
SEQ ID NO: 6175	NKG2D_1scFv	scFv that binds NKG2D	QVHLQESGPGLVKPSETLSLTCTVSDDSISSYYWSWIRQ PPGKGLEWIGHISYSGSANYNPSLKSRTVISVDTSKNQF SLKLSSVTAADTAVYYCANWDDAFNIWQGTMVTVSSGG

TABLE 15-continued

Exemplary variable regions of NKp46, NKG2D,
or CD16-targeting antigen binding domains

SEQ ID NO	Ab ID	Description	Sequence
			GGSGGGGGGGGGGGSEIVLTQSPGTLSSLSPGERATL SCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYCQQYGSSPWTF GQGTKEIK
SEQ ID NO: 6176	NKG2D_1VH	VH that binds NKG2D	QVHLQESGPGLVKPSETLSLTCTVSDDSISYYWSWIQ PPGKGLEWIGHISYSGSANYNPSLKSRTVISVDTSKNQF SLKLSSVTAADTAVYYCANWDDAFNIWGQGTMTVTVSS
SEQ ID NO: 6177	NKG2D_1VL	VL that binds NKG2D	EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQ KPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFLTISR LEPEDFAVYYCQQYGSSPWTFGQGTKEIK
SEQ ID NO: 6178	NKG2D_2scFv	scFv that binds NKG2D	EVQLVQSGAEVKEPGESLKISCKNSGYSFTNYWVGWVRQ MPGKGLEWMGIIYPGDSDTYSRSPSFQGVТИSADKSINT AYLQWSSLKAQDTAMYYCGRLTMRGIIIGYFDYWGQGT LTVSSGGGGGGGGGGGGGGGGGGGGGGSEIVLTQSPATLSS SPGERATLSCRASQSVSSYLAWSQQKPGQAPRLLIYDAS NRATGIPARFSGSGSGTDFLTISLEPEDFAVYYCQQR SNWPWTFGQGTKEIK
SEQ ID NO: 6179	NKG2D_2VH	VH that binds NKG2D	EVQLVQSGAEVKEPGESLKISCKNSGYSFTNYWVGWVRQ MPGKGLEWMGIIYPGDSDTYSRSPSFQGVТИSADKSINT AYLQWSSLKAQDTAMYYCGRLTMRGIIIGYFDYWGQGT LTVSS
SEQ ID NO: 6180	NKG2D_2VL	VL that binds NKG2D	EIVLTQSPATLSSLSPGERATLSCRASQSVSSYLAWSQQK PGQAPRLLIYDASNRATGIPARFSGSGSGTDFLTISL EPEDFAVYYCQQRSNWPWTFGQGTKEIK
SEQ ID NO: 6181	NKp46scFv	scFv that binds NKp46	QVQLQQSGPELVKPGAVKMSCKASGYTFDYVINWGKQ RSGQGLEWIGEIYPGSGTNYYNEKFKAQATLTADKSSNI AYMQLSSLTSEDAVYPCARRGRYGLYAMDYWGQGTSVT VSSGGGGGGGGGGGGGGGGSDIQMTQTTSSLASLG DRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLH SGVPSRFSGSGSGTDYSLTINNLEQEDIATYFCQQGNTR PWTFGGGTKLEIK
SEQ ID NO: 6182	NKp46VH	VH that binds NKp46	QVQLQQSGPELVKPGAVKMSCKASGYTFDYVINWGKQ RSGQGLEWIGEIYPGSGTNYYNEKFKAQATLTADKSSNI AYMQLSSLTSEDAVYPCARRGRYGLYAMDYWGQGTSVT VSS
SEQ ID NO: 6183	NKp46VL	VL that binds NKp46	DIQMTQTTSSLSASLGDRTVITCRASQDISNYLNWYQQK PDGTVKLLIYYTSRLHSGVPSPRSFSGSGSGTDSLTINNL EQEDIATYFCQQGNTRPWTFGGGTKLEIK
SEQ ID NO: 6184	CD16scFv	scFv that binds CD16	EVQLVESGGGVVRPGGSLRLSCAASGFTFDYGMWSVRQ APGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKNS LYLQMNSLRAEDTAVYYCARGRSLLFDYWGQGTLVTSR GGGGSGGGGGGGGGSELTQDPAVSVALGQTVRITCQGD SLRSYYASWYQQKPGQAPVLVIYGKNNRPGSIPDRFSGS SSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGT KLTVL
SEQ ID NO: 6185	CD16VH	VH that binds CD16	EVQLVESGGGVVRPGGSLRLSCAASGFTFDYGMWSVRQ APGKGLEWVSGINWNGGSTGYADSVKGRFTISRDNAKNS LYLQMNSLRAEDTAVYYCARGRSLLFDYWGQGTLVTSR
SEQ ID NO: 6186	CD16VL	VL that binds CD16	SSELTDQDPAVSVALGQTVRITCQGDSSLRSYYASWYQQK GQAPVLVIYGKNNRPGSIPDRFSGSSSGNTASLTITGAQ AEDEADYYCNSRDSSGNHVVFGGGT KLTVL

In one embodiment, the NK cell engager is a ligand of NKp30, e.g., is a B7-6, e.g., comprises the amino acid sequence of: DLKVEMMAGGTQITPLNDNVTIFCN-
FYSQPLNITSMGITWFWKSLTFDKEVKVFEFFGD
HQEAFRPGAIVSPWRLKSGDASLRLPGIQLEEAGEY-
RCEVVVTPLKAQGTVQLEVVASP
DQVGMKENEDKYMCESSGFYPEAINIT-
WEKQTQKFPHPIEISEDVITGPTIKNM

ASRLLL-

60 DGTFNVTSCLKLNSSQEDPGTVYQCVVRHASLHTPL
RSNFTLTAARHSLSETEKTDNFS (SEQ ID NO: 7233), a
fragment thereof, or an amino acid sequence substantially
identical thereto (e.g., 95% to 99.9% identical thereto, or
having at least one amino acid alteration, but not more than
five, ten or fifteen alterations (e.g., substitutions, deletions,
or insertions, e.g., conservative substitutions) to the amino
acid sequence of SEQ ID NO: 7233.

In other embodiments, the NK cell engager is a ligand of NKP44 or NKP46, which is a viral HA. Viral hemagglutinins (HA) are glyco proteins which are on the surface of viruses. HA proteins allow viruses to bind to the membrane of cells via sialic acid sugar moieties which contributes to the fusion of viral membranes with the cell membranes (see e.g., Eur J Immunol. 2001 September; 31(9):2680-9 "Recognition of viral hemagglutinins by NKP44 but not by NKP30"; and Nature. 2001 Feb. 22; 409(6823):1055-60 "Recognition of haemagglutinins on virus-infected cells by NKP46 activates lysis by human NK cells" the contents of each of which are incorporated by reference herein).

In other embodiments, the NK cell engager is a ligand of NKG2D chosen from MICA, MICB, or ULBP1, e.g., wherein:

- (i) MICA comprises the amino acid sequence: EPHSL-RYNLTLSWDGSVQSGFLTEVHLDGQP-
FLRCDRQKCRACKPQQWAEVDVLGNK
TWDRETRDLTGNKDLRMTLAHKDQKEG-
LHSLQEIRVCEIHEDNSTRSSQHFYYDGEL
FLSQNLETKEWTMPQSSRAQTLAMNVRNFLKE-
DAMKTTHYHAMHADCLQKLQRYLK
SGVLLRRTVPPMVNVTRSEASEGNITVT-
CRASGFYPWNITLSWRQDGVSLSHDTQQWG
DVLPGNGTYQTWVATRICQGEEQRFT-
CYMEHSGNHSTHPVPSGKVLVLQSHW (SEQ ID NO: 7234), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7234);
- (ii) MICB comprises the amino acid sequence: AEPHSL-RYNLMVLSQDESVPQSGFLAEGHLDGQPFLRY-
DRQKRRAKPKQQWAEVDVLGA KTWDYTET-
EDLTENGQDLRRLTHIKDQKGLHSLQEIRVCEI-
HEDSSTRGRSRHFYYDGEL
FLSQNLETQESTVPQSSRAQTLAMNVTNFKE-
DAMKTTHYRAMQADCLQKLQRYLK
SGVAIRRTVPPMVNVTCSEVESEGNTVT-
CRASSFYPRNITLWRQDGVSLSHNTQWG
DVLPGNGTYQTWVATRIRQGEEQRFT-
CYMEHSGNHGTHPVPSSGKVLVLQSQRTD (SEQ ID NO: 7235), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7235; or
- (iii) ULBP1 comprises the amino acid sequence:
GWVDTHLCYDFIITPKSRPEPWCE-
VQGLVDERPFLHYDCVNHKAKAFASLGKKVNV
TKTWEEQTETLRDVDFLKGQLLDIQVENLPIE-
PLTLQARMSCEHEAHGHGRGSWQFL
FNGQKFLFDSDNNRKWTALHPGAKKMTEK-
WEKNRDVTMFFQKISLGDCKMWLEEF
MYWEQMLDPTKPPSLAPG (SEQ ID NO: 7236), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7236.

In other embodiments, the NK cell engager is a ligand of DNAM1 chosen from NECTIN2 or NECL5, e.g., wherein:

- (i) NECTIN2 comprises the amino acid sequence: QDVRVQLPEVRGQLGGTVELPCHLLPPVPGLY-ISLVTWQRPDAPANHQNVAAFPKM
GPSFPSPKPGSERLSFSVSAKQSTGQDTEAELQ-DATLALHGLTVEDEGNYTCEFATFPKGS
VRGMTWLRLVIAKPKNQAEA-QKVTFSDPPTVVALCISKEGRPPA-RISWLSSLDWAKEETQ
LAGTVTVTSRFTLVPSGRADGVTVCKVEHESF
EEPALIPVTLVSRVYPPEVSIISGYD DNWYLGRT-DATLSCDVRSNPEPTGYDWSTTSQTFPT-
SAVAQGSQQLVIHAVDSLNFNTTFV CTVT-
NAVGMGRAEQVIFVRETPNTAGAGATGG (SEQ ID NO: 7237), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7237; or
 - (ii) NECL5 comprises the amino acid sequence: WPPP GTG D VV VQAPTQV PGFL GD S VT L PC YL Q
VPNMEV THV S Q L T W A R H G E S G S M A V
FHQTQGP SY S E K S R L E F V A A R L G A E L R -
N A S L R M F G L R V E D E G N Y T C L F V T F P Q G S R S V D
I W L R V L A K P Q N T A E V Q K V Q L T G E P V P -
M A R C V S T G R P P A Q I T W H S D L G G M P N T S Q V P G
F L S G T V T V T S L W I L V P S S Q V D G K N V T C K V E H E S -
F E K P Q L L T V N L T V Y Y P P E V S I S G Y D N N
W Y L G Q N E A T L T C D A R S N P E P T G Y N W S T T M G -
P L P P F A V A Q G A Q L L I R P V D K P I N T T L I C N V T N A L -
G A R Q A E L T V Q V K E G P P S E H S G I S R N (SEQ ID NO: 7238), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7238).
- In yet other embodiments, the NK cell engager is a ligand of DAP10, which is an adapter for NKG2D (see e.g., Proc Natl Acad Sci USA. 2005 May 24; 102(21): 7641-7646; and Blood, 15 Sep. 2011 Volume 118, Number 11, the full contents of each of which is incorporated by reference herein).
- In other embodiments, the NK cell engager is a ligand of CD16, which is a CD16a/b ligand, e.g., a CD16a/b ligand further comprising an antibody Fc region (see e.g., Front Immunol. 2013; 4: 76 discusses how antibodies use the Fc to trigger NK cells through CD16, the full contents of which are incorporated herein).
- In other embodiments, the NK cell engager is a ligand of CRTAM, which is NECL2, e.g., wherein NECL2 comprises the amino acid sequence: QNLFTKDVTVIEGEVATISCQVKSDDSVIQLLNPNRQTIYFRDFR-PLKDSRFQLLNFSSS ELKVS LTNV SISDE-GRYFCQLYTDPPQESYTTITVLVPPRNLMIDIQKDTAVE-GEEIEVNC
TAMASKPATTIRWFKGNT E LKGKSEVEEWS-
DMYTVTSQMLKVHKEDDGVPVICQVE
HPAVTGNLQTQRYLEVQYKPKVH IQMTYPLQGL-TREGDALELTCEAIGKPKQPVMTWV RVD-
DEM P Q H A V L S G P N L F I N N L N K T D N G T Y R C E A S N I V -
GKAHS D Y M L Y V Y D P P T T I P P P
TTTTTTTTTTTTTILTIITDSRAGEEGSIRAVDH (SEQ

ID NO: 7239), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7239.

In other embodiments, the NK cell engager is a ligand of CD27, which is CD70, e.g., wherein CD70 comprises the amino acid sequence: QRFAQAQQLPLESLGWDAEL-QLNHTGPQQDPRLYWQGGPALGRSFLHGPELDKGQ-LRIHRDGIYVMHIVQVTLAICSSSTASRHHPTTLAVG-ICSPASRSISLLRLSFHQGCTIASQR-LTPLARGDTLCTNLTGTLLPSRNTDETFGVQWVRP (SEQ ID NO: 7240), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7240.

In other embodiments, the NK cell engager is a ligand of PSGL1, which is L-selectin (CD62L), e.g., wherein L-selectin comprises the amino acid sequence: WTYHY-SEKPMNWQRARRFCRDNYTDLVAIQNKAEIYEY-LEKTLFPSRSRYYWIGIRKIGGI-WTWVGTNKSLTEEAENWDGEPEPNK-KNKEDCVEIYIKRNKDAGKWNDDACHKLKAA-LCY-TASCQPWSCEGHGECVEIN-NYTCNCVDVGYGPQCQFVIQCEPLEAPELGTMDCTH-PLGNFSFSSQCAFSCSEGNTNLGIEETTCGPGFNWSS-PEPTCQVIQCEPLSAPDLGIMNC SH-PLASFSFTSACT-FICSEGTE-LIGKKKTICESSGIWSNPSPICQKLDKSFSMIKEGDYN (SEQ ID NO: 7241), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7241.

In other embodiments, the NK cell engager is a ligand of CD96, which is NECL5, e.g., wherein NECL5 comprises the amino acid sequence: WPPPGTGVVQAPTQVPGFLGDSVTPCYLQVPN-MEVTHVSQLTWARHGESGSMAV-FHQQTQGPSYS-ESKRLEFVAARLGAELRNASLRMFLRVEDEGNYT-CLFVTFPQGSRSVD-IWLRLAKPQNTAEVQKVQLTGEVPVMARCVSTG-GRPPAQITWHSDLGGMPNTSQVPG-FLSGTVTVT-SLWILVPSSQVDGKNVCKVEHES-FEKPQLLTVNLTVYYPPPEVSISGYDNN-WYLGQNEATLCDARSNPEPTGYNWSTTMGPLPP-FAVAQQAQLLIRPVDKPINTTLCIN-VTNALGAR-QAELTVQVKEGPPSEHSGISRN (SEQ ID NO: 7238), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7238.

In other embodiments, the NK cell engager is a ligand of CD100 (SEMA4D), which is CD72, e.g., wherein CD72 comprises the amino acid sequence: RYLQVSQQLQQTNRVLLEVNTNSSLRQLRLKITQLGQ-SAEDLQGSRRELAQSQEALQVEQ-RAHQAAEGQLQ-ACQADRQKTKETLQSEEQQRRALEQKLSN-MENRLKPFITCGSADTCC-PSGWIMHQKSCFYISLTSKNWQESQKQCETLSSK-LATFSEIYPQSHSYYFLNSLLPNGGS

GNSYWTGLSSNKDWKLTDDTQR-TRTYAQSSKCNVKHKTWSWWTLESECSRSSLPYICE-MTAFRFPD (SEQ ID NO: 7242), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7242.

- 10 In other embodiments, the NK cell engager is a ligand of NKp80, which is CLEC2B (AICL), e.g., wherein CLEC2B (AICL) comprises the amino acid sequence: KLTRDSQSLCPYDWIGFQNKCYYFSKEE-GDWNSSKYNCSTQHADLTIIDNIEEMNFLRR
- 15 YKCSSDHWIGLKMAKNRTGQWVD-GATFTKSFGMRGSEGCAYLSDDGAAATARCYTER-KWICRKRIH (SEQ ID NO: 7243), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7243.

In other embodiments, the NK cell engager is a ligand of CD244, which is CD48, e.g., wherein CD48 comprises the amino acid sequence: QGHLVHMTVSGSNVTLNISEL-PENYKQLTWFTFDQKIVEWDSRKSKYFESKFKGR-VRLDpqSGALYISKVQKEDNSTYIMRVLKKTG-NEQEWKIKLQVLDPPVPKPVKIEKIEDM-DDN-30 CYKLKSCVIPGESVNYTWYGDKRPFPKELQNSVLET-TLMPHNYSRCYTCQVSNSVS-SKNGTVCLSPPCCTLARS (SEQ ID NO: 7244), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7244.

In some embodiments, the NK cell engager is a viral hemagglutinin (HA), HA is a glycoprotein found on the surface of influenza viruses. It is responsible for binding the virus to cells with sialic acid on the membranes, such as cells in the upper respiratory tract or erythrocytes. HA has at least 18 different antigens. These subtypes are named H1 through H18. NCRs can recognize viral proteins. NKp46 has been shown to be able to interact with the HA of influenza and the HA-NA of Paramyxovirus, including Sendai virus and Newcastle disease virus. Besides NKp46, NKp44 can also functionally interact with HA of different influenza subtypes.

Antibody Molecules

In an embodiment, the anti-NKp30 antibody molecule is a monospecific antibody molecule and binds a single epitope on NKp30. E.g., a monospecific antibody molecule having a plurality of immunoglobulin variable domain sequences, each of which binds the same epitope.

In another embodiment, the anti-NKp30 antibody molecule is a multispecific or multifunctional antibody molecule, e.g., it comprises a plurality of immunoglobulin variable domains sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, e.g., the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment

ment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, e.g., the different proteins (or different subunits of a multimeric protein). In an embodiment a multispecific antibody molecule comprises a third, fourth or fifth immunoglobulin variable domain. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule, a trispecific antibody molecule, or a tetraspecific antibody molecule.

In an embodiment a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, e.g., the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, e.g., the different proteins (or different subunits of a multimeric protein). In an embodiment a bispecific antibody molecule comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody having binding specificity for a first epitope and a half antibody having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a scFv or a Fab, or fragment thereof, have binding specificity for a first epitope and a scFv or a Fab, or fragment thereof, have binding specificity for a second epitope.

In an embodiment, an antibody molecule comprises a diabody, and a single-chain molecule, as well as an antigen-binding fragment of an antibody (e.g., Fab, F(ab')₂, and Fv). For example, an antibody molecule can include a heavy (H) chain variable domain sequence (abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein as VL). In an embodiment an antibody molecule comprises or consists of a heavy chain and a light chain (referred to herein as a half antibody). In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab', F(ab')₂, Fc, Fd, Fd', Fv, single chain antibodies (scFv for example), single variable domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (e.g., humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (e.g., IgG1, IgG2, IgG3, and IgG4) of antibodies. The preparation of antibody molecules can be monoclonal or polyclonal. An antibody molecule can also be a human, humanized, CDR-grafted, or in vitro generated antibody. The antibody can have a heavy chain constant

region chosen from, e.g., IgG1, IgG2, IgG3, or IgG4. The antibody can also have a light chain chosen from, e.g., kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

Examples of antigen-binding fragments of an antibody molecule include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb) fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), see e.g., Bird et al. (1988) *Science* 242:423-426; and Huston et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883; (viii) a single domain antibody. These antibody fragments are obtained using conventional techniques known to those with skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

Antibody molecules include intact molecules as well as functional fragments thereof. Constant regions of the antibody molecules can be altered, e.g., mutated, to modify the properties of the antibody (e.g., to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

Antibody molecules can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to another aspect of the invention, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are disclosed in WO 9404678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VH molecule can be derived from antibodies raised in Camelidae species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides Camelidae may produce heavy chain antibodies naturally devoid of light chain; such VHs are within the scope of the invention.

The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW).

The extent of the framework region and CDRs has been precisely defined by a number of methods (see, Kabat, E. A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C. et al. (1987) *J. Mol. Biol.* 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software. See, generally, e.g., *Protein Sequence and Structure*

Analysis of Antibody Variable Domains. In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg).

The terms “complementarity determining region,” and “CDR,” as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. In general, there are three CDRs in each heavy chain variable region (HCDR1, HCDR2, HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, LCDR3).

The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of known schemes, including those described by Kabat et al. (1991), “Sequences of Proteins of Immunological Interest,” 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (“Kabat” numbering scheme), Al-Lazikani et al., (1997) *JMB* 273, 927-948 (“Chothia” numbering scheme). As used herein, the CDRs defined according the “Chothia” number scheme are also sometimes referred to as “hypervariable loops.”

For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3). Under Chothia, the CDR amino acids in the VH are numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3).

Each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

The antibody molecule can be a polyclonal or a monoclonal antibody.

The terms “monoclonal antibody” or “monoclonal antibody composition” as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope. A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (e.g., recombinant methods).

The antibody can be recombinantly produced, e.g., produced by phage display or by combinatorial methods.

Phage display and combinatorial methods for generating antibodies are known in the art (as described in, e.g., Ladner et al. U.S. Pat. No. 5,223,409; Kang et al. International Publication No. WO 92/18619; Dower et al. International Publication No. WO 91/17271; Winter et al. International Publication WO 92/20791; Markland et al. International Publication No. WO 92/15679; Breitling et al. International Publication WO 93/01288; McCafferty et al. International Publication No. WO 92/01047; Garrard et al. International Publication No. WO 92/09690; Ladner et al. International Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum Antibody Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734; Hawkins et al. (1992) *J Mol Biol* 226:889-896; Clackson et al. (1991) *Nature* 352:624-628; Gram et al. (1992) *PNAS* 89:3576-3580; Garrad et al. (1991) *Bio/Technology* 9:1373-1377; Hoogenboom et al. (1991) *Nuc Acid Res* 19:4133-4137; and Barbas et al. (1991) *PNAS* 88:7978-7982, the contents of all of which are incorporated by reference herein).

In one embodiment, the antibody is a fully human antibody (e.g., an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, e.g., a rodent (mouse or rat), goat, primate (e.g., monkey), camel antibody. Preferably, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (see, e.g., Wood et al. International Application WO 91/00906, Kucherlapati et al. PCT publication WO 91/10741; Lonberg et al. International Application WO 92/03918; Kay et al. International Application 92/03917; Lonberg, N. et al. 1994 *Nature* 368:856-859; Green, L. L. et al. 1994 *Nature Genet.* 7:13-21; Morrison, S. L. et al. 1994 *Proc. Natl. Acad. Sci. USA* 81:6851-6855; Bruggeman et al. 1993 *Year Immunol* 7:33-40; Tuailon et al. 1993 *PNAS* 90:3720-3724; Bruggeman et al. 1991 *Eur J Immunol* 21:1323-1326).

An antibody molecule can be one in which the variable region, or a portion thereof, e.g., the CDRs, are generated in a non-human organism, e.g., a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibody molecules generated in a non-human organism, e.g., a rat or mouse, and then modified, e.g., in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

An “effectively human” protein is a protein that does substantially not evoke a neutralizing antibody response, e.g., the human anti-murine antibody (HAMA) response.

HAMA can be problematic in a number of circumstances, e.g., if the antibody molecule is administered repeatedly, e.g., in treatment of a chronic or recurrent disease condition. A HAMA response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (see, e.g., Saleh et al., *Cancer Immunol. Immunother.*, 32:180-190 (1990)) and also because of potential allergic reactions (see, e.g., LoBuglio et al., *Hybridoma*, 5:5117-5123 (1986)).

Chimeric antibodies can be produced by recombinant DNA techniques known in the art (see Robinson et al., International Patent Publication PCT/US86/02269; Akira, et al., European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison et al., European Patent Application 173,494; Neuberger et al., International Application WO 86/01533; Cabilly et al. U.S. Pat. No. 4,816,567; Cabilly et al., European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043); Liu et al. (1987) *PNAS* 84:3439-3443; Liu et al., 1987, *J Immunol.* 139:3521-3526; Sun et al. (1987) *PNAS* 84:214-218; Nishimura et al., 1987, *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al., 1988, *J. Natl Cancer Inst.* 80:1553-1559).

A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and/or light immunoglobulin chains) replaced with a donor CDR. The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding to the antigen. Preferably, the donor will be a rodent antibody, e.g., a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the

immunoglobulin providing the CDRs is called the "donor" and the immunoglobulin providing the framework is called the "acceptor." In one embodiment, the donor immunoglobulin is a non-human (e.g., rodent). The acceptor framework is a naturally-occurring (e.g., a human) framework or a consensus framework, or a sequence about 85% or higher, preferably 90%, 95%, 99% or higher identical thereto.

As used herein, the term "consensus sequence" refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (See e.g., Winnacker, From Genes to Clones (Verlagsgesellschaft, Weinheim, Germany 1987)). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A "consensus framework" refers to the framework region in the consensus immunoglobulin sequence.

An antibody molecule can be humanized by methods known in the art (see e.g., Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi et al., 1986, *BioTechniques* 4:214, and by Queen et al. U.S. Pat. Nos. 5,585,089, 5,693,761 and 5,693,762, the contents of all of which are hereby incorporated by reference).

Humanized or CDR-grafted antibody molecules can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced. See e.g., U.S. Pat. No. 5,225,539; Jones et al. 1986 *Nature* 321:552-525; Verhoeyan et al. 1988 *Science* 239: 1534; Beidler et al. 1988 *J. Immunol.* 141:4053-4060; Winter U.S. Pat. No. 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare the humanized antibodies of the present invention (UK Patent Application GB 2188638A, filed on Mar. 26, 1987; Winter U.S. Pat. No. 5,225,539), the contents of which is expressly incorporated by reference.

Also within the scope of the invention are humanized antibody molecules in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in U.S. Pat. No. 5,585,089, e.g., columns 12-16 of U.S. Pat. No. 5,585,089, e.g., columns 12-16 of U.S. Pat. No. 5,585,089, the contents of which are hereby incorporated by reference. Other techniques for humanizing antibodies are described in Padlan et al. EP 519596 A1, published on Dec. 23, 1992.

The antibody molecule can be a single chain antibody. A single-chain antibody (scFv) may be engineered (see, for example, Colcher, D. et al. (1999) *Ann NY Acad Sci* 880: 263-80; and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

In yet other embodiments, the antibody molecule has a heavy chain constant region chosen from, e.g., the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, e.g., the (e.g., human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, e.g., the (e.g., human) light chain constant regions of kappa or lambda. The constant region can be altered, e.g., mutated, to modify the properties of the antibody (e.g., to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement function). In one embodiment the antibody has: effector function; and can fix complement.

In other embodiments the antibody does not recruit effector cells; or fix complement. In another embodiment, the antibody has reduced or no ability to bind an Fc receptor. For example, it is a isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, e.g., it has a mutagenized or deleted Fc receptor binding region.

Methods for altering an antibody constant region are known in the art. Antibodies with altered function, e.g., altered affinity for an effector ligand, such as FcR on a cell, 10 or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (see e.g., EP 388,151 A1, U.S. Pat. Nos. 5,624,821 and 5,648,260, the contents of all of which are hereby incorporated by reference). Similar type of alterations could be described which if applied to the murine, or other species immunoglobulin would reduce or eliminate these functions.

An antibody molecule can be derivatized or linked to another functional molecule (e.g., another peptide or protein). 20 As used herein, a "derivatized" antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin. Accordingly, the antibody molecules 25 of the invention are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (e.g., a bispecific antibody or a diabody), a detectable agent, a cytotoxic agent, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

One type of derivatized antibody molecule is produced by crosslinking two or more antibodies (of the same type or of different types, e.g., to create bispecific antibodies). Suitable 40 crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (e.g., m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (e.g., disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.

Multispecific or Multifunctional Antibody Molecules

Exemplary structures of multispecific and multifunctional molecules defined herein are described throughout. Exemplary structures are further described in: Weidle U et al. 50 (2013) The Intriguing Options of Multispecific Antibody Formats for Treatment of Cancer. *Cancer Genomics & Proteomics* 10: 1-18 (2013); and Spiess C et al. (2015) Alternative molecular formats and therapeutic applications for bispecific antibodies. *Molecular Immunology* 67: 95-106; the full contents of each of which is incorporated by reference herein).

In embodiments, multispecific antibody molecules can comprise more than one antigen-binding site, where different sites are specific for different antigens. In embodiments, 60 multispecific antibody molecules can bind more than one (e.g., two or more) epitopes on the same antigen. In embodiments, multispecific antibody molecules comprise an antigen-binding site specific for a target cell (e.g., cancer cell) and a different antigen-binding site specific for an immune effector cell. In one embodiment, the multispecific antibody molecule is a bispecific antibody molecule. Bispecific antibody molecules can be classified into five different structural

groups: (i) bispecific immunoglobulin G (BsIgG); (ii) IgG appended with an additional antigen-binding moiety; (iii) bispecific antibody fragments; (iv) bispecific fusion proteins; and (v) bispecific antibody conjugates.

BsIgG is a format that is monovalent for each antigen. Exemplary BsIgG formats include but are not limited to crossMab, DAF (two-in-one), DAF (four-in-one), Dutamab, DT-IgG, knobs-in-holes common LC, knobs-in-holes assembly, charge pair, Fab-arm exchange, SEEDbody, tricomab, LUZ-Y, Fcab, κλ-body, orthogonal Fab. See Spiess et al. Mol. Immunol. 67(2015):95-106. Exemplary BsIgGs include catumaxomab (Fresenius Biotech, Trion Pharma, Neopharm), which contains an anti-CD3 arm and an anti-EpCAM arm; and ertumaxomab (Neovii Biotech, Fresenius Biotech), which targets CD3 and HER2. In some embodiments, BsIgG comprises heavy chains that are engineered for heterodimerization. For example, heavy chains can be engineered for heterodimerization using a “knobs-into-holes” strategy, a SEED platform, a common heavy chain (e.g., in κλ-bodies), and use of heterodimeric Fc regions. See Spiess et al. Mol. Immunol. 67(2015):95-106. Strategies that have been used to avoid heavy chain pairing of homodimers in BsIgG include knobs-in-holes, duobody, asymmetric, charge pair, HA-TF, SEEDbody, and differential protein A affinity. See Id. BsIgG can be produced by separate expression of the component antibodies in different host cells and subsequent purification/assembly into a BsIgG. BsIgG can also be produced by expression of the component antibodies in a single host cell. BsIgG can be purified using affinity chromatography, e.g., using protein A and sequential pH elution.

IgG appended with an additional antigen-binding moiety is another format of bispecific antibody molecules. For example, monospecific IgG can be engineered to have bispecificity by appending an additional antigen-binding unit onto the monospecific IgG, e.g., at the N- or C-terminus of either the heavy or light chain. Exemplary additional antigen-binding units include single domain antibodies (e.g., variable heavy chain or variable light chain), engineered protein scaffolds, and paired antibody variable domains (e.g., single chain variable fragments or variable fragments). See Id. Examples of appended IgG formats include dual variable domain IgG (DVD-Ig), IgG(H)-scFv, scFv-(H)IgG, IgG(L)-scFv, scFv-(L)IgG, IgG(L,H)-Fv, IgG(H)-V, V(H)-IgG, IgG(L)-V, V(L)-IgG, KIH IgG-scFab, 2scFv-IgG, IgG-2scFv, scFv4-Ig, zybody, and DVI-IgG (four-in-one). See Spiess et al. Mol. Immunol. 67(2015):95-106. An example of an IgG-scFv is MM-141 (Merrimack Pharmaceuticals), which binds IGF-1R and HER3. Examples of DVD-Ig include ABT-981 (AbbVie), which binds IL-1 α and IL-1 β ; and ABT-122 (AbbVie), which binds TNF and IL-17A.

Bispecific antibody fragments (BsAb) are a format of bispecific antibody molecules that lack some or all of the antibody constant domains. For example, some BsAb lack an Fc region. In embodiments, bispecific antibody fragments include heavy and light chain regions that are connected by a peptide linker that permits efficient expression of the BsAb in a single host cell. Exemplary bispecific antibody fragments include but are not limited to nanobody, nanobody-HAS, BiTE, Diabody, DART, TandAb, scDiabody, scDiabody-CH3, Diabody-CH3, triple body, minibody, minibody, TriBi minibody, scFv-CH3 KIH, Fab-scFv, scFv-CH-CL-scFv, F(ab')2, F(ab')2-scFv2, scFv-KIH, Fab-scFv-Fc, tetravalent HCAb, scDiabody-Fc, Diabody-Fc, tandem scFv-Fc, and intrabody. See Id. For example, the BiTE format comprises tandem scFvs, where the component scFvs bind to CD3 on T cells and a surface antigen on cancer cells

Bispecific fusion proteins include antibody fragments linked to other proteins, e.g., to add additional specificity and/or functionality. An example of a bispecific fusion protein is an immTAC, which comprises an anti-CD3 scFv linked to an affinity-matured T-cell receptor that recognizes HLA-presented peptides. In embodiments, the dock-and-lock (DNL) method can be used to generate bispecific antibody molecules with higher valency. Also, fusions to albumin binding proteins or human serum albumin can be 10 extend the serum half-life of antibody fragments. See Id.

In embodiments, chemical conjugation, e.g., chemical conjugation of antibodies and/or antibody fragments, can be used to create BsAb molecules. See Id. An exemplary bispecific antibody conjugate includes the CovX-body format, in which a low molecular weight drug is conjugated site-specifically to a single reactive lysine in each Fab arm or an antibody or fragment thereof. In embodiments, the conjugation improves the serum half-life of the low molecular weight drug. An exemplary CovX-body is CVX-241 15 (NCT01004822), which comprises an antibody conjugated to two short peptides inhibiting either VEGF or Ang2. See Id.

The antibody molecules can be produced by recombinant expression, e.g., of at least one or more component, in a host 25 system. Exemplary host systems include eukaryotic cells (e.g., mammalian cells, e.g., CHO cells, or insect cells, e.g., SF9 or S2 cells) and prokaryotic cells (e.g., *E. coli*). Bispecific antibody molecules can be produced by separate expression of the components in different host cells and 30 subsequent purification/assembly. Alternatively, the antibody molecules can be produced by expression of the components in a single host cell. Purification of bispecific antibody molecules can be performed by various methods such as affinity chromatography, e.g., using protein A and 35 sequential pH elution. In other embodiments, affinity tags can be used for purification, e.g., histidine-containing tag, myc tag, or streptavidin tag.

CDR-Grafted Scaffolds

In embodiments, the antibody molecule is a CDR-grafted 40 scaffold domain. In embodiments, the scaffold domain is based on a fibronectin domain, e.g., fibronectin type III domain. The overall fold of the fibronectin type III (Fn3) domain is closely related to that of the smallest functional antibody fragment, the variable domain of the antibody 45 heavy chain. There are three loops at the end of Fn3; the positions of BC, DE and FG loops approximately correspond to those of CDR1, 2 and 3 of the VH domain of an antibody. Fn3 does not have disulfide bonds; and therefore Fn3 is stable under reducing conditions, unlike antibodies and their fragments (see, e.g., WO 98/56915; WO 01/64942; WO 00/34784). An Fn3 domain can be modified (e.g., using CDRs or hypervariable loops described herein) or varied, e.g., to select domains that bind to an antigen/marker/cell 50 described herein.

In embodiments, a scaffold domain, e.g., a folded domain, is based on an antibody, e.g., a “minibody” scaffold created by deleting three beta strands from a heavy chain variable domain of a monoclonal antibody (see, e.g., Tramontano et al., 1994, J Mol. Recognit. 7:9; and Martin et al., 1994, 55 EMBO J. 13:5303-5309). The “minibody” can be used to present two hypervariable loops. In embodiments, the scaffold domain is a V-like domain (see, e.g., Coia et al. WO 99/45110) or a domain derived from tandemstatin, which is a 74 residue, six-strand beta sheet sandwich held together by 60 two disulfide bonds (see, e.g., McConnell and Hoess, 1995, J Mol. Biol. 250:460). For example, the loops of tandemstatin can be modified (e.g., using CDRs or hypervariable 65

loops) or varied, e.g., to select domains that bind to a marker/antigen/cell described herein. Another exemplary scaffold domain is a beta-sandwich structure derived from the extracellular domain of CTLA-4 (see, e.g., WO 00/60070).

Other exemplary scaffold domains include but are not limited to T-cell receptors; MHC proteins; extracellular domains (e.g., fibronectin Type III repeats, EGF repeats); protease inhibitors (e.g., Kunitz domains, ecotin, BPTI, and so forth); TPR repeats; trifoil structures; zinc finger domains; DNA-binding proteins; particularly monomeric DNA binding proteins; RNA binding proteins; enzymes, e.g., proteases (particularly inactivated proteases), RNase; chaperones, e.g., thioredoxin, and heat shock proteins; and intracellular signaling domains (such as SH2 and SH3 domains). See, e.g., US 20040009530 and U.S. Pat. No. 7,501,121, incorporated herein by reference.

In embodiments, a scaffold domain is evaluated and chosen, e.g., by one or more of the following criteria: (1) amino acid sequence, (2) sequences of several homologous domains, (3) 3-dimensional structure, and/or (4) stability data over a range of pH, temperature, salinity, organic solvent, oxidant concentration. In embodiments, the scaffold domain is a small, stable protein domain, e.g., a protein of less than 100, 70, 50, 40 or 30 amino acids. The domain may include one or more disulfide bonds or may chelate a metal, e.g., zinc.

Antibody-Based Fusions

A variety of formats can be generated which contain additional binding entities attached to the N or C terminus of antibodies. These fusions with single chain or disulfide stabilized Fvs or Fabs result in the generation of tetravalent molecules with bivalent binding specificity for each antigen. Combinations of scFvs and scFabs with IgGs enable the production of molecules which can recognize three or more different antigens.

Antibody-Fab Fusion

Antibody-Fab fusions are bispecific antibodies comprising a traditional antibody to a first target and a Fab to a second target fused to the C terminus of the antibody heavy chain. Commonly the antibody and the Fab will have a common light chain. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. et al. (1997) *Nature Biotech* 15:159.

Antibody-scFv Fusion

Antibody-scFv Fusions are bispecific antibodies comprising a traditional antibody and a scFv of unique specificity fused to the C terminus of the antibody heavy chain. The scFv can be fused to the C terminus through the Heavy Chain of the scFv either directly or through a linker peptide. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. et al. (1997) *Nature Biotech* 15:159.

Variable Domain Immunoglobulin DVD

A related format is the dual variable domain immunoglobulin (DVD), which are composed of VH and VL domains of a second specificity place upon the N termini of the V domains by shorter linker sequences.

Other exemplary multispecific antibody formats include, e.g., those described in the following US20160114057A1, US20130243775A1, US20140051833, US20130022601, US20150017187A1, US20120201746A1, 5 US20150133638A1, US20130266568A1, US20160145340A1, WO2015127158A1, US20150203591A1, US20140322221A1, US20130303396A1, US20110293613, US20130017200A1, US20160102135A1, WO2015197598A2, 10 WO2015197582A1, U.S. Pat. No. 9,359,437, US20150018529, WO2016115274A1, WO2016087416A1, US20080069820A1, U.S. Pat. Nos. 9,145,588B, 7,919,257, and US20150232560A1. Exemplary multispecific molecules utilizing a full antibody-Fab/scFab format include those described in the following, U.S. Pat. No. 9,382,323B2, US20140072581A1, US20140308285A1, 15 US20130165638A1, US20130267686A1, US20140377269A1, U.S. Pat. No. 7,741,446B2, and 20 WO1995009917A1. Exemplary multispecific molecules utilizing a domain exchange format include those described in the following, US20150315296A1, WO2016087650A1, US20160075785A1, WO2016016299A1, US20160130347A1, US20150166670, U.S. Pat. No. 8,703, 25 132B2, US20100316645, U.S. Pat. No. 8,227,577B2, US20130078249.

Fc-Containing Entities (Mini-Antibodies)

Fc-containing entities, also known as mini-antibodies, can be generated by fusing scFv to the C-termini of constant 30 heavy region domain 3 (CH3-scFv) and/or to the hinge region (scFv-hinge-Fc) of an antibody with a different specificity. Trivalent entities can also be made which have disulfide stabilized variable domains (without peptide linker) fused to the C-terminus of CH3 domains of IgGs.

Fc-Containing Multispecific Molecules

In some embodiments, the multispecific molecules disclosed herein includes an immunoglobulin constant region (e.g., an Fc region). Exemplary Fc regions can be chosen from the heavy chain constant regions of IgG1, IgG2, IgG3 40 or IgG4; more particularly, the heavy chain constant region of human IgG1, IgG2, IgG3, or IgG4.

In some embodiments, the immunoglobulin chain constant region (e.g., the Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, 45 antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.

In other embodiments, an interface of a first and second immunoglobulin chain constant regions (e.g., a first and a second Fc region) is altered, e.g., mutated, to increase or 50 decrease dimerization, e.g., relative to a non-engineered interface, e.g., a naturally-occurring interface. For example, dimerization of the immunoglobulin chain constant region (e.g., the Fc region) can be enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired protuberance-cavity ("knob-in-a hole"), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer to homomultimer forms, e.g., relative to a non-engineered interface.

In some embodiments, the multispecific molecules 60 include a paired amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1. For example, the immunoglobulin chain constant region (e.g., Fc region) can include a paired 65 amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), and T366W (e.g., corresponding to a protuberance or knob).

In other embodiments, the multifunctional molecule includes a half-life extender, e.g., a human serum albumin or an antibody molecule to human serum albumin.

Heterodimerized Antibody Molecules & Methods of Making

Various methods of producing multispecific antibodies have been disclosed to address the problem of incorrect heavy chain pairing. Exemplary methods are described below. Exemplary multispecific antibody formats and methods of making said multispecific antibodies are also disclosed in e.g., Speiss et al. Molecular Immunology 67 (2015) 95-106; and Klein et al mAbs 4:6, 653-663; November/December 2012; the entire contents of each of which are incorporated by reference herein.

Heterodimerized bispecific antibodies are based on the natural IgG structure, wherein the two binding arms recognize different antigens. IgG derived formats that enable defined monovalent (and simultaneous) antigen binding are generated by forced heavy chain heterodimerization, combined with technologies that minimize light chain mispairing (e.g., common light chain). Forced heavy chain heterodimerization can be obtained using, e.g., knob-in-hole OR strand exchange engineered domains (SEED).

Knob-in-Hole

Knob-in-Hole as described in U.S. Pat. Nos. 5,731,116, 7,476,724 and Ridgway, J. et al. (1996) *Prot. Engineering* 9(7): 617-621, broadly involves: (1) mutating the CH3 domain of one or both antibodies to promote heterodimerization; and (2) combining the mutated antibodies under conditions that promote heterodimerization. "Knobs" or "protuberances" are typically created by replacing a small amino acid in a parental antibody with a larger amino acid (e.g., T366Y or T366W); "Holes" or "cavities" are created by replacing a larger residue in a parental antibody with a smaller amino acid (e.g., Y407T, T366S, L368A and/or Y407V).

For bispecific antibodies including an Fc domain, introduction of specific mutations into the constant region of the heavy chains to promote the correct heterodimerization of the Fc portion can be utilized. Several such techniques are reviewed in Klein et al. (mAbs (2012) 4:6, 1-11), the contents of which are incorporated herein by reference in their entirety. These techniques include the "knobs-into-holes" (KiH) approach which involves the introduction of a bulky residue into one of the CH3 domains of one of the antibody heavy chains. This bulky residue fits into a complementary "hole" in the other CH3 domain of the paired heavy chain so as to promote correct pairing of heavy chains (see e.g., U.S. Pat. No. 7,642,228).

Exemplary KiH mutations include S354C, T366W in the "knob" heavy chain and Y349C, T366S, L368A, Y407V in the "hole" heavy chain. Other exemplary KiH mutations are provided in Table 1, with additional optional stabilizing Fc cysteine mutations.

TABLE 1

Exemplary Fc KiH mutations and optional Cysteine mutations		
Position	Knob Mutation	Hole Mutation
T366	T366W	T366S
L368	—	L368A
Y407	—	Y407V

TABLE 1-continued

Exemplary Fc KiH mutations and optional Cysteine mutations		
Additional Cysteine Mutations to form a stabilizing disulfide bridge		
Position	Knob CH3	Hole CH3
S354 Y349	S354C —	— Y349C

Other Fc mutations are provided by Igawa and Tsunoda who identified 3 negatively charged residues in the CH3 domain of one chain that pair with three positively charged residues in the CH3 domain of the other chain. These specific charged residue pairs are: E356-K439, E357-K370, D399-K409 and vice versa. By introducing at least two of the following three mutations in chain A: E356K, E357K and D399K, as well as K370E, K409D, K439E in chain B, alone or in combination with newly identified disulfide bridges, they were able to favor very efficient heterodimerization while suppressing homodimerization at the same time (Martens T et al. A novel one-armed antic-Met antibody inhibits glioblastoma growth in vivo. *Clin Cancer Res* 2006; 12:6144-52; PMID:17062691). Xencor defined 41 variant pairs based on combining structural calculations and sequence information that were subsequently screened for maximal heterodimerization, defining the combination of S364H, F405A (HA) on chain A and Y349T, T394F on chain B (TF) (Moore G L et al. A novel bispecific antibody format enables simultaneous bivalent and monovalent co-engagement of distinct target antigens. *MAbs* 2011; 3:546-57; PMID: 22123055).

Other exemplary Fc mutations to promote heterodimerization of multispecific antibodies include those described in the following references, the contents of each of which is incorporated by reference herein, WO2016071377A1, US20140079689A1, US20160194389A1, US20160257763, WO2016071376A2, WO2015107026A1, WO2015107025A1, WO2015107015A1, US20150353636A1, US20140199294A1, U.S. Pat. No. 7,750,128B2, US20160229915A1, US20150344570A1, U.S. Pat. No. 8,003,774A1, US20150337049A1, US20150175707A1, US20140242075A1, US20130195849A1, US20120149876A1, US20140200331A1, U.S. Pat. No. 9,309,311B2, U.S. Pat. No. 8,586,713, US20140037621A1, US20130178605A1, US20140363426A1, US20140051835A1 and US20110054151A1.

Stabilizing cysteine mutations have also been used in combination with KiH and other Fc heterodimerization promoting variants, see e.g., U.S. Pat. No. 7,183,076. Other exemplary cysteine modifications include, e.g., those disclosed in US20140348839A1, U.S. Pat. No. 7,855,275B2, and U.S. Pat. No. 9,000,130B2.

Strand Exchange Engineered Domains (SEED)

Heterodimeric Fc platform that support the design of bispecific and asymmetric fusion proteins by devising strand-exchange engineered domain (SEED) C(H)3 heterodimers are known. These derivatives of human IgG and IgA C(H)3 domains create complementary human SEED C(H)3 heterodimers that are composed of alternating segments of human IgA and IgG C(H)3 sequences. The resulting pair of SEED C(H)3 domains preferentially associates to form heterodimers when expressed in mammalian cells. SEEDbody (Sb) fusion proteins consist of [IgG1 hinge]-C(H)2-[SEED C(H)3], that may be genetically linked to one

or more fusion partners (see e.g., Davis J H et al. SEED bodies: fusion proteins based on strand exchange engineered domain (SEED) CH3 heterodimers in an Fc analogue platform for asymmetric binders or immunofusions and bispecific antibodies. Protein Eng Des Sel 2010; 23:195-202; PMID:20299542 and U.S. Pat. No. 8,871,912. The contents of each of which are incorporated by reference herein). Duobody

“Duobody” technology to produce bispecific antibodies with correct heavy chain pairing are known. The DuoBody technology involves three basic steps to generate stable bispecific human IgG1 antibodies in a post-production exchange reaction. In a first step, two IgG1s, each containing single matched mutations in the third constant (CH3) domain, are produced separately using standard mammalian recombinant cell lines. Subsequently, these IgG1 antibodies are purified according to standard processes for recovery and purification. After production and purification (post-production), the two antibodies are recombined under tailored laboratory conditions resulting in a bispecific antibody product with a very high yield (typically >95%) (see e.g., Labrijn et al, PNAS 2013; 110(13):5145-5150 and Labrijn et al. Nature Protocols 2014; 9(10):2450-63, the contents of each of which are incorporated by reference herein).

Electrostatic Interactions

Methods of making multispecific antibodies using CH3 amino acid changes with charged amino acids such that homodimer formation is electrostatically unfavorable are disclosed. EP1870459 and WO 2009089004 describe other strategies for favoring heterodimer formation upon co-expression of different antibody domains in a host cell. In these methods, one or more residues that make up the heavy chain constant domain 3 (CH3), CH3-CH3 interfaces in both CH3 domains are replaced with a charged amino acid such that homodimer formation is electrostatically unfavorable and heterodimerization is electrostatically favorable. Additional methods of making multispecific molecules using electrostatic interactions are described in the following references, the contents of each of which is incorporated by reference herein, include US20100015133, U.S. Pat. No. 8,592,562B2, U.S. Pat. No. 9,200,060B2, US20140154254A1, and U.S. Pat. No. 9,358,286A1.

Common Light Chain

Light chain mispairing needs to be avoided to generate homogenous preparations of bispecific IgGs. One way to achieve this is through the use of the common light chain principle, i.e. combining two binders that share one light chain but still have separate specificities. An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable light chain to interact with each of the heteromeric variable heavy chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common light chain as disclosed in, e.g., U.S. Pat. No. 7,183,076B2, US20110177073A1, EP2847231A1, WO2016079081A1, and EP3055329A1, the contents of each of which is incorporated by reference herein.

CrossMab

Another option to reduce light chain mispairing is the CrossMab technology which avoids non-specific L chain mispairing by exchanging CH1 and CL domains in the Fab of one half of the bispecific antibody. Such crossover variants retain binding specificity and affinity, but make the two arms so different that L chain mispairing is prevented. The CrossMab technology (as reviewed in Klein et al. Supra) involves domain swapping between heavy and light

chains so as to promote the formation of the correct pairings. Briefly, to construct a bispecific IgG-like CrossMab antibody that could bind to two antigens by using two distinct light chain-heavy chain pairs, a two-step modification process is applied. First, a dimerization interface is engineered into the C-terminus of each heavy chain using a heterodimerization approach, e.g., Knob-into-hole (KiH) technology, to ensure that only a heterodimer of two distinct heavy chains from one antibody (e.g., Antibody A) and a second antibody (e.g., Antibody B) is efficiently formed. Next, the constant heavy 1 (CH1) and constant light (CL) domains of one antibody are exchanged (Antibody A), keeping the variable heavy (VH) and variable light (VL) domains consistent. The exchange of the CH1 and CL domains ensured that the modified antibody (Antibody A) light chain would only efficiently dimerize with the modified antibody (antibody A) heavy chain, while the unmodified antibody (Antibody B) light chain would only efficiently dimerize with the unmodified antibody (Antibody B) heavy chain; and thus only the desired bispecific CrossMab would be efficiently formed (see e.g., Cain, C. SciBX 4(28); doi:10.1038/scibx.2011.783, the contents of which are incorporated by reference herein).

Common Heavy Chain

An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable heavy chain to interact with each of the heteromeric variable light chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common heavy chain are disclosed in, e.g., US20120184716, US20130317200, and US20160264685A1, the contents of each of which is incorporated by reference herein.

Amino Acid Modifications

Alternative compositions and methods of producing multispecific antibodies with correct light chain pairing include various amino acid modifications. For example, Zymeworks describes heterodimers with one or more amino acid modifications in the CH1 and/or CL domains, one or more amino acid modifications in the VH and/or VL domains, or a combination thereof, which are part of the interface between the light chain and heavy chain and create preferential pairing between each heavy chain and a desired light chain such that when the two heavy chains and two light chains of the heterodimer pair are co-expressed in a cell, the heavy chain of the first heterodimer preferentially pairs with one of the light chains rather than the other (see e.g., WO2015181805). Other exemplary methods are described in WO2016026943 (Argen-X), US20150211001, US20140072581A1, US20160039947A1, and US20150368352.

Lambda/Kappa Formats

Multispecific molecules (e.g., multispecific antibody molecules) that include the lambda light chain polypeptide and a kappa light chain polypeptides, can be used to allow for heterodimerization. Methods for generating bispecific antibody molecules comprising the lambda light chain polypeptide and a kappa light chain polypeptides are disclosed in PCT/US17/53053 filed on Sep. 22, 2017, incorporated herein by reference in its entirety.

In embodiments, the multispecific molecules includes a multispecific antibody molecule, e.g., an antibody molecule comprising two binding specificities, e.g., a bispecific antibody molecule. The multispecific antibody molecule includes:

a lambda light chain polypeptide 1 (LLCP1) specific for a first epitope;

83

a heavy chain polypeptide 1 (HCP1) specific for the first epitope;
 a kappa light chain polypeptide 2 (KLCP2) specific for a second epitope; and
 a heavy chain polypeptide 2 (HCP2) specific for the second epitope.

“Lambda light chain polypeptide 1 (LLCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, an LLCP1 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP1. LLCP1, together with its HCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope). As described elsewhere herein, LLCP1 has a higher affinity for HCP1 than for HCP2.

“Kappa light chain polypeptide 2 (KLCP2)”, as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP2. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, a KLCP2 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP2. KLCP2, together with its HCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

“Heavy chain polypeptide 1 (HCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an LLCP1, (ii) to complex preferentially, as described herein to LLCP1 as opposed to KLCP2; and (iii) to complex preferentially, as described herein, to an HCP2, as opposed to another molecule of HCP1. HCP1, together with its LLCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope).

“Heavy chain polypeptide 2 (HCP2)”, as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an KLCP2, (ii) to complex preferentially, as described herein to KLCP2 as opposed to LLCP1; and (iii) to complex preferentially, as described herein, to an HCP1, as opposed to another molecule of HCP2. HCP2, together

84

with its KLCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

In some embodiments of the multispecific antibody molecule disclosed herein:

LLCP1 has a higher affinity for HCP1 than for HCP2; and/or

KLCP2 has a higher affinity for HCP2 than for HCP1.

In embodiments, the affinity of LLCP1 for HCP1 is sufficiently greater than its affinity for HCP2, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75, 80, 90, 95, 98, 99, 99.5, or 99.9% of the multispecific antibody molecule molecules have a LLCP1 complexed, or interfaced with, a HCP1.

In some embodiments of the multispecific antibody molecule disclosed herein:

the HCP1 has a greater affinity for HCP2, than for a second molecule of HCP1; and/or

the HCP2 has a greater affinity for HCP1, than for a second molecule of HCP2.

In embodiments, the affinity of HCP1 for HCP2 is sufficiently greater than its affinity for a second molecule of HCP1, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75%, 80, 90, 95, 98, 99, 99.5 or 99.9% of the multispecific antibody molecule molecules have a HCP1 complexed, or interfaced with, a HCP2.

In another aspect, disclosed herein is a method for making, or producing, a multispecific antibody molecule. The method includes:

(i) providing a first heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both));

(ii) providing a second heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both));

(iii) providing a lambda chain polypeptide (e.g., a lambda light variable region (VL λ), a lambda light constant chain (VL λ), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH); and

(iv) providing a kappa chain polypeptide (e.g., a lambda light variable region (VL κ), a lambda light constant chain (VL κ), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH),

under conditions where (i)-(iv) associate.

In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization.

In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in a single cell, e.g., a single mammalian cell, e.g., a CHO cell. In embodiments, (i)-(iv) are expressed in the cell.

In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in different cells, e.g., different mammalian cells, e.g., two or more CHO cell. In embodiments, (i)-(iv) are expressed in the cells.

In one embodiment, the method further comprises purifying a cell-expressed antibody molecule, e.g., using a lambda-and/or-kappa-specific purification, e.g., affinity chromatography.

In embodiments, the method further comprises evaluating the cell-expressed multispecific antibody molecule. For example, the purified cell-expressed multispecific antibody molecule can be analyzed by techniques known in the art, include mass spectrometry. In one embodiment, the purified cell-expressed antibody molecule is cleaved, e.g., digested with papain to yield the Fab moieties and evaluated using mass spectrometry.

In embodiments, the method produces correctly paired kappa/lambda multispecific, e.g., bispecific, antibody molecules in a high yield, e.g., at least 75%, 80, 90, 95, 98, 99, 99.5 or 99.9%.

In other embodiments, the multispecific, e.g., a bispecific, antibody molecule that includes:

- (i) a first heavy chain polypeptide (HCP1) (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both)), e.g., wherein the HCP1 binds to a first epitope;
- (ii) a second heavy chain polypeptide (HCP2) (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both)), e.g., wherein the HCP2 binds to a second epitope;
- (iii) a lambda light chain polypeptide (LLCP1) (e.g., a lambda light variable region (VLI), a lambda light constant chain (VL_k), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH), e.g., wherein the LLCP1 binds to a first epitope; and (iv) a kappa light chain polypeptide (KLCP2) (e.g., a lambda light variable region (VL_k), a lambda light constant chain (VL_k), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH), e.g., wherein the KLCP2 binds to a second epitope.

In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization. In embodiments, the multispecific antibody molecule has a first binding specificity that includes a hybrid VL1-CL1 heterodimerized to a first heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a knob modification) and a second binding specificity that includes a hybrid VL_k-CL_k heterodimerized to a second heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a hole modification).

Linkers

The multispecific or multifunctional molecule disclosed herein can further include a linker, e.g., a linker between one or more of: the antigen binding domain and the cytokine molecule, the antigen binding domain and the immune cell engager, the antigen binding domain and the stromal modifying moiety, the cytokine molecule and the immune cell engager, the cytokine molecule and the stromal modifying moiety, the immune cell engager and the stromal modifying moiety, the antigen binding domain and the immunoglobulin chain constant region, the cytokine molecule and the immunoglobulin chain constant region, the immune cell engager and the immunoglobulin chain constant region, or the stromal modifying moiety and the immunoglobulin chain constant region. In embodiments, the linker is chosen from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker, or a combination thereof.

In one embodiment, the multispecific molecule can include one, two, three or four linkers, e.g., a peptide linker.

In one embodiment, the peptide linker includes Gly and Ser. In some embodiments, the peptide linker is selected from GGGGS (SEQ ID NO: 42); GGGGSGGGGS (SEQ ID NO: 43); GGGGSGGGGSGGGGS (SEQ ID NO: 44); and DVPSGPAGGGGSGGGGS (SEQ ID NO: 45). In some embodiments, the peptide linker is a A(EAAAK)nA (SEQ ID NO: 6154) family of linkers (e.g., as described in Protein Eng. (2001) 14 (8): 529-532). These are stiff helical linkers with n ranging from 2-5. In some embodiments, the peptide linker is selected from AEAAAKEAAAKAAA (SEQ ID NO: 75); AEAAAKEAAAKEAAAKAAA (SEQ ID NO: 76); AEAAAKEAAAKEAAAKEAAAKAAA (SEQ ID NO: 77); and AEAAAKEAAAKEAAAKEAAKEAAKAAA (SEQ ID NO: 78).

Targeting Moieties

In one embodiment, the anti-NKp30 antibody molecule further comprises a second antigen binding moiety, e.g., tumor targeting moiety, that binds to a cancer antigen, e.g., a tumor antigen or a stromal antigen. In some embodiments, the cancer antigen is, e.g., a mammalian, e.g., a human, cancer antigen. In other embodiments, the antibody molecule further comprises a second binding moiety that binds to an immune cell antigen, e.g., a mammalian, e.g., a human, immune cell antigen. In other embodiments, the antibody molecule further comprises a second binding moiety that binds to a viral antigen. For example, the antibody molecule binds specifically to an epitope, e.g., linear or conformational epitope, on the cancer antigen, the immune cell antigen.

In some embodiments, the multispecific (e.g., bi-, tri-, tetra-specific) molecule, includes, e.g., is engineered to contain, one or more tumor specific targeting moieties that direct the molecule to a tumor cell. In certain embodiments, the multispecific molecules disclosed herein include a tumor-targeting moiety. The tumor targeting moiety can be chosen from an antibody molecule (e.g., an antigen binding domain as described herein), a receptor or a receptor fragment, or a ligand or a ligand fragment, or a combination thereof. In some embodiments, the tumor targeting moiety associates with, e.g., binds to, a tumor cell (e.g., a molecule, e.g., antigen, present on the surface of the tumor cell). In certain embodiments, the tumor targeting moiety targets, e.g., directs the multispecific molecules disclosed herein to a cancer (e.g., a cancer or tumor cells). In some embodiments, the cancer is chosen from a hematological cancer, a solid cancer, a metastatic cancer, or a combination thereof.

In some embodiments, the multispecific molecule, e.g., the tumor-targeting moiety, binds to a solid tumor antigen or a stromal antigen. The solid tumor antigen or stromal antigen can be present on a solid tumor, or a metastatic lesion thereof. In some embodiments, the solid tumor is chosen from one or more of pancreatic (e.g., pancreatic adenocarcinoma), breast, colorectal, lung (e.g., small or non-small cell lung cancer), skin, ovarian, or liver cancer. In one embodiment, the solid tumor is a fibrotic or desmoplastic solid tumor. For example, the solid tumor antigen or stromal antigen can be present on a tumor, e.g., a tumor of a class typified by having one or more of: limited tumor perfusion, compressed blood vessels, or fibrotic tumor interstitium.

In certain embodiments, the solid tumor antigen is chosen from one or more of: PDL1, CD47, mesothelin, ganglioside 2 (GD2), prostate stem cell antigen (PSCA), prostate specific membrane antigen (PMSA), prostate-specific antigen (PSA), carcinoembryonic antigen (CEA), Ron Kinase, c-Met, Immature laminin receptor, TAG-72, BING-4, Calcium-activated chloride channel 2, Cyclin-B1, 9D7, Ep-

CAM, EphA3, Her2/neu, Telomerase, SAP-1, Survivin, NY-ESO-1/LAGE-1, PRAME, SSX-2, Melan-A/MART-1, Gp100/pmel17, Tyrosinase, TRP-1/-2, MC1R, β -catenin, BRCA1/2, CDK4, CML66, Fibronectin, p53, Ras, TGF-B receptor, AFP, ETA, MAGE, MUC-1, CA-125, BAGE, GAGE, NY-ESO-1, β -catenin, CDK4, CDC27, CD47, a actinin-4, TRP1/gp75, TRP2, gp100, Melan-A/MART1, gangliosides, WT1, EphA3, Epidermal growth factor receptor (EGFR), CD20, MART-2, MART-1, MUC1, MUC2, MUM1, MUM2, MUM3, NA88-1, NPM, OA1, OGT, RCC, RUI1, RUI2, SAGE, TRG, TRP1, TSTA, Folate receptor alpha, L1-CAM, CAIX, EGFRvIII, gpA33, GD3, GM2, VEGFR, Integrins (Integrin alphaVbeta3, Integrin alpha5Beta1), Carbohydrates (Le), IGF1R, EPHA3, TRAILR1, TRAILR2, or RANKL. In some embodiments, the solid tumor antigen is chosen from: PDL1, Mesothelin, CD47, GD2, PMSA, PSCA, CEA, Ron Kinase, or c-Met. Exemplary amino acid and nucleotide sequences for tumor targeting moieties are disclosed in WO 2017/165464, see e.g., pages 102-108, 172-290, incorporated herein by reference.

In some embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises a targeting moiety, e.g., a binding specificity, that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.

In some embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises a targeting moiety, e.g., a binding specificity, that binds to an infected cell, e.g., a viral infected cell.

T Cell Engagers

In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more T cell engager that mediate binding to and/or activation of a T cell. Accordingly, in some embodiments, the T cell engager is selected from an antigen binding domain or ligand that binds to (e.g., and in some embodiments activates) one or more of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226. In other embodiments, the T cell engager is selected from an antigen binding domain or ligand that binds to and does not activate one or more of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226.

Exemplary T cell engagers are disclosed in WO 2017/165464, incorporated herein by reference.

Cytokine Molecules

In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more cytokine molecules, e.g., immunomodulatory (e.g., proinflammatory) cytokines and variants, e.g., functional variants, thereof. Accordingly, in some embodiments, the cytokine molecule is an interleukin or a variant, e.g., a functional variant thereof. In some embodiments the interleukin is a proinflammatory interleukin. In some embodiments the interleukin is chosen from interleukin-2 (IL-2), interleukin-12 (IL-12), interleukin-15 (IL-15), interleukin-18 (IL-18), interleukin-21 (IL-21), interleukin-7 (IL-7), or interferon gamma. In some embodiments, the cytokine molecule is a proinflammatory cytokine.

In certain embodiments, the cytokine is a single chain cytokine. In certain embodiments, the cytokine is a multi-chain cytokine (e.g., the cytokine comprises 2 or more (e.g., 2) polypeptide chains. An exemplary multichain cytokine is IL-12.

Examples of useful cytokines include, but are not limited to, GM-CSF, IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-21, IFN- α , IFN- γ , MIP-1 α , MIP-1 β , TGF- β , TNF- α , and TNF β . In one embodiment the cytokine of the multispecific or multifunctional polypeptide is a cytokine selected from the group of GM-CSF, IL-2, IL-7, IL-8, IL-10, IL-12, IL-15, IL-21, IFN- α , IFN- γ , MIP-1 α , MIP-1 β and TGF- β . In one embodiment the cytokine of the i the multispecific or multifunctional polypeptide is a cytokine selected from the group of IL-2, IL-7, IL-10, IL-12, IL-15, IFN- α , and IFN- γ . In certain embodiments the cytokine is mutated to remove N- and/or O-glycosylation sites. Elimination of glycosylation increases homogeneity of the product obtainable in recombinant production.

In one embodiment, the cytokine of the multispecific or multifunctional polypeptide is IL-2. In a specific embodiment, the IL-2 cytokine can elicit one or more of the cellular responses selected from the group consisting of: proliferation in an activated T lymphocyte cell, differentiation in an activated T lymphocyte cell, cytotoxic T cell (CTL) activity, proliferation in an activated B cell, differentiation in an activated B cell, proliferation in a natural killer (NK) cell, differentiation in a NK cell, cytokine secretion by an activated T cell or an NK cell, and NK/lymphocyte activated killer (LAK) antitumor cytotoxicity. In another particular embodiment the IL-2 cytokine is a mutant IL-2 cytokine having reduced binding affinity to the .alpha.-subunit of the IL-2 receptor. Together with the beta- and gamma-subunits (also known as CD122 and CD132, respectively), the .alpha.-subunit (also known as CD25) forms the heterotrimeric high-affinity IL-2 receptor, while the dimeric receptor consisting only of the β - and γ -subunits is termed the intermediate-affinity IL-2 receptor. As described in PCT patent application number PCT/EP2012/051991, which is incorporated herein by reference in its entirety, a mutant IL-2 polypeptide with reduced binding to the .alpha.-subunit of the IL-2 receptor has a reduced ability to induce IL-2 signaling in regulatory T cells, induces less activation-induced cell death (AICD) in T cells, and has a reduced toxicity profile in vivo, compared to a wild-type IL-2 polypeptide. The use of such an cytokine with reduced toxicity is particularly advantageous in a multispecific or multifunctional polypeptide according to the invention, having a long serum half-life due to the presence of an Fc domain. In one embodiment, the mutant IL-2 cytokine of the multispecific or multifunctional polypeptide according to the invention comprises at least one amino acid mutation that reduces or abolishes the affinity of the mutant IL-2 cytokine to the .alpha.-subunit of the IL-2 receptor (CD25) but preserves the affinity of the mutant IL-2 cytokine to the intermediate-affinity IL-2 receptor (consisting of the β and γ subunits of the IL-2 receptor), compared to the non-mutated IL-2 cytokine. In one embodiment the one or more amino acid mutations are amino acid substitutions. In a specific embodiment, the mutant IL-2 cytokine comprises one, two or three amino acid substitutions at one, two or three position(s) selected from the positions corresponding to residue 42, 45, and 72 of human IL-2. In a more specific embodiment, the mutant IL-2 cytokine comprises three amino acid substitutions at the positions corresponding to residue 42, 45 and 72 of human IL-2. In an even more specific embodiment, the mutant IL-2 cytokine is human IL-2 comprising the amino acid substitutions F42A, Y45A and L72G. In one embodiment the mutant IL-2 cytokine additionally comprises an amino acid mutation at a position corresponding to position 3 of human IL-2, which eliminates the O-glycosylation site of IL-2. Particularly, said additional

amino acid mutation is an amino acid substitution replacing a threonine residue by an alanine residue. A particular mutant IL-2 cytokine useful in the invention comprises four amino acid substitutions at positions corresponding to residues 3, 42, 45 and 72 of human IL-2. Specific amino acid substitutions are T3A, F42A, Y45A and L72G. As demonstrated in PCT patent application number PCT/EP2012/051991 and in the appended Examples, said quadruple mutant IL-2 polypeptide (IL-2 qm) exhibits no detectable binding to CD25, reduced ability to induce apoptosis in T cells, reduced ability to induce IL-2 signaling in T.sub.reg cells, and a reduced toxicity profile in vivo. However, it retains ability to activate IL-2 signaling in effector cells, to induce proliferation of effector cells, and to generate IFN- γ as a secondary cytokine by NK cells.

The IL-2 or mutant IL-2 cytokine according to any of the above embodiments may comprise additional mutations that provide further advantages such as increased expression or stability. For example, the cysteine at position 125 may be replaced with a neutral amino acid such as alanine, to avoid the formation of disulfide-bridged IL-2 dimers. Thus, in certain embodiments the IL-2 or mutant IL-2 cytokine of the multispecific or multifunctional polypeptide according to the invention comprises an additional amino acid mutation at a position corresponding to residue 125 of human IL-2. In one embodiment said additional amino acid mutation is the amino acid substitution C125A.

Exemplary cytokine molecules are disclosed in WO 2017/165464, see e.g., pages 108-118, 169-172, incorporated herein by reference.

TGF- β Inhibitor

In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more modulators of TGF- β (e.g., a TGF- β inhibitor). In some embodiments, the TGF- β inhibitor binds to and inhibits TGF- β , e.g., reduces the activity of TGF- β . In some embodiments, the TGF- β inhibitor inhibits (e.g., reduces the activity of) TGF- β 1. In some embodiments, the TGF- β inhibitor inhibits (e.g., reduces the activity of) TGF- β 2. In some embodiments, the TGF- β inhibitor inhibits (e.g., reduces the activity of) TGF- β 3. In some embodiments, the TGF- β inhibitor inhibits (e.g., reduces the activity of) TGF- β 1 and TGF- β 3. In some embodiments, the TGF- β inhibitor inhibits (e.g., reduces the activity of) TGF- β 1, TGF- β 2, and TGF- β 3.

In some embodiments, the TGF- β inhibitor comprises a portion of a TGF- β receptor (e.g., an extracellular domain of a TGF- β receptor) that is capable of inhibiting (e.g., reducing the activity of) TGF- β , or functional fragment or variant thereof. In some embodiments, the TGF- β inhibitor comprises a TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof). In some embodiments, the TGF- β inhibitor comprises a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof). In some embodiments, the TGF- β inhibitor comprises a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof). In some embodiments, the TGF- β inhibitor comprises a TGFBR2 polypeptide (e.g., an

extracellular domain of TGFBR2 or functional variant thereof) and a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof).

Exemplary TGF- β receptor polypeptides that can be used as TGF- β inhibitors have been disclosed in U.S. Pat. Nos. 8,993,524, 9,676,863, 8,658,135, US20150056199, US20070184052, and WO2017037634, all of which are herein incorporated by reference in their entirety.

In some embodiments, the TGF- β inhibitor comprises an extracellular domain of TGFBR1 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3095, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3096, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3097, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3104, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3105, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

In some embodiments, the TGF- β inhibitor comprises an extracellular domain of TGFBR2 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3098, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3099, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3100, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3101, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3102, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3103, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

In some embodiments, the TGF- β inhibitor comprises an extracellular domain of TGFBR3 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3106, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises an extracellular domain of SEQ ID NO: 3107, or a sequence substantially identical thereto (e.g., a sequence

91

that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF- β inhibitor comprises the amino acid sequence of SEQ ID NO: 3108, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

92

In some embodiments, the TGF- β inhibitor comprises no more than one TGF- β receptor extracellular domain. In some embodiments, the TGF- β inhibitor comprises two or more (e.g., two, three, four, five, or more) TGF- β receptor extracellular domains, linked together, e.g., via a linker.

TABLE 4

Exemplary amino acid sequences of TGF- β polypeptides or TGF- β receptor polypeptides		
SEQ ID NO	Description	Amino acid sequence
SEQ ID NO: 1 3092	Immature (P01137-1)	MPPSGLRLLLLLPLLWLLVTPGRPAAGLSTCKTIDMELVKRKRIE AIRGQILSKRLASPPSQGEVPPGPLPEAVLALYNSTRDRVAGESAE PEPEADYYAKEVTRVLVMEVTHNEIYDKFKQSTHSIYMFNTSELR EAVPEPVLLSRAELRLRLKLKVQEYQKYSNNSWRYLSNRLLA PSDSEWLSPDVTGVVRQWLSRGGEIEGFRLSAHCSCSRDNLTQVD INGFTTGRRGDLATIHGMNRPFLLMATPLERAQHQLQSSRHRRALDT NYCFSSTEKCCVRLQYIDFRKDLGKWNIHEPKGYHANFCLGPCPYI WSLDTQYSKVLALYNOHNPAGASAAPCCVPQALEPLPIVYYVGRKPKV EQLSNMIVRSCKCS
SEQ ID NO: 1 3117	Human TGF- β (P01137-1)	LSTCKTIDMELVKRKRIEAIRGQILSKRLASPPSQGEVPPGPLPEA VLALYNSTRDRVAGESAEPEPEADYYAKEVTRVLVMEVTHNEIYDK FKQSTHSIYMFNTSELRLEAVPEPVLLSRAELRLRLKLKVQEYQHVEL YQKYSNNSWRYLSNRLLAPSDSPEWLSFDVTGVVRQWLSRGGEIEGF RLSAHCSCDSRDNTLQVDINGFTTGRRGDLATIHGMNRPFLLMATP LERAQHQLQSSRHRRALDTNYCFSSTEKCCVRLQYIDFRKDLGKWNI HEPKGYHANFCLGPCPYIWSLDTQYSKVLALYNOHNPAGASAAPCCVP QALEPLPIVYYVGRKPKEVQLSNMIVRSCKCS
SEQ ID NO: 2 3093	Immature (P61812-1)	MHYCVLASFILHLHVTLVALSLSLTCSTLDMDQFMRKRKIEAIRGQILSK LKLTSPPEDYPEPEEVPPVEVISIYINSTDRDLSQEAKSRRAAACERERS DEEYYAKEVYKIDMPPFFPSENAIPPTFYRPFYFRIVRFDVSAMEKNA SNLVKAEPFRVFRLQNPKARVEPQRILEYQILKSKDLSPTQRYIDS VVKTRAEGEWLSFDVTDAVHEWLHKDRNLGFKISLHCPCTTFVPSN NYIIPNKSEELEARFAGIDGTSTYSGDQKTIKSTRKKNSGKTPHLL LMLLPSPYRLESQQTNRRKRALDAAYCPRNVQDNCLLRPLYIDFKRD LGWKWIHEPKGYNANCAGACPYLWSSDTQHSRVLSLYNTINPEASA SPCCVSQDLEPLTILYYIGKTPKIEQLSNMIVKSCKCS
SEQ ID NO: 2 3118	Human TGF- β (P61812-1)	LSTCSTLDMDQFMRKRKIEAIRGQILSKLKLTSPPEDYPEPEEVPPEV ISIYINSTDRDLSQEAKSRRAAACERERSDEEYYAKEVYKIDMPPFFPS ENAIPPTFYRPFYFRIVRFDVSAMEKNA SNLVKAEPFRVFRLQNPKARV PEQRILEYQILKSKDLSPTQRYIDS KVVKTRAEGEWLSFDVTDAV EWLHHKDRNLGFKISLHCPCTTFVPSNNYIIPNKSEELEARFAGIDG TSTYSGDQKTIKSTRKKNSGKTPHLLMLLPSPYRLESQQTNRRK ALDAAYCPRNVQDNCLLRPLYIDFKRD LGWKWIHEPKGYNANCAGA CPYLWSSDTQHSRVLSLYNTINPEASA PCCVSQDLEPLTILYYIGK TPKIEQLSNMIVKSCKCS
SEQ ID NO: 3 3094	Immature (P10600-1)	MKMHLQRALVVLALLNFATVSLSLSTCTLDGFHIKKKRVEAIRGQI LSKRLRTSPPEPTVMTHVYPQVLALYNSTRELLLEEMHGereeGCTQE NTESBYAKEIHKFDMIQGLAHEHNEALVCPKGITSKVFVNVSVEK NRTNLFRAEFRLVRLVPNPSSKRNEQRIELFQILRDPDEHIAKQRYIGG KNLPTRGTAEBWLSPDVTREWLRLRRESNLGLEIISIHCPCHTFQPN GDILENIHEVMEIKFGVDNEDDHGRGDLGRLKKQKDHHNPHLILMM IPPHRLDNPQGGQRKKRDLTNYCFCRNLEENCCVRLPLYIDFRQDLG WKWVHEPKGYYANFCGCPYLRSAADTTSTVGLYNTLNPEASASP CCVPQDLEPLTILYYVGRTPKVEQLSNMIVKSCKCS
SEQ ID NO: 3 3119	Human TGF- β (P10600-1)	LSTCTTLDGFHIKKKRVEAIRGQILSKLKLTSPPEPTVMTHVYPQVL ALYNSTRELLLEEMHGereeGCTQE NTESBYAKEIHKFDMIQGLAHE NELAVCPKGITSKVFVNVSVEK NRTNLFRAEFRLVRLVPNPSSKR EQRIELFQILRDPDEHIAKQRYIGGKNLPTRGTAEWLSFDVTDTREW LLRRESNLGLEIISIHCPCHTFQPN DILENIHEVMEIKFGVDNEDD HGRGDLGRLKKQKD F IHNPHLILMMIIPPFRLDNPQGGQRKKRDL NYCFCRNLEENCCVRLPLYIDFRQDLGKWVHEPKGYYANFCGCPY RSADTTSTVGLYNTLNPEASASPCCVPQDLEPLTILYYVGRTPK EQLSNMIVKSCKCS
SEQ ID NO: 3 3095	Immature TGFBRI isoform 1 (P36897-1)	MEAAVAAPRPLLVLAAAAAAAAAALLPGATAHQCFCHLCTKDNT CVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGS VTTTYCCNQDHCKNIELPPTVKSSPGLGPVLEAVIAGPVCFCV CISL MLMVYICHNRTVIFIHRVPNEEDPSLDRPFISEGTTLKD LIYDMTTS GSGSLPLLVQRTIARTIVLQESIGKGRFGEVWRGKWRGEVAVKIF SSREERSWFREAEIYQTVMRLHENILGFIAADNKDNGTWTQLWLVS YHEHGSLSFDYLNRYT VTEGMIKALSTASGLAHLHMEIVGTQGKPA IAHRLDKSKNIVLKNGTCCIADLGLAVRHD SATD TIDIA PNP HRVGT

TABLE 4-continued

 Exemplary amino acid sequences of TGF- β polypeptides
 or TGF- β receptor polypeptides

SEQ	ID NO	Description	Amino acid sequence
			KRYMAPEVLDDSIINMKHFESFKRADIYAMGLVFWEIARRCSIGGIHE DYQLPYYDLVPSDPSVEEMRKVVCEQKLRPNIPNRWQSCEALRVMAK IMRECWYANGAARLTALRIKKTLSQLSQEGIKM
SEQ	Human		LQCFCHLCTKDNTFCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVCAPSSKTGSVTTTYCCNQDHCKNIELPPTVKSSPGLGPVELA AVIAGPVCFCV CISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFISEG TTLKDLIYDMTTSGSGSGLPLLVORTIARTIVLQESIGKGRFGEVWR GKWRGEEVAKIFSSREERSWFREAEIYQTVMRLHENILGFIAADNK DNGWTQWLVLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTASGLAH LHMEIVGTQGKPAIAHRLDKSKNIVLKKNGTCCIADLGLAVRHDSAT DTIDIANPCHRVTGKRYMAPEVLDDSIINMKHFESFKRADIYAMGLVF EIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLRPNIPN RWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQEGIKM
3120	TGFBR1 isoform 1 (P36897-1)		
SEQ	Immature		MEAAAAPRPRLLLLVLAACAAAAALLPGATALQCFCHLCTKDNT CVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGS VTTTYCCNQDHCKNIELPPTGPFVKSSPGLGPVELAAVIAGPVCFCV CISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFISEGTTLKDLDIYD MTTSGSGSGLPLLVORTIARTIVLQESIGKGRFGEVWRGKWRGEEVA VKIFSSREERSWFREAEIYQTVMRLHENILGFIAADNKDNGTWTQLW LVSVDYHEHGSLFDYLNRYTVTVEGMIKLALSTASGLAHLMIEIVGTQ GKPAIAHRLDKSKNIVLKKNGTCCIADLGLAVRHD SATDTIDIANP RVGKRYMAPEVLDDSIINMKHFESFKRADIYAMGLVFWEIARRCSIG GIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLRPNIPNRWQSCEALR VMAKIMRECWYANGAARLTALRIKKTLSQLSQEGIKM
3096	TGFBR1 isoform 2 (P36897-2)		
SEQ	Human		LQCFCHLCTKDNTFCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVCAPSSKTGSVTTTYCCNQDHCKNIELPPTGPFVKSSPGLGP VELAAVIAGPVCFCV CISLMLMVYICHNRTVIHHRVPNEEDPSLDRP FISEGTTLKDLDIYDMTTSGSGSGLPLLVORTIARTIVLQESIGKGRF GEVWRGKWRGEEVAVKIFSSREERSWFREAEIYQTVMRLHENILGF IAADNKDNGTWTQLWLVLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTA SGLAHLHMEIVGTQGKPAIAHRLDKSKNIVLKKNGTCCIADLGLAVR HDSATDTIDIANPCHRVTGKRYMAPEVLDDSIINMKHFESFKRADIYAM GLVFWEIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLR PNIPNRWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQEG IKM
3121	isoform 2 (P36897-2)		
SEQ	Immature		MEAAAAPRPRLLLLVLAACAAAAALLPGATALQCFCHLCTKDNT CVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGS VTTTYCCNQDHCKNIELPPTGFLPLVQRTIARTIVLQESIGKGRFGE VWRGKWRGEEVAVKIFSSREERSWFREAEIYQTVMRLHENILGFIAA DNKDNGTWTQLWLVLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTASG LAHLHMEIVGTQGKPAIAHRLDKSKNIVLKKNGTCCIADLGLAVRHD SATDTIDIANPCHRVTGKRYMAPEVLDDSIINMKHFESFKRADIYAM GLVFWEIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLR PNIPNRWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQEG IKM
3097	TGFBR1 isoform 3 (P36897-3)		
SEQ	Human		LQCFCHLCTKDNTFCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVCAPSSKTGSVTTTYCCNQDHCKNIELPPTGFLPLVQRTIART IVLQESIGKGRFGEVWRGKWRGEEVAVKIFSSREERSWFREAEIYQT VMLRHENILGFIAADNKDNGTWTQLWLVLVSDYHEHGSLFDYLNRYTV TVEGMIKLALSTASGLAHLHMEIVGTQGKPAIAHRLDKSKNIVLKKN GTCCIADLGLAVRHD SATDTIDIANPCHRVTGKRYMAPEVLDDSIIN MKHFESFKRADIYAMGLVFWEIARRCSIGGIHEDYQLPYYDLVPSD PSVEEMRKVVCEQKLRPNIPNRWQSCEALRVMAKIMRECWYANGAARLT ALRIKKTLSQLSQEGIKM
3122	isoform 3 (P36897-3)		
SEQ	Human		LQCFCHLCTKDNTFCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVCAPSSKTGSVTTTYCCNQDHCKNIELPPTVKSSPGLGPVEL
3104	TGFBR1 fragment 1		
SEQ	Human		ALQCFCHLCTKDNTFCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIP RDRPFVCAPSSKTGSVTTTYCCNQDHCKNIEL
3105	TGFBR1 fragment 2		
SEQ	Immature		MGRGLLRLGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNNGAVKF PQLCKFCDFVRSTCDNQKSCMSNCNSITSICEKPQEVCVAWRKNDEN ITLETVCCHDPKLPYHDFILEDAAASPCKCIMKEKKPGETFFMCSCSSD ECNDNIIFSSEYNTSNPDLLVIFQVTGISLLPPLGVVAISVIIIFYC YRVNRQQQLSSTWETGKTRKLMFESEHCAIILEDDRSDISSTCANNI HNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYE
3098	TGFBR2 isoform B (short isoform)		

TABLE 4-continued

Exemplary amino acid sequences of TGF- β polypeptides or TGF- β receptor polypeptides		
SEQ ID NO	Description	Amino acid sequence
(P37173-1)		YEASWKTEKDIFSDINLKHENILQFLTAEEKTELGKQYWLTAFHAKGNLQEYLTRHVISWEDLRKGSSLARGIAHLHSDDHTPCGRPKMPIVHRDLKSSNILVKNDLTCLCDFGSLRLDPTLSVDDLANSQVGQTARYMAPEEVLESRMNLLENVESFKQTYMAPEEVLESRMNLLENVESFKQTEPPFGSKVREHPCVESMKDNVLTECWDHDPEARLTAQCVAAERFSELEHLDRLSGRSCSEEKIPEDGSLNTTK
SEQ ID NO: 3123	Human TGFBR2 isoform B (short isoform)	TIPPHVQKSNNNDMIVTDNNNGAVKFPQLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIFSEEEYNTSNPDLLLVIFQVTGISLLPPLGVAISVIIIFCYCRVNQQQLSSTWETGKTRKLMEFSEHCACIILEDDRSDISSTCANNINHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENILQFLTAEEKTELGKQYWLTAFHAKGNLQEYLTRHVISWEDLRKGSSLARGIAHLHSDDHTPCGRPKMPIVHRDLKSSNILVKNDLTCLCDFGSLRLDPTLSVDDLANSQVGQTARYMAPEEVLESRMNLLENVESFKQTDVYSMALVWEMTSRCNAVGEVKDYEPPFGSKVREHPCVESMKDNVLDRGRPEIIPSFWLNHQGIQMVCETLTECWDHDPEARLTAQCVAAERFSELEHLDRLSGRSCSEEKIPEDGSLNTTK
SEQ ID NO: 3099	Human TGFBR2 isoform A (long isoform)	MGRGLLRLGLWPLHIVLWTRIASTIPPHVQKSVDVEMEAQKDEIICPSCNRTAHLRHINNDMIVTDNNGAVKFPQLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIFSEEEYNTSNPDLLLVIFQVTGISLLPPLGVAISVIIIFCYCRVNQQQLSSTWETGKTRKLMEFSEHCACIILEDDRSDISSTCANNINHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENILQFLTAEEKTELGKQYWLTAFHAKGNLQEYLTRHVISWEDLRKGSSLARGIAHLHSDDHTPCGRPKMPIVHRDLKSSNILVKNDLTCLCDFGSLRLDPTLSVDDLANSQVGQTARYMAPEEVLESRMNLLENVESFKQTDVYSMALVWEMTSRCNAVGEVKDYEPPFGSKVREHPCVESMKDNVLDRGRPEIIPSFWLNHQGIQMVCETLTECWDHDPEARLTAQCVAAERFSELEHLDRLSGRSCSEEKIPEDGSLNTTK
SEQ ID NO: 3124	Human TGFBR2 isoform A (long isoform)	TIPPHVQKSVDVEMEAQKDEIICPSCNRTAHLRHINNDMIVTDNNGAVKFPQLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIFSEEEYNTSNPDLLVIFOVTGISLLPPLGVAISVIIIIFCYCRVNQQQLSSTWETGKTRKLMEFSEHCACIILEDDRSDISSTCANNINHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENILQFLTAEEKTELGKQYWLTAFHAKGNLQEYLTRHVISWEDLRKGSSLARGIAHLHSDDHTPCGRPKMPIVHRDLKSSNILVKNDLTCLCDFGSLRLDPTLSVDDLANSQVGQTARYMAPEEVLESRMNLLENVESFKQTDVYSMALVWEMTSRCNAVGEVKDYEPPFGSKVREHPCVESMKDNVLDRGRPEIIPSFWLNHQGIQMVCETLTECWDHDPEARLTAQCVAAERFSELEHLDRLSGRSCSEEKIPEDGSLNTTK
SEQ ID NO: 3100	Human TGFBR2 fragment 1 (ECD of human TGFBR2 isoform B)	TIPPHVQKSNNNDMIVTDNNNGAVKFPQLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIFSEEEYNTSNPD
SEQ ID NO: 3101	Human TGFBR2 fragment 2	IIPPHVQKSNNNDMIVTDNNNGAVKFPQLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIFSEEEYNTSNPD
SEQ ID NO: 3102	Human TGFBR2 fragment 3 (ECD of human TGFBR2 isoform A)	TIPPHVQKSVDVEMEAQKDEIICPSCNRTAHLRHINNDMIVTDNNGAVKFPQLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIFSEEEYNTSNPD
SEQ ID NO: 3103	Human TGFBR2 fragment 4	QLCKFCDFVRSTCDNQKSCMSNCITSICEKPQEVCAVWRKNDENITLETVCCHDPKLPHYHDFILEDAAASKCIMKEKKKPGETFFMCSSDECNDNIIF

TABLE 4-continued

 Exemplary amino acid sequences of TGF- β polypeptides
 or TGF- β receptor polypeptides

SEQ	ID NO	Description	Amino acid sequence
SEQ	Immature		MTSHYVIAIFALMSSCLATAGPEPGALCELS PVSASHPVQALMESFT
ID NO:	human		VLSGCASRGTTGLPQE VHVLNLR TAGQGPGQLQREVTLHLNP ISSV
3106	TGFBR3		IHHHKSVVFLNNSPHPLVWHLKTERLATGVSRFLVSEGSSVQFSSA
	isoform 1		NFSLTAETEERNFPHGNEHLLNWARKEYGAVT SFTELKIARNIYIKV
(Q03167-1)			GEDQVFPPCKNCIGKNFLS LNYLABYLQPKAAEGCVMSSQCPQNNEEVHI
			I ELITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLILIKCKKS VNW
			VIKSPDVKGSLKIIAPNSI GFGKESERSMTMTKSIRDDIPSTQGNLV
			KWALDNGYS PITSYTMAPVANRFHLRLENNAEEMGDEEVHTI PPELR
			ILLDPGALPALQNPPIRGE GEGQNGGLPFPFDISRRVWNEEGEDGLP
			RPKDPVIPS QOLFPGLREPEEVQGSVDIALSVKCDNEKMI VAVEKDS
			FQASGYSGMDVTLLDPTCAKAMNGTHFVLESPLNGCGTRPRNSALDG
			VVYYNSIVI QVPALGDSSGWP DGYEDLES GDNGFPGDMEGDA SFT
			RPEIVVFNC SLQQVRNPSSFQEQPHGNITFN MELYNTDLFLVPSQGV
			FSVPENGHVYEVSVT KAEQELGFAI QTCFISPYSNPDRMSHYTIIE
			NICPKDESVKFYSPKRVHFPI PQADMDKKRFSVFKPVFNTSLLFLQ
			CELTLC MKHPQKL PKCVPD EACTSLDASIIWAMMQNKKTFTKP
			LAVI HEEAESKEKGPSMKEPNPIS PPIFHGLDTLTVMGIAFAAFVIG
			ALLTGALWYI YSHTGETAGRQVPTSPPASENSAAHSIGSTQSTPC
			SSSSSTA
SEQ	Human		GPEPGALCELS PVSASHPVQALMESFTVLSGCASRGTTGLPQE VHVL
ID NO:	TGFBR3		NLRTAGQGPQQLQREVTLHLNP ISSVHIFIHKSVVFLNNSPHPLVWH
3125	isoform 1		LKTERLATGVSRFLVSEGSSVQFSSANFSLTAETEERNFPHGNEHL
(Q03167-1)			LNWARKEYGAVT SFTELKIARNIYIKVGEDQVFP PKCNI GKNFLSLN
			YLAEYLQPKAAEGCVMSSQCPQNNEEVHII ELITPNSNPYSAFQVDITI
			DIRPSQEDLEVVKNLILIKCKKS VNWVIKSF DVKGSLKIIAPNSIG
			FGKESERSMTMTKSIRDDIPSTQGNLV KWALDNGYS PITSYTMAPVA
			NRFHLRLENNAEEMGDEEVHTI PPELRILLDPGALPALQNPPIRGE
			GQNGGLPFPFDISRRVWNEEGEDGLP RPKDPVIPS QOLFPGLREPE
			EVQGSVDIALSVKCDNEKMI VAVEKDSFQASGYSGMDVILLDPTCA
			KMNGTHFVLESPLNGCGTRPRWSALDG VVYYNSIVI QVPALGDSSG
			PDGYEDLES GDNGFPGDMEGDA SFT FTRPEIVVFNC SLQQRNPSSF
			QE QPHGNITFN MELYNTDLFLVPSQGVFSVPENGHVYEVSVT KAEQ
			ELGFAI QT CFISPYSNPDRMSHYTIIE NICKPKDESVKFYSPKRVHF
			IPQADMDKKRFSVFKPVFNTSLLFLQCELTLC MKHPQKL PKCV
			PPDEACTSLDASIIWAMMQNKKTFTKP LAVI HEEAESKEKGPSMKEP
			NPIS PPIFHGLDTLTVMGIAFAAFVIG ALLTGALWYI YSHTGETAGR
			QVPTSPPASENSAAHSIGSTQSTPCSSSSSTA
SEQ	Immature		MTSHYVIAIFALMSSCLATAGPEPGALCELS PVSASHPVQALMESFT
ID NO:	human		VLSGCASRGTTGLPQE VHVLNLR TAGQGPGQLQREVTLHLNP ISSVH
3107	TGFBR3		IHHHKSVVFLNNSPHPLVWHLKTERLATGVSRFLVSEGSSVQFSSAN
	isoform 2		FSLTAETEERNFPHGNEHLLNWARKEYGAVT SFTELKIARNIYIKV
(Q03167-2)			EDQVFPPCKNCIGKNFLS LNYLABYLQPKAAEGCVMSSQCPQNNEEVHII
			ELITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLILIKCKKS VNWV
			I KSF DVKGSLKIIAPNSI GFGKESERSMTMTKSIRDDIPSTQGNLVK
			WALDNGYS PITSYTMAPVANRFHLRLENNEEMGDEEVHTI PPELRIL
			LDPGALPALQNPPIRGE GQNGGLPFPFDISRRVWNEEGEDGLP RPK
			KDPVIPS QOLFPGLREPEEVQGSVDIALSVKCDNEKMI VAVEKDSFQ
			ASGYSGMDVILLDPTCAKAMNGTHFVLESPLNGCGTRPRWSALDGVV
			YYNSIVI QVPALGDSSGWP DGYEDLES GDNGFPGDMEGDA SFT FTRP
			EIVVFNCSLQQRNPSSFQEQPHGNITFN MELYNTDLFLVPSQGVFS
			VPENGHVYEVSVT KAEQELGFAI QT CFISPYSNPDRMSHYTIIE NICKPKDESVKFYSPKRVHF
			IPQADMDKKRFSVFKPVFNTSLLFLQCELTLC MKHPQKL PKCV
			PPDEACTSLDASIIWAMMQNKKTFTKP LAVI HEEAESKEKGPSMKEP
			NPIS PPIFHGLDTLTVMGIAFAAFVIG ALLTGALWYI YSHTGETAGR
			QVPTSPPASENSAAHSIGSTQSTPCSSSSSTA
SEQ	Human		GPEPGALCELS PVSASHPVQALMESFTVLSGCASRGTTGLPQE VHVL
ID NO:	TGFBR3		NLRTAGQGPQQLQREVTLHLNP ISSVHIFIHKSVVFLNNSPHPLVWH
3126	isoform 2		LKTERLATGVSRFLVSEGSSVQFSSANFSLTAETEERNFPHGNEHL
(Q03167-2)			LNWARKEYGAVT SFTELKIARNIYIKVGEDQVFP PKCNI GKNFLSLN
			YLAEYLQPKAAEGCVMSSQCPQNNEEVHII ELITPNSNPYSAFQVDITI
			DIRPSQEDLEVVKNLILIKCKKS VNWVIKSF DVKGSLKIIAPNSIG
			FGKESERSMTMTKSIRDDIPSTQGNLV KWALDNGYS PITSYTMAPVA
			NRFHLRLENNAEEMGDEEVHTI PPELRILLDPGALPALQNPPIRGE
			GQNGGLPFPFDISRRVWNEEGEDGLP RPKDPVIPS QOLFPGLREPE
			VQGSVDIALSVKCDNEKMI VAVEKDSFQASGYSGMDVILLDPTCAK
			MNGTHFVLESPLNGCGTRPRWSALDG VVYYNSIVI QVPALGDSSG
			PDGYEDLES GDNGFPGDMEGDA SFT FTRPEIVVFNC SLQQRNPSSFQ
			EQPHGNITFN MELYNTDLFLVPSQGVFSVPENGHVYEVSVT KAEQ
			ELGFAI QT CFISPYSNPDRMSHYTIIE NICKPKDESVKFYSPKRVHF

TABLE 4-continued

Exemplary amino acid sequences of TGF- β polypeptides or TGF- β receptor polypeptides		
SEQ ID NO	Description	Amino acid sequence
		PQADMDDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHPQKLPKCVP PDEACTSLASI IWAMM MONKKTFTKPLAVI HHEAESKEKGPSMKEPN PISPP IFHGLDTLTVMGIAFAAFVIGALLTGALWYI YSHTAGRQ QVPTSPPASENSSAAHSIGSTQSTPCSSSSA
SEQ 3108	Human ID NO: TGFB3 fragment 1	GPEPGALCELSPVSAHPVQALMESFTVLSGCASRGTTGLPQEvhVL NLRTAGQGPQLQREVTLHLNPPISSHIFIKSVVFLLNSPHPLVWH LKTERLATGVSRFLVSEGSVVQFSSANSLTAETEERNFPHGNEHL LNWARKEYAVTSFTELKIARNIYIKVGEDQVFPPKCNI GKNFLSLN YLAELQPKAEGCVMSQOPQNEEVHIIELITPNSNPYSAFQVDITI DIRPSQEDLEVVKNLILIKCKKS VNWVIKSF DVKGSLKIIAPNSIG FGKESERSMTMKSI RDDIPSTQGNLVKWLADNGYS PITSYTMAPVA NRFLRL ENNAEEMGDEEVHTI PPELRILLDPGALPALQNPPIRGGE GQNGGLPFPFPDI SRVWNNEEGEDGLPRPKDPVIPSILQFPGLREPE EVQGSVDIALSVKCDNEKMI VAVEKDSFQASGYSGMDVTLLDPTCKA KMNGTHFVLESPLNGCGTRPRWSALDG VVYYNSIVIQVPA LGDSSGW PDGYEDLES GDNGFPGDMDEGDA SFTRPEIVVFNCSLQQVRNPSSF QEQPQHGNITNMELYNTDLFLVPSQGVFSPENGHVYVEVSVTKAEQ ELGFAI QTFCFISPYSNPDRMSHYTIENI CPKDESVKFYSPKRVHF IPQADMDDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHPQKLPKC PPDEACTSLASI IWAMM QNKKTFTKPLAVI HHEAESKEKGPSMKEP NPISPP IFHGLDTLTV
SEQ 3192	hCH1-hFc_Hole-ID NO: 3x4GS-TGFbR2	ASTKGPSVFP LAPSSKSTSGGTA ALGCLVKDYFPEPVTVWSN GALT SGVHTFP AVLQSSGLYSLSSVTV PSSSLGTQTYICNVNHKP SNTKV DKRVEPKSCDKTHTCPCPAPEELLGGPSVFLFPPKPKD TLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVSV LTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAKGQPREPVCTLP PSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQOPENNYKTTPPVLD SDGSFFLVS KLTVDKSRWQQGNV FSCVMHEALHNHTQKSLSLSPG XGGGGSGGGGGGGGSIPPHVQKS VNNNDMIVTDNNGAVKFQPLCKFC DVRFSTCDNQKSCMSNC SITSICEK PQEVC VAWRKNDENITLETVC HDPKL PYH FILEDAASPKCIMKEKKKPGETFFMCSSDECNDNII FSEEYNTSNPD, where in X is K or absent
SEQ 3193	hCH1-hFc_Knob-ID NO: 3x4GS-TGFbR2	ASTKGPSVFP LAPSSKSTSGGTA ALGCLVKDYFPEPVTVWSN GALT SGVHTFP AVLQSSGLYSLSSVTV PSSSLGTQTYICNVNHKP SNTKV DKRVEPKSCDKTHTCPCPAPEELLGGPSVFLFPPKPKD TLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVSV LTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAKGQPREPVCTLP PCREEMTKNQVSLCLVKGFYPSDI AVEWESNGQOPENNYKTTPPVLD SDGSFFLVS KLTVDKSRWQQGNV FSCVMHEALHNHTQKSLSLSPG XGGGGSGGGGGGGGSIPPHVQKS VNNNDMIVTDNNGAVKFQPLCKFC DVRFSTCDNQKSCMSNC SITSICEK PQEVC VAWRKNDENITLETVC HDPKL PYH FILEDAASPKCIMKEKKKPGETFFMCSSDECNDNII FSEEYNTSNPD, where in X is K or absent
SEQ 3194	hFc_Hole-ID NO: 3x4GS-TGFbR2	DKTHTCPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVSVLTVLHQDWL NGKEYCKVSNKALPAPI EKTISKAKGQPREPVCTLPSSREEMTKN QVSLSCLVKGFYPSDI AVEWESNGQOPENNYKTTPPVLDSDGSFFLVS KLTVDKSRWQQGNV FSCVMHEALHNHTQKSLSLSPG XGGGGSGGG GSGGGGSIPPHVQKS VNNNDMIVTDNNGAVKFQPLCKFC D VRFSTCDN QKSCMSNC SITSICEK PQEVC VAWRKNDENITLETVC HDPKL PYH FILEDAASPKCIMKEKKKPGETFFMCSSDECNDNII FSEEYNTSN PD, where in X is K or absent
SEQ 3195	hFc_Knob-ID NO: 3x4GS-TGFbR2	DKTHTCPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVSVLTVLHQDWL NGKEYCKVSNKALPAPI EKTISKAKGQPREPVCTLPSSREEMTKN QVSLSCLVKGFYPSDI AVEWESNGQOPENNYKTTPPVLDSDGSFFLVS KLTVDKSRWQQGNV FSCVMHEALHNHTQKSLSLSPG XGGGGSGGG GSGGGGSIPPHVQKS VNNNDMIVTDNNGAVKFQPLCKFC D VRFSTCDN QKSCMSNC SITSICEK PQEVC VAWRKNDENITLETVC HDPKL PYH FILEDAASPKCIMKEKKKPGETFFMCSSDECNDNII FSEEYNTSN PD, where in X is K or absent
SEQ 3196	TGfbR2-3x4GS-ID NO: hCH1-hFc_Hole	IPPHVQKS VNNNDMIVTDNNGAVKFQPLCKFC D VRFSTCDNQKSCMSN CSITSICEK PQEVC VAWRKNDENITLETVC HDPKL PYH FILEDAAS SPK CIMKEKKKPGETFFMCSSDECNDNII FSEEYNTSNPDGGGG GGGGSGGGGSA STKGPSPVFP LAPSSKSTSGGTA ALGCLVKDYFPEPV TVWSN GALTSGVHTFP AVLQSSGLYSLSSVTV PSSSLGTQTYICN VNHKPSNTKVDKRVEPKSCDKTHTCPCPAPEELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ

TABLE 4-continued

Exemplary amino acid sequences of TGF- β polypeptides or TGF- β receptor polypeptides		
SEQ ID NO	Description	Amino acid sequence
		YNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ PREPQVCTLPPSREEMTKNQVSLCAVKGFYPSDIAVEWESNGQOPEN NYKTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMEHALHNHY TQKSLSLSPGX, where in X is K or absent
SEQ ID NO: hCh1-hFc_Knob 3197	TGFbR2-3x4GS-	IPPHVQKVSNNDMIVTDNNNGAVKFPQLCKFCDFVRFSTCDNQKSCMSN CSITSICEKPQEVCVAWRKNDENITLETVCHDPKLKYHDFILEDAA SPKCIMKEKKPGETFFMCSSDECNDNIIIFSEEEYNTSNPDGGGS GGGGSGGGGASTKGPSVPFLAPSSKSTSGGTAAALGCLVKDYFPEPV TVSWSGALTSGVHTFPVALQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKRVEPKSCDKTHTCPCCPAPELLGGPSVFLFPPKPK DTLMISRTEVTCVVVDVSHEDPEVKFNWYWDGVEVHNAKTKPREEQ YNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ PREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQOPEN NYKTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEHALHNHY TQKSLSLSPGX, where in X is K or absent
SEQ ID NO: hCL Ig_v1 3198	TGFbR2-3x4G5-	IPPHVQKVSNNDMIVTDNNNGAVKFPQLCKFCDFVRFSTCDNQKSCMSN CSITSICEKPQEVCVAWRKNDENITLETVCHDPKLKYHDFILEDAA SPKCIMKEKKPGETFFMCSSDECNDNIIIFSEEEYNTSNPDGGGS GGGGSGGGGSGQPKANPTVLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADGSPVKAGVETTKPSKQSNNKYAASSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: hCL Ig_vk 3199	TGF β R2-3x4GS-	IPPHVQKVSNNDMIVTDNNNGAVKFPQLCKFCDFVRFSTCDNQKSCMSN CSITSICEKPQEVCVAWRKNDENITLETVCHDPKLKYHDFILEDAA SPKCIMKEKKPGETFFMCSSDECNDNIIIFSEEEYNTSNPDGGGS GGGGSGGGGSRTVAAPSVIFPPSDEQLKSGTASVVCCLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSTTLSKADYEKFIK VYACEVTHQGLSSPVTKSFNRGEC

Stromal Modifying Moieties

In other embodiments, the anti-NKp30 antibody molecule (e.g., the multispecific antibody molecule) further comprises one or more stromal modifying moieties. Stromal modifying moieties described herein include moieties (e.g., proteins, e.g., enzymes) capable of degrading a component of the stroma, e.g., an ECM component, e.g., a glycosaminoglycan, e.g., hyaluronan (also known as hyaluronic acid or HA), chondroitin sulfate, chondroitin, dermatan sulfate, heparin sulfate, heparin, entactin, tenascin, aggrecan and keratin sulfate; or an extracellular protein, e.g., collagen, laminin, elastin, fibrinogen, fibronectin, and vitronectin.

In some embodiments, the stromal modifying moiety is an enzyme. For example, the stromal modifying moiety can include, but is not limited to a hyaluronidase, a collagenase, a chondroitinase, a matrix metalloproteinase (e.g., macrophage metalloelastase).

Exemplary amino acid and nucleotide sequences for stromal modifying moieties are disclosed in WO 2017/165464, see e.g., pages 131-136, 188-193, incorporated herein by reference.

Nucleic Acids

Nucleic acids encoding the aforementioned antibody molecules, e.g., multispecific or multifunctional molecules. are also disclosed.

In certain embodiments, the invention features nucleic acids comprising nucleotide sequences that encode heavy and light chain variable regions and CDRs or hypervariable loops of the antibody molecules, as described herein. For example, the invention features a first and second nucleic acid encoding heavy and light chain variable regions, respectively, of an antibody molecule chosen from one or more of the antibody molecules disclosed herein. The nucleic acid can comprise a nucleotide sequence as set forth

in the tables herein, or a sequence substantially identical thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in the tables herein).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a heavy chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, e.g., conserved substitutions). In other embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a light chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, e.g., conserved substitutions). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs or hypervariable loops from heavy and light chain variable regions having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, e.g., conserved substitutions).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a heavy chain variable region having the nucleotide sequence as set forth in the tables herein, a sequence substantially homologous thereto

103

(e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a light chain variable region having the nucleotide sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs or hypervariable loops from heavy and light chain variable regions having the nucleotide sequence as set forth in the tables herein, or a sequence substantially homologous thereto (e.g., a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding a cytokine molecule, an immune cell engager, or a stromal modifying moiety disclosed herein.

In another aspect, the application features host cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell, as described in more detail hereinbelow.

Vectors

Further provided herein are vectors comprising the nucleotide sequences encoding a multispecific or multifunctional molecule described herein. In one embodiment, the vectors comprise nucleotides encoding a multispecific or multifunctional molecule described herein. In one embodiment, the vectors comprise the nucleotide sequences described herein. The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

Additionally, cells which have stably integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow for the selection of transfected host cells. The marker may provide, for example, prototropy to an auxotrophic host, biocide resistance (e.g., antibiotics), or resistance to heavy metals such as copper, or the like. The selectable marker gene can be either directly linked to the DNA sequences to be expressed, or introduced into the same cell by cotransformation. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcriptional promoters, enhancers, and termination signals.

Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based trans-

104

fection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity.

Methods and conditions for culturing the resulting transfected cells and for recovering the antibody molecule produced are known to those skilled in the art, and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

10 Cells

In another aspect, the application features host cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell.

15 The host cell can be a eukaryotic cell, e.g., a mammalian cell, an insect cell, a yeast cell, or a prokaryotic cell, e.g., *E. coli*. For example, the mammalian cell can be a cultured cell or a cell line. Exemplary mammalian cells include lymphocytic cell lines (e.g., NSO), Chinese hamster ovary cells

20 (CHO), COS cells, oocyte cells, and cells from a transgenic animal, e.g., mammary epithelial cell.

The invention also provides host cells comprising a nucleic acid encoding an antibody molecule as described herein.

25 In one embodiment, the host cells are genetically engineered to comprise nucleic acids encoding the antibody molecule.

30 In one embodiment, the host cells are genetically engineered by using an expression cassette. The phrase "expression cassette," refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.

35 The invention also provides host cells comprising the vectors described herein.

40 The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells. Suitable insect cells include, but are not limited to, Sf9 cells.

45 Uses

Methods described herein include treating a disorder, e.g., a cancer, an autoimmune or inflammatory disorder, or an infectious disorder, in a subject by using an anti-NKP30 antibody molecule, e.g., a multispecific molecule, described herein, e.g., using a pharmaceutical composition described herein. Also provided are methods for reducing or ameliorating a symptom of a disorder, e.g., a cancer, an autoimmune or inflammatory disorder, or an infectious disorder, in a subject, as well as methods for inhibiting the growth of a diseased cell, e.g., cancer cell, and/or killing or depleting one or more diseased cells, e.g., cancer cells. In embodiments, the methods described herein decrease the size of a tumor and/or decrease the number of cancer cells in a subject administered with a described herein or a pharmaceutical composition described herein.

50 In embodiments, the antibody molecule, e.g., multispecific molecules or pharmaceutical composition, is administered to the subject parenterally. In embodiments, the antibody molecule or pharmaceutical composition is administered to the subject intravenously, subcutaneously, intratumorally, intranodally, intramuscularly, intradermally, or intraperitoneally. In embodiments, the cells are adminis-

105

tered, e.g., injected, directly into a tumor or lymph node. In embodiments, the cells are administered as an infusion (e.g., as described in Rosenberg et al., *New Eng. J. of Med.* 319:1676, 1988) or an intravenous push. In embodiments, the cells are administered as an injectable depot formulation.

In embodiments, the subject is a mammal. In embodiments, the subject is a human, monkey, pig, dog, cat, cow, sheep, goat, rabbit, rat, or mouse. In embodiments, the subject is a human. In embodiments, the subject is a pediatric subject, e.g., less than 18 years of age, e.g., less than 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 or less years of age. In embodiments, the subject is an adult, e.g., at least 18 years of age, e.g., at least 19, 20, 21, 22, 23, 24, 25, 25-30, 30-35, 35-40, 40-50, 50-60, 60-70, 70-80, or 80-90 years of age.

Cancers

In embodiments, the cancer is a hematological cancer, a solid tumor or a metastatic lesion thereof. In some embodiments, the anti-NKp30 antibody molecule used to treat the cancer further comprises a tumor targeting moiety, e.g., a tumor targeting moiety as described herein.

In embodiments, the hematological cancer is a leukemia or a lymphoma. As used herein, a "hematologic cancer" refers to a tumor of the hematopoietic or lymphoid tissues, e.g., a tumor that affects blood, bone marrow, or lymph nodes. Exemplary hematologic malignancies include, but are not limited to, leukemia (e.g., acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), hairy cell leukemia, acute monocytic leukemia (AMoL), chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia (JMML), or large granular lymphocytic leukemia), lymphoma (e.g., AIDS-related lymphoma, cutaneous T-cell lymphoma, Hodgkin lymphoma (e.g., classical Hodgkin lymphoma or nodular lymphocyte-predominant Hodgkin lymphoma), mycosis fungoides, non-Hodgkin lymphoma (e.g., B-cell non-Hodgkin lymphoma (e.g., Burkitt lymphoma, small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, or mantle cell lymphoma) or T-cell non-Hodgkin lymphoma (mycosis fungoides, anaplastic large cell lymphoma, or precursor T-lymphoblastic lymphoma)), primary central nervous system lymphoma, Sezary syndrome, Waldenström macroglobulinemia), chronic myeloproliferative neoplasm, Langerhans cell histiocytosis, multiple myeloma/plasma cell neoplasm, myelodysplastic syndrome, or myelodysplastic/myeloproliferative neoplasm.

In embodiments, the cancer is a solid cancer. Exemplary solid cancers include, but are not limited to, ovarian cancer, rectal cancer, stomach cancer, testicular cancer, cancer of the anal region, uterine cancer, colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, Kaposi's sarcoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, brain stem glioma, pituitary adenoma, epidermoid cancer, carcinoma of the cervix squamous cell cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the vagina, sarcoma of soft tissue, cancer of the urethra, carcinoma of the vulva, cancer of the penis, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, spinal axis tumor, neoplasm of the central

106

nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, metastatic lesions of said cancers, or combinations thereof.

In certain embodiments, the cancer is an epithelial, mesenchymal or hematologic malignancy. In certain embodiments, the cancer treated is a solid tumor (e.g., carcinoid, carcinoma or sarcoma), a soft tissue tumor (e.g., a heme malignancy), and a metastatic lesion, e.g., a metastatic lesion of any of the cancers disclosed herein. In one embodiment, the cancer treated is a fibrotic or desmoplastic solid tumor, e.g., a tumor having one or more of: limited tumor perfusion, compressed blood vessels, fibrotic tumor interstitium, or increased interstitial fluid pressure. In one embodiment, the solid tumor is chosen from one or more of 10 pancreatic (e.g., pancreatic adenocarcinoma or pancreatic ductal adenocarcinoma), breast, colon, colorectal, lung (e.g., small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC)), skin, ovarian, liver cancer, esophageal cancer, endometrial cancer, gastric cancer, head and neck cancer, kidney, or prostate cancer.

Examples of cancer include, but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia or lymphoid malignancies. More particular examples of such cancers are noted below and include: squamous cell cancer (e.g. epithelial squamous cell cancer), lung cancer including small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung and squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial cancer or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, 20 hepatic carcinoma, anal carcinoma, penile carcinoma, as well as head and neck cancer. The term "cancer" includes primary malignant cells or tumors (e.g., those whose cells have not migrated to sites in the subject's body other than the site of the original malignancy or tumor) and secondary malignant cells or tumors (e.g., those arising from metastasis, the migration of malignant cells or tumor cells to secondary sites that are different from the site of the original tumor).

Other examples of cancers or malignancies include, but are not limited to: Acute Childhood Lymphoblastic Leukemia, Acute Lymphoblastic Leukemia, Acute Lymphocytic Leukemia, Acute Myeloid Leukemia, Adrenocortical Carcinoma, Adult (Primary) Hepatocellular Cancer, Adult (Primary) Liver Cancer, Adult Acute Lymphocytic Leukemia, 45 Adult Acute Myeloid Leukemia, Adult Hodgkin's Disease, Adult Hodgkin's Lymphoma, Adult Lymphocytic Leukemia, Adult Non-Hodgkin's Lymphoma, Adult Primary Liver Cancer, Adult Soft Tissue Sarcoma, AIDS-Related Lymphoma, AIDS-Related Malignancies, Anal Cancer, Astrocytoma, Bile Duct Cancer, Bladder Cancer, Bone Cancer, Brain Stem Glioma, Brain Tumors, Breast Cancer, Cancer of the Renal Pelvis and Ureter, Central Nervous System (Primary) Lymphoma, Central Nervous System Lymphoma, Cerebellar Astrocytoma, Cerebral Astrocytoma, Cervical 50 Cancer, Childhood (Primary) Hepatocellular Cancer, Childhood (Primary) Liver Cancer, Childhood Acute Lymphoblastic Leukemia, Childhood Acute Myeloid Leukemia, Childhood Brain Stem Glioma, Childhood Cerebellar Astrocytoma, Childhood Cerebral Astrocytoma, Childhood 55 Extracranial Germ Cell Tumors, Childhood Hodgkin's Disease, Childhood Hodgkin's Lymphoma, Childhood Hypothalamic and Visual Pathway Glioma, Childhood Lympho-

107

blastic Leukemia, Childhood Medulloblastoma, Childhood Non-Hodgkin's Lymphoma, Childhood Pineal and Supratentorial Primitive Neuroectodermal Tumors, Childhood Primary Liver Cancer, Childhood Rhabdomyosarcoma, Childhood Soft Tissue Sarcoma, Childhood Visual Pathway and Hypothalamic Glioma, Chronic Lymphocytic Leukemia, Chronic Myelogenous Leukemia, Colon Cancer, Cutaneous T-Cell Lymphoma, Endocrine Pancreas Islet Cell Carcinoma, Endometrial Cancer, Ependymoma, Epithelial Cancer, Esophageal Cancer, Ewing's Sarcoma and Related Tumors, Exocrine Pancreatic Cancer, Extracranial Germ Cell Tumor, Extragonadal Germ Cell Tumor, Extrahepatic Bile Duct Cancer, Eye Cancer, Female Breast Cancer, Gaucher's Disease, Gallbladder Cancer, Gastric Cancer, Gastrointestinal Carcinoid Tumor, Gastrointestinal Tumors, Germ Cell Tumors, Gestational Trophoblastic Tumor, Hairy Cell Leukemia, Head and Neck Cancer, Hepatocellular Cancer, Hodgkin's Disease, Hodgkin's Lymphoma, Hypergammaglobulinemia, Hypopharyngeal Cancer, Intestinal Cancers, Intraocular Melanoma, Islet Cell Carcinoma, Islet Cell Pancreatic Cancer, Kaposi's Sarcoma, Kidney Cancer, Laryngeal Cancer, Lip and Oral Cavity Cancer, Liver Cancer, Lung Cancer, Lymphoproliferative Disorders, Macroglobulinemia, Male Breast Cancer, Malignant Mesothelioma, Malignant Thymoma, Medulloblastoma, Melanoma, Mesothelioma, Metastatic Occult Primary Squamous Neck Cancer, Metastatic Primary Squamous Neck Cancer, Metastatic Squamous Neck Cancer, Multiple Myeloma, Multiple Myeloma/Plasma Cell Neoplasm, Myelodysplastic Syndrome, Myelogenous Leukemia, Myeloid Leukemia, Myeloproliferative Disorders, Nasal Cavity and Paranasal Sinus Cancer, Nasopharyngeal Cancer, Neuroblastoma, Non-Hodgkin's Lymphoma During Pregnancy, Nonmelanoma Skin Cancer, Non-Small Cell Lung Cancer, Occult Primary Metastatic Squamous Neck Cancer, Oropharyngeal Cancer, Osteo-/Malignant Fibrous Sarcoma, Osteosarcoma/Malignant Fibrous Histiocytoma, Osteosarcoma/Malignant Fibrous Histiocytoma of Bone, Ovarian Epithelial Cancer, Ovarian Germ Cell Tumor, Ovarian Low Malignant Potential Tumor, Pancreatic Cancer, Paraproteinemias, Purpura, Parathyroid Cancer, Penile Cancer, Pheochromocytoma, Pituitary Tumor, Plasma Cell Neoplasm/Multiple Myeloma, Primary Central Nervous System Lymphoma, Primary Liver Cancer, Prostate Cancer, Rectal Cancer, Renal Cell Cancer, Renal Pelvis and Ureter Cancer, Retinoblastoma, Rhabdomyosarcoma, Salivary Gland Cancer, Sarcoidosis Sarcomas, Sezary Syndrome, Skin Cancer, Small Cell Lung Cancer, Small Intestine Cancer, Soft Tissue Sarcoma, Squamous Neck Cancer, Stomach Cancer, Supratentorial Primitive Neuroectodermal and Pineal Tumors, T-Cell Lymphoma, Testicular Cancer, Thymoma, Thyroid Cancer, Transitional Cell Cancer of the Renal Pelvis and Ureter, Transitional Renal Pelvis and Ureter Cancer, Trophoblastic Tumors, Ureter and Renal Pelvis Cell Cancer, Urethral Cancer, Uterine Cancer, Uterine Sarcoma, Vaginal Cancer, Visual Pathway and Hypothalamic Glioma, Vulvar Cancer, Waldenstrom's Macroglobulinemia, Wilms' Tumor, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

In other embodiments, the multispecific molecule, as described above and herein, is used to treat a hyperproliferative disorder, e.g., a hyperproliferative connective tissue disorder (e.g., a hyperproliferative fibrotic disease). In one embodiment, the hyperproliferative fibrotic disease is multisystemic or organ-specific. Exemplary hyperproliferative fibrotic diseases include, but are not limited to, multisystemic (e.g., systemic sclerosis, multifocal fibrosclerosis,

108

sclerodermatous graft-versus-host disease in bone marrow transplant recipients, nephrogenic systemic fibrosis, scleroderma), and organ-specific disorders (e.g., fibrosis of the eye, lung, liver, heart, kidney, pancreas, skin and other organs). In other embodiments, the disorder is chosen from liver cirrhosis or tuberculosis. In other embodiments, the disorder is leprosy.

In embodiments, the multispecific molecules (or pharmaceutical composition) are administered in a manner appropriate to the disease to be treated or prevented. The quantity and frequency of administration will be determined by such factors as the condition of the patient, and the type and severity of the patient's disease. Appropriate dosages may be determined by clinical trials. For example, when "an effective amount" or "a therapeutic amount" is indicated, the precise amount of the pharmaceutical composition (or multispecific molecules) to be administered can be determined by a physician with consideration of individual differences in tumor size, extent of infection or metastasis, age, weight, and condition of the subject. In embodiments, the pharmaceutical composition described herein can be administered at a dosage of 10^4 to 10^9 cells/kg body weight, e.g., 10^5 to 10^6 cells/kg body weight, including all integer values within those ranges. In embodiments, the pharmaceutical composition described herein can be administered multiple times at these dosages. In embodiments, the pharmaceutical composition described herein can be administered using infusion techniques described in immunotherapy (see, e.g., Rosenberg et al., *New Eng. J. of Med.* 319:1676, 1988).

In embodiments, the cancer is a myeloproliferative neoplasm, e.g., primary or idiopathic myelofibrosis (MF), essential thrombocythemia (ET), polycythemia vera (PV), or chronic myelogenous leukemia (CIVIL). In embodiments, the cancer is myelofibrosis. In embodiments, the subject has myelofibrosis. In embodiments, the subject has a calreticulin mutation, e.g., a calreticulin mutation disclosed herein. In embodiments, the subject does not have the JAK2-V617F mutation. In embodiments, the subject has the JAK2-V617F mutation. In embodiments, the subject has a MPL mutation. In embodiments, the subject does not have a MPL mutation.

In embodiments, the cancer is a solid cancer. Exemplary solid cancers include, but are not limited to, ovarian cancer, rectal cancer, stomach cancer, testicular cancer, cancer of the anal region, uterine cancer, colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, Kaposi's sarcoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, brain stem glioma, pituitary adenoma, epidermoid cancer, carcinoma of the cervix squamous cell cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the vagina, sarcoma of soft tissue, cancer of the urethra, carcinoma of the vulva, cancer of the penis, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, spinal axis tumor, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, metastatic lesions of said cancers, or combinations thereof.

Inflammatory and Autoimmune Disorders

In some embodiments, the anti-NKp30 antibody molecules, e.g., the multispecific antibody molecules, disclosed herein can be used to treat inflammatory and autoimmune diseases, and graft vs. host disease (GvHD). In some embodiments, the antibody molecules, e.g., the multispecific

109

antibody molecules, disclosed herein deplete autoreactive T cells, e.g., by directing an NK cell, e.g., an NKp30-expressing cell, to an autoreactive T cell. In some embodiments, the anti-NKp30 antibody molecule further comprises a binding specificity that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.

As used herein, the term “autoimmune” disease, disorder, or condition refers to a disease where the body’s immune system attacks its own cells or tissues. An autoimmune disease can result in the production of autoantibodies that are inappropriately produced and/or excessively produced to a self-antigen or autoantigen. Autoimmune diseases include, but are not limited to, cardiovascular diseases, rheumatoid diseases, glandular diseases, gastrointestinal diseases, cutaneous diseases, hepatic diseases, neurological diseases, muscular diseases, nephric diseases, diseases related to reproduction, connective tissue diseases and systemic diseases. In some embodiments, the autoimmune disease is mediated by T cells, B cells, innate immune cells (e.g., macrophages, eosinophils, or natural killer cells), or complement-mediated pathways.

Examples of autoimmune disorders that may be treated by administering the antibodies of the present invention include, but are not limited to, alopecia areata, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison’s disease, autoimmune diseases of the adrenal gland, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune oophoritis and orchitis, autoimmune thrombocytopenia, Behcet’s disease, bullous pemphigoid, cardiomyopathy, celiac sprue-dermatitis, chronic fatigue immune dysfunction syndrome (CFIDS), chronic inflammatory demyelinating polyneuropathy, Churg-Strauss syndrome, cicatrical pemphigoid, CREST syndrome, cold agglutinin disease, Crohn’s disease, discoid lupus, essential mixed cryoglobulinemia, fibromyalgia-fibromyositis, glomerulonephritis, Graves’ disease, Guillain-Barre, Hashimoto’s thyroiditis, idiopathic pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA neuropathy, juvenile arthritis, lichen planus, lupus erythematosus, Meniere’s disease, mixed connective tissue disease, multiple sclerosis, Neuromyelitis optica (NMO), type 1 or immune-mediated diabetes mellitus, myasthenia gravis, pemphigus vulgaris, pernicious anemia, polyarteritis nodosa, polychondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, Raynaud’s phenomenon, Reiter’s syndrome, Rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren’s syndrome, stiff-man syndrome, systemic lupus erythematosus, lupus erythematosus, takayasu arteritis, temporal arteritis/giant cell arteritis, transverse myelitis, ulcerative colitis, uveitis, vasculitides such as dermatitis herpetiformis vasculitis, vitiligo, and Wegener’s granulomatosis. In some embodiments, the autoimmune disorder is SLE or Type-1 diabetes.

Examples of inflammatory disorders which can be prevented, treated or managed in accordance with the methods of the invention include, but are not limited to, asthma, encephalitis, inflammatory bowel disease, chronic obstructive pulmonary disease (COPD), allergic disorders, septic shock, pulmonary fibrosis, undifferentiated spondyloarthropathy, undifferentiated arthropathy, arthritis, inflammatory osteolysis, and chronic inflammation resulting from chronic viral or bacterial infections.

Thus, the anti-NKp30 antibody molecules, e.g., multispecific molecules, of the present invention have utility in the treatment of inflammatory and autoimmune diseases.

110

Infectious Diseases

In some embodiments, the anti-NKp30 antibody molecules, e.g., the multispecific antibody molecules, disclosed herein can be used to treat infectious diseases. In some embodiments, the antibody molecules, e.g., the multispecific antibody molecules, disclosed herein deplete cells expressing a viral or bacterial antigen. In some embodiments, the anti-NKp30 antibody molecule further comprises a binding specificity that binds to an antigen present on the surface of an infected cell, e.g., a viral infected cell.

Some examples of pathogenic viruses causing infections treatable by methods include HIV, hepatitis (A, B, or C), herpes virus (e.g., VZV, HSV-1, HAV-6, HSV-II, and CMV, Epstein Barr virus), adenovirus, influenza virus, flaviviruses, echovirus, rhinovirus, coxsackie virus, coronaviruses, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus and arboviral encephalitis virus. In one embodiment, the infection is an influenza infection.

In another embodiment, the infection is a hepatitis infection, e.g., a Hepatitis B or C infection.

Exemplary viral disorders that can be treated include, but are not limited to, Epstein Bar Virus (EBV), influenza virus, HIV, SIV, tuberculosis, malaria and HCMV.

Some examples of pathogenic bacteria causing infections treatable by methods of the invention include syphilis, chlamydia, rickettsial bacteria, mycobacteria, staphylococci, streptococci, pneumonococci, meningococci and conococci, klebsiella, proteus, serratia, pseudomonas, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lymes disease bacteria. The anti-NKp30 antibody molecules can be used in combination with existing treatment modalities for the aforesaid infections. For example, Treatments for syphilis include penicillin (e.g., penicillin G.), tetracycline, doxycycline, ceftriaxone and azithromycin.

Diagnostic Uses

In one aspect, the present invention provides a diagnostic method for detecting the presence of a NKp30 protein in vitro (e.g., in a biological sample, such as a tissue biopsy, e.g., from a cancerous tissue) or in vivo (e.g., in vivo imaging in a subject). The method includes: (i) contacting the sample with an antibody molecule described herein, or administering to the subject, the antibody molecule; (optionally) (ii) contacting a reference sample, e.g., a control sample (e.g., a control biological sample, such as plasma, tissue, biopsy) or a control subject); and (iii) detecting formation of a complex between the antibody molecule, and the sample or subject, or the control sample or subject, wherein a change, e.g., a statistically significant change, in the formation of the complex in the sample or subject relative to the control sample or subject is indicative of the presence of NKp30 in the sample. The antibody molecule can be directly or indirectly labeled with a detectable substance to facilitate detection of the bound or unbound antibody. Suitable detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials and radioactive materials, as described above and described in more detail below.

The term “sample,” as it refers to samples used for detecting polypeptides includes, but is not limited to, cells, cell lysates, proteins or membrane extracts of cells, body fluids, or tissue samples.

Complex formation between the antibody molecule and NKp30 can be detected by measuring or visualizing either the binding molecule bound to the NKp30 antigen or

111

unbound binding molecule. Conventional detection assays can be used, e.g., an enzyme-linked immunosorbent assays (ELISA), a radioimmunoassay (RIA) or tissue immunohistochemistry. Alternative to labeling the antibody molecule, the presence of NKp30 can be assayed in a sample by a competition immunoassay utilizing standards labeled with a detectable substance and an unlabeled antibody molecule. In this assay, the biological sample, the labeled standards and the antibody molecule are combined and the amount of labeled standard bound to the unlabeled binding molecule is determined. The amount of NKp30 in the sample is inversely proportional to the amount of labeled standard bound to the antibody molecule.

EXAMPLES

The Examples below are set forth to aid in the understanding of the inventions but are not intended to, and should not be construed to, limit its scope in any way.

Example 1: Immunization of Armenian Hamster to Generate Anti-NKp30 Antibodies

Briefly, armenian hamster were immunized with the extracellular domain of human NKp30 protein in complete Freund's adjuvant and boosted twice on day 14 and day 28 with NKp30 in incomplete Freund's adjuvant (IFA). On day 56 one more boost in IFA was given and the animals harvested three days later. Spleens were collected and fused with P3X63Ag8.653 murine myeloma cell line. 0.9×10^5 cells/well in 125 μ L were seated in 96 well plate and fed with 125 μ L of I-20+2ME+HAT (IMDM (4 g/L glucose) supplemented with 20% fetal bovine serum, 4 mM L-glutamine, 1 mM sodium pyruvate, 50 U penicillin, 50 μ g streptomycin and 50 μ M 2-ME in the absence or presence of HAT or HT for selection, and Hybridoma Cloning Factor (1% final) on days 7, 11 and thereafter as needed. At approximately 2 weeks after fusion (cells are about 50% confluent), supernatant was collected and assayed for binding.

Example 2: Hybridoma Screen for NKp30 mAbs

Expi293 cells were transfected with BG160 (hNKp30 cell antigen) 18 hours prior to screening. The day of screening, transfected cells were diluted to 0.05×10^6 /mL and anti-Armenian hamster Fc Alexa Fluor 488 added to a final concentration of 0.4 μ g/mL. 50 μ L (2,500 cells) of this mixture was added to each well of a 384 well plate. The same density of untransfected 293 cells with secondary were used as a negative control. 5 μ L of hybridoma supernatant was added to the cell mixture and the plate incubated for 1 hour at 37° C. The plates were then imaged on Mirrorball. Positive clones were identified and subcloned by serial dilution to obtain clonal selected hybridoma. After reconfirmation using the same protocols the hybridoma cells were harvested and the corresponding heavy and light chain sequences recovered. The DNA was subcloned into pcDNA3.4 for subsequent expression of the corresponding antibodies and further validation.

Example 3: Binding of NKp30 Antibodies to NK92 Cells

NK-92 cells were washed with PBS containing 0.5% BSA and 0.1% sodium azide (staining buffer) and added to 96-well V-bottom plates with 200,000 cells/well. Hamster NKp30 antibodies were added to the cells in 2.0 fold serial

112

dilutions and incubated for 1 hour at room temperature. The plates were washed twice with staining buffer. The secondary antibody against hamster IgG conjugated to AF647 (Jackson, 127-605-160) was added at 1:100 dilution (1.4 mg/ml stock) and incubated with the cells for 30 minutes at 4° C. followed by washing with staining buffer. Cells were subsequently fixed for 10 minutes with 4% paraformaldehyde at room temperature. The plates were read on CytoFLEX LS (Beckman Coulter). Data was calculated as the percent-AF747 positive population (FIG. 1).

Example 4: Bioassay to Measure Activity of NKp30 Antibodies Using NK92 Cell Line

NKp30 antibodies were three-fold serially diluted in PBS and incubated at 2-8° C. overnight in flat bottom 96 well plates. Plates were washed twice in PBS and 40,000 NK-92 cells were added in growth medium containing IL-2. Plates were incubated at 37° C., 5% CO₂, humidified incubator for 16-24 hours before supernatants were collected. IFN γ levels in supernatants was measured following MSD assay instructions (FIG. 2). Supernatant collected from cells incubated with hamster isotype IgG was used as negative control and supernatants from cells incubated with NKp30 monoclonal antibody (R&D, clone 210847) was utilized as a positive control. Data were generated using hamster anti-NKp30 mAbs.

Example 5: Generation and Characterization of Humanized Anti-NKp30 Antibodies

A series of hamster anti-NKp30 antibodies were selected. These antibodies were shown to bind to human NKp30 and cynomolgus NKp30 and induce IFN γ production from NK-90 cells (data not shown). The VH and VL sequences of exemplary hamster anti-NKp30 antibodies 15E1, 9G1, 15H6, 9D9, 3A12, and 12D10 are disclosed in Table 9. The VH and VL sequences of exemplary humanized anti-NKp30 antibodies based on 15E1, 9G1, and 15H6 are also disclosed in Table 9. The Kabat CDRs of these antibodies are disclosed in Table 18 and Table 8.

Two humanized constructs based on 15E1 were selected. The first construct BJM0407 is a Fab comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7302 and a lambda light chain variable region comprising the amino acid sequence of SEQ ID NO: 7305. Its corresponding scFv construct BJM0859 comprises the amino acid sequence of SEQ ID NO: 7310. The second construct BJM0411 is a Fab comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7302 and a kappa light chain variable region comprising the amino acid sequence of SEQ ID NO: 7309. Its corresponding scFv construct BJM0860 comprises the amino acid sequence of SEQ ID NO: 7311. BJM0407 and BJM0411 showed comparable biophysical characteristics, e.g., binding affinity to NKp30 and thermal stability. The scFv constructs BJM0859 and BJM0860 also showed comparable biophysical properties.

INCORPORATION BY REFERENCE

All publications, patents, and Accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference.

113
EQUIVALENTS

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become

114

apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

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US 12,384,842 B2

659

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<210> SEQ ID NO 3070

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<210> SEQ ID NO 3090

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<210> SEQ ID NO 3091

<400> SEQUENCE: 3091

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<210> SEQ ID NO 3092

<211> LENGTH: 390

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

US 12,384,842 B2

663**664**

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<400> SEQUENCE: 3092

Met Pro Pro Ser Gly Leu Arg Leu Leu Leu Leu Leu Pro Leu Leu
 1 5 10 15
 Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr
 20 25 30
 Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala
 35 40 45
 Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
 50 55 60
 Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
 65 70 75 80
 Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Glu Pro Glu
 85 90 95
 Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
 100 105 110
 Met Val Glu Thr His Asn Glu Ile Tyr Asp Lys Phe Lys Gln Ser Thr
 115 120 125
 His Ser Ile Tyr Met Phe Phe Asn Thr Ser Glu Leu Arg Glu Ala Val
 130 135 140
 Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu
 145 150 155 160
 Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
 165 170 175
 Asn Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser
 180 185 190
 Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu
 195 200 205
 Ser Arg Gly Gly Glu Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser
 210 215 220
 Cys Asp Ser Arg Asp Asn Thr Leu Gln Val Asp Ile Asn Gly Phe Thr
 225 230 235 240
 Thr Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro
 245 250 255
 Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu Gln
 260 265 270
 Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
 275 280 285
 Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
 290 295 300
 Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
 305 310 315 320
 Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
 325 330 335
 Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
 340 345 350
 Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
 355 360 365
 Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
 370 375 380
 Arg Ser Cys Lys Cys Ser
 385 390

US 12,384,842 B2

665**666**

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<210> SEQ ID NO 3093

<211> LENGTH: 414

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3093

Met His Tyr Cys Val Leu Ser Ala Phe Leu Ile Leu His Leu Val Thr			
1	5	10	15

Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe			
20	25	30	

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu			
35	40	45	

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Glu Val Pro			
50	55	60	

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu			
65	70	75	80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu			
85	90	95	

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe			
100	105	110	

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg			
115	120	125	

Ile Val Arg Phe Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu			
130	135	140	

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg			
145	150	155	160

Val Pro Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp			
165	170	175	

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr			
180	185	190	

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His			
195	200	205	

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu			
210	215	220	

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro			
225	230	235	240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr			
245	250	255	

Ser Thr Tyr Thr Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys			
260	265	270	

Lys Asn Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser			
275	280	285	

Tyr Arg Leu Glu Ser Gln Gln Thr Asn Arg Arg Lys Lys Arg Ala Leu			
290	295	300	

Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg			
305	310	315	320

Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His			
325	330	335	

Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr			
340	345	350	

Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn			
355	360	365	

Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp			
370	375	380	

US 12,384,842 B2

667**668**

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Leu	Glu	Pro	Leu	Thr	Ile	Leu	Tyr	Tyr	Ile	Gly	Lys	Thr	Pro	Lys	Ile
385						390			395						400

Glu	Gln	Leu	Ser	Asn	Met	Ile	Val	Lys	Ser	Cys	Lys	Cys	Ser	
						405			410					

<210> SEQ ID NO 3094

<211> LENGTH: 412

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3094

Met	Lys	Met	His	Leu	Gln	Arg	Ala	Leu	Val	Val	Leu	Ala	Leu	Leu	Asn
1							5		10			15			

Phe	Ala	Thr	Val	Ser	Leu	Ser	Leu	Ser	Thr	Cys	Thr	Thr	Leu	Asp	Phe
							20		25			30			

Gly	His	Ile	Lys	Lys	Lys	Arg	Val	Glu	Ala	Ile	Arg	Gly	Gln	Ile	Leu
							35		40		45				

Ser	Lys	Leu	Arg	Leu	Thr	Ser	Pro	Pro	Glu	Pro	Thr	Val	Met	Thr	His
							50		55		60				

Val	Pro	Tyr	Gln	Val	Leu	Ala	Leu	Tyr	Asn	Ser	Thr	Arg	Glu	Leu	Leu
65							70		75			80			

Glu	Glu	Met	His	Gly	Glu	Arg	Glu	Glu	Gly	Cys	Thr	Gln	Glu	Asn	Thr
							85		90			95			

Glu	Ser	Glu	Tyr	Tyr	Ala	Lys	Glu	Ile	His	Lys	Phe	Asp	Met	Ile	Gln
							100		105			110			

Gly	Leu	Ala	Glu	His	Asn	Glu	Leu	Ala	Val	Cys	Pro	Lys	Gly	Ile	Thr
							115		120			125			

Ser	Lys	Val	Phe	Arg	Phe	Asn	Val	Ser	Ser	Val	Glu	Lys	Asn	Arg	Thr
							130		135			140			

Asn	Leu	Phe	Arg	Ala	Glu	Phe	Arg	Val	Leu	Arg	Val	Pro	Asn	Pro	Ser
145							150		155			160			

Ser	Lys	Arg	Asn	Glu	Gln	Arg	Ile	Glu	Leu	Phe	Gln	Ile	Leu	Arg	Pro
							165		170			175			

Asp	Glu	His	Ile	Ala	Lys	Gln	Arg	Tyr	Ile	Gly	Gly	Lys	Asn	Leu	Pro
							180		185			190			

Thr	Arg	Gly	Thr	Ala	Glu	Trp	Leu	Ser	Phe	Asp	Val	Thr	Asp	Thr	Val
							195		200			205			

Arg	Glu	Trp	Leu	Leu	Arg	Arg	Glu	Ser	Asn	Leu	Gly	Leu	Glu	Ile	Ser
							210		215			220			

Ile	His	Cys	Pro	Cys	His	Thr	Phe	Gln	Pro	Asn	Gly	Asp	Ile	Leu	Glu
225							230		235			240			

Asn	Ile	His	Glu	Val	Met	Glu	Ile	Lys	Phe	Lys	Gly	Val	Asp	Asn	Glu
							245		250			255			

Asp	Asp	His	Gly	Arg	Gly	Asp	Leu	Gly	Arg	Leu	Lys	Lys	Gln	Lys	Asp
							260		265			270			

His	His	Asn	Pro	His	Leu	Ile	Leu	Met	Met	Ile	Pro	Pro	His	Arg	Leu
							275		280			285			

Asp	Asn	Pro	Gly	Gln	Gly	Gly	Gln	Arg	Lys	Lys	Arg	Ala	Leu	Asp	Thr
							290		295			300			

Asn	Tyr	Cys	Phe	Arg	Asn	Leu	Glu	Glu	Asn	Cys	Cys	Val	Arg	Pro	Leu
305							310		315			320			

Tyr	Ile	Asp	Phe	Arg	Gln	Asp	Leu	Gly	Trp	Lys	Trp	Val	His	Glu	Pro
							325		330			335			

Lys	Gly	Tyr	Tyr	Ala	Asn	Phe	Cys	Ser	Gly	Pro	Cys	Pro	Tyr	Leu	Arg
							340		345			350			

669

670

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<210> SEQ ID NO 3095
<211> LENGTH: 503
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3095

Met Glu Ala Ala Val Ala Ala Pro Arg Pro Arg Leu Leu Leu Leu Val
 1 5 10 15

Ala Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys
35 40 45

Val	Thr	Asp	Gly	Leu	Cys	Phe	Val	Ser	Val	Thr	Glu	Thr	Thr	Asp	Lys
50						55					60				

Val Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg

Asp Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr

Thr Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro

Thr Thr Val Lys Ser Ser Pro Gly Leu Gly Pro Val Glu Leu Ala Ala

Val Ile Ala Gly Pro Val Cys Phe Val Cys Ile Ser Leu Met Leu Met

Val Tyr Ile Cys His Asn Arg Thr Val Ile His His Arg Val Pro Asn

Glu Glu Asp Pro Ser Leu Asp Arg Pro Phe Ile Ser Glu Gly Thr Thr

180 185 190

195 200 205

210 215 220

225 230 235 240

ser Ile Phe Arg Glu Ala Glu Ile Tyr Gln Thr Val Met Leu Arg His
245 250 255

Glu Asn Ile Leu Gly Phe Ile Ala Ala Asp Asn Lys Asp Asn Gly Thr
260 265 270

Trp Thr Gln Leu Trp Leu Val Ser Asp Tyr His Glu His Gly Ser Leu
275 280 285

Leu Ala Leu Ser Thr Ala Ser Gly Leu Ala His Leu His Met Glu Ile

US 12,384,842 B2

671**672**

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305	310	315	320
Val Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser			
325	330	335	
Lys Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys Ile Ala Asp Leu			
340	345	350	
Gly Leu Ala Val Arg His Asp Ser Ala Thr Asp Thr Ile Asp Ile Ala			
355	360	365	
Pro Asn His Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu			
370	375	380	
Asp Asp Ser Ile Asn Met Lys His Phe Glu Ser Phe Lys Arg Ala Asp			
385	390	395	400
Ile Tyr Ala Met Gly Leu Val Phe Trp Glu Ile Ala Arg Arg Cys Ser			
405	410	415	
Ile Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr Tyr Asp Leu Val			
420	425	430	
Pro Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val Val Cys Glu Gln			
435	440	445	
Lys Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser Cys Glu Ala Leu			
450	455	460	
Arg Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr Ala Asn Gly Ala			
465	470	475	480
Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ser Gln Leu Ser			
485	490	495	
Gln Gln Glu Gly Ile Lys Met			
500			

<210> SEQ ID NO 3096
<211> LENGTH: 507
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3096

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

US 12,384,842 B2

673

674

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Glu Gly Thr Thr Leu Lys Asp Leu Ile Tyr Asp Met Thr Thr Ser Gly
180 185 190

Ser Gly Ser Gly Leu Pro Leu Leu Val Gln Arg Thr Ile Ala Arg Thr
195 200 205

Ile Val Leu Gln Glu Ser Ile Gly Lys Gly Arg Phe Gly Glu Val Trp
210 215 220

Arg Gly Lys Trp Arg Gly Glu Glu Val Ala Val Lys Ile Phe Ser Ser
225 230 235 240

Arg Glu Glu Arg Ser Trp Phe Arg Glu Ala Glu Ile Tyr Gln Thr Val
245 250 255

Met Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ala Asp Asn Lys
260 265 270

Asp Asn Gly Thr Trp Thr Gln Leu Trp Leu Val Ser Asp Tyr His Glu
275 280 285

His Gly Ser Leu Phe Asp Tyr Leu Asn Arg Tyr Thr Val Thr Val Glu
290 295 300

Gly Met Ile Lys Leu Ala Leu Ser Thr Ala Ser Gly Leu Ala His Leu
305 310 315 320

His Met Glu Ile Val Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg
325 330 335

Asp Leu Lys Ser Lys Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys
340 345 350

Ile Ala Asp Leu Gly Leu Ala Val Arg His Asp Ser Ala Thr Asp Thr
355 360 365

Ile Asp Ile Ala Pro Asn His Arg Val Gly Thr Lys Arg Tyr Met Ala
370 375 380

Pro Glu Val Leu Asp Asp Ser Ile Asn Met Lys His Phe Glu Ser Phe
385 390 395 400

Lys Arg Ala Asp Ile Tyr Ala Met Gly Leu Val Phe Trp Glu Ile Ala
405 410 415

Arg Arg Cys Ser Ile Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr
420 425 430

Tyr Asp Leu Val Pro Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val
435 440 445

Val Cys Glu Gln Lys Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser
450 455 460

Cys Glu Ala Leu Arg Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr
465 470 475 480

Ala Asn Gly Ala Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu
485 490 495

Ser Gln Leu Ser Gln Gln Glu Gly Ile Lys Met
500 505

<210> SEQ ID NO 3097

<211> LENGTH: 426

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3097

Met Glu Ala Ala Val Ala Ala Pro Arg Pro Arg Leu Leu Leu Val
1 5 10 15

Leu Ala Ala Ala Ala Ala Ala Ala Leu Leu Pro Gly Ala Thr
20 25 30

Ala Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys
35 40 45

US 12,384,842 B2

675**676**

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Val	Thr	Asp	Gly	Leu	Cys	Phe	Val	Ser	Val	Thr	Glu	Thr	Thr	Asp	Lys
50				55					60						
Val	Ile	His	Asn	Ser	Met	Cys	Ile	Ala	Glu	Ile	Asp	Leu	Ile	Pro	Arg
65				70					75				80		
Asp	Arg	Pro	Phe	Val	Cys	Ala	Pro	Ser	Ser	Lys	Thr	Gly	Ser	Val	Thr
	85							90				95			
Thr	Thr	Tyr	Cys	Cys	Asn	Gln	Asp	His	Cys	Asn	Lys	Ile	Glu	Leu	Pro
					100				105			110			
Thr	Thr	Gly	Leu	Pro	Leu	Leu	Val	Gln	Arg	Thr	Ile	Ala	Arg	Thr	Ile
	115				120					125					
Val	Leu	Gln	Glu	Ser	Ile	Gly	Lys	Gly	Arg	Phe	Gly	Glu	Val	Trp	Arg
	130				135			140							
Gly	Lys	Trp	Arg	Gly	Glu	Glu	Val	Ala	Val	Lys	Ile	Phe	Ser	Ser	Arg
145				150					155			160			
Glu	Glu	Arg	Ser	Trp	Phe	Arg	Glu	Ala	Glu	Ile	Tyr	Gln	Thr	Val	Met
	165				170				175			175			
Leu	Arg	His	Glu	Asn	Ile	Leu	Gly	Phe	Ile	Ala	Ala	Asp	Asn	Lys	Asp
	180				185				190						
Asn	Gly	Thr	Trp	Thr	Gln	Leu	Trp	Leu	Val	Ser	Asp	Tyr	His	Glu	His
	195				200				205						
Gly	Ser	Leu	Phe	Asp	Tyr	Leu	Asn	Arg	Tyr	Thr	Val	Thr	Val	Glu	Gly
	210				215				220						
Met	Ile	Lys	Leu	Ala	Leu	Ser	Thr	Ala	Ser	Gly	Leu	Ala	His	Leu	His
225				230				235				240			
Met	Glu	Ile	Val	Gly	Thr	Gln	Gly	Lys	Pro	Ala	Ile	Ala	His	Arg	Asp
	245				250				255						
Leu	Lys	Ser	Lys	Asn	Ile	Leu	Val	Lys	Lys	Asn	Gly	Thr	Cys	Cys	Ile
	260				265				270						
Ala	Asp	Leu	Gly	Leu	Ala	Val	Arg	His	Asp	Ser	Ala	Thr	Asp	Thr	Ile
	275				280				285						
Asp	Ile	Ala	Pro	Asn	His	Arg	Val	Gly	Thr	Lys	Arg	Tyr	Met	Ala	Pro
	290				295			300							
Glu	Val	Leu	Asp	Asp	Ser	Ile	Asn	Met	Lys	His	Phe	Glu	Ser	Phe	Lys
305					310				315			320			
Arg	Ala	Asp	Ile	Tyr	Ala	Met	Gly	Leu	Val	Phe	Trp	Glu	Ile	Ala	Arg
	325				330				335						
Arg	Cys	Ser	Ile	Gly	Gly	Ile	His	Glu	Asp	Tyr	Gln	Leu	Pro	Tyr	Tyr
	340				345				350						
Asp	Leu	Val	Pro	Ser	Asp	Pro	Ser	Val	Glu	Glu	Met	Arg	Lys	Val	Val
	355				360				365						
Cys	Glu	Gln	Lys	Leu	Arg	Pro	Asn	Ile	Pro	Asn	Arg	Trp	Gln	Ser	Cys
	370				375				380						
Glu	Ala	Leu	Arg	Val	Met	Ala	Lys	Ile	Met	Arg	Glu	Cys	Trp	Tyr	Ala
385				390				395			400				
Asn	Gly	Ala	Ala	Arg	Leu	Thr	Ala	Leu	Arg	Ile	Lys	Lys	Thr	Leu	Ser
	405				410				415						
Gln	Leu	Ser	Gln	Gln	Glu	Gly	Ile	Lys	Met						
	420				425										

<210> SEQ ID NO 3098

<211> LENGTH: 567

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

US 12,384,842 B2

677**678**

-continued

<400> SEQUENCE: 3098

Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
 1 5 10 15

Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Val
 20 25 30

Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val Lys Phe Pro
 35 40 45

Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
 50 55 60

Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
 65 70 75 80

Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
 85 90 95

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
 100 105 110

Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
 115 120 125

Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Asp Glu Cys Asn
 130 135 140

Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu
 145 150 155 160

Leu Leu Val Ile Phe Gln Val Thr Gly Ile Ser Leu Leu Pro Pro Leu
 165 170 175

Gly Val Ala Ile Ser Val Ile Ile Phe Tyr Cys Tyr Arg Val Asn
 180 185 190

Arg Gln Gln Lys Leu Ser Ser Thr Trp Glu Thr Gly Lys Thr Arg Lys
 195 200 205

Leu Met Glu Phe Ser Glu His Cys Ala Ile Ile Leu Glu Asp Asp Arg
 210 215 220

Ser Asp Ile Ser Ser Thr Cys Ala Asn Asn Ile Asn His Asn Thr Glu
 225 230 235 240

Leu Leu Pro Ile Glu Leu Asp Thr Leu Val Gly Lys Gly Arg Phe Ala
 245 250 255

Glu Val Tyr Lys Ala Lys Leu Lys Gln Asn Thr Ser Glu Gln Phe Glu
 260 265 270

Thr Val Ala Val Lys Ile Phe Pro Tyr Glu Glu Tyr Ala Ser Trp Lys
 275 280 285

Thr Glu Lys Asp Ile Phe Ser Asp Ile Asn Leu Lys His Glu Asn Ile
 290 295 300

Leu Gln Phe Leu Thr Ala Glu Glu Arg Lys Thr Glu Leu Gly Lys Gln
 305 310 315 320

Tyr Trp Leu Ile Thr Ala Phe His Ala Lys Gly Asn Leu Gln Glu Tyr
 325 330 335

Leu Thr Arg His Val Ile Ser Trp Glu Asp Leu Arg Lys Leu Gly Ser
 340 345 350

Ser Leu Ala Arg Gly Ile Ala His Leu His Ser Asp His Thr Pro Cys
 355 360 365

Gly Arg Pro Lys Met Pro Ile Val His Arg Asp Leu Lys Ser Ser Asn
 370 375 380

Ile Leu Val Lys Asn Asp Leu Thr Cys Cys Leu Cys Asp Phe Gly Leu
 385 390 395 400

Ser Leu Arg Leu Asp Pro Thr Leu Ser Val Asp Asp Leu Ala Asn Ser
 405 410 415

US 12,384,842 B2

679**680**

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Gly Gln Val Gly Thr Ala Arg Tyr Met Ala Pro Glu Val Leu Glu Ser
 420 425 430

Arg Met Asn Leu Glu Asn Val Glu Ser Phe Lys Gln Thr Asp Val Tyr
 435 440 445

Ser Met Ala Leu Val Leu Trp Glu Met Thr Ser Arg Cys Asn Ala Val
 450 455 460

Gly Glu Val Lys Asp Tyr Glu Pro Pro Phe Gly Ser Lys Val Arg Glu
 465 470 475 480

His Pro Cys Val Glu Ser Met Lys Asp Asn Val Leu Arg Asp Arg Gly
 485 490 495

Arg Pro Glu Ile Pro Ser Phe Trp Leu Asn His Gln Gly Ile Gln Met
 500 505 510

Val Cys Glu Thr Leu Thr Glu Cys Trp Asp His Asp Pro Glu Ala Arg
 515 520 525

Leu Thr Ala Gln Cys Val Ala Glu Arg Phe Ser Glu Leu Glu His Leu
 530 535 540

Asp Arg Leu Ser Gly Arg Ser Cys Ser Glu Glu Lys Ile Pro Glu Asp
 545 550 555 560

Gly Ser Leu Asn Thr Thr Lys
 565

<210> SEQ ID NO 3099

<211> LENGTH: 592

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3099

Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
 1 5 10 15

Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Asp
 20 25 30

Val Glu Met Glu Ala Gln Lys Asp Glu Ile Ile Cys Pro Ser Cys Asn
 35 40 45

Arg Thr Ala His Pro Leu Arg His Ile Asn Asn Asp Met Ile Val Thr
 50 55 60

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
 65 70 75 80

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
 85 90 95

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Ala Val
 100 105 110

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
 115 120 125

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
 130 135 140

Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe Met
 145 150 155 160

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
 165 170 175

Glu Tyr Asn Thr Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Val
 180 185 190

Thr Gly Ile Ser Leu Leu Pro Pro Leu Gly Val Ala Ile Ser Val Ile
 195 200 205

Ile Ile Phe Tyr Cys Tyr Arg Val Asn Arg Gln Gln Lys Leu Ser Ser

US 12,384,842 B2

681**682**

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210	215	220
Thr Trp Glu Thr Gly Lys	Thr Arg Lys Leu Met	Glu Phe Ser Glu His
225	230	235
240		
Cys Ala Ile Ile Leu Glu Asp Asp Arg Ser Asp Ile Ser Ser	Thr Cys	
245	250	255
Ala Asn Asn Ile Asn His Asn Thr Glu Leu Leu Pro Ile Glu Leu Asp		
260	265	270
Thr Leu Val Gly Lys Gly Arg Phe Ala Glu Val Tyr Lys Ala Lys Leu		
275	280	285
Lys Gln Asn Thr Ser Glu Gln Phe Glu Thr Val Ala Val Lys Ile Phe		
290	295	300
Pro Tyr Glu Glu Tyr Ala Ser Trp Lys Thr Glu Lys Asp Ile Phe Ser		
305	310	315
320		
Asp Ile Asn Leu Lys His Glu Asn Ile Leu Gln Phe Leu Thr Ala Glu		
325	330	335
Glu Arg Lys Thr Glu Leu Gly Lys Gln Tyr Trp Leu Ile Thr Ala Phe		
340	345	350
His Ala Lys Gly Asn Leu Gln Glu Tyr Leu Thr Arg His Val Ile Ser		
355	360	365
Trp Glu Asp Leu Arg Lys Leu Gly Ser Ser Leu Ala Arg Gly Ile Ala		
370	375	380
His Leu His Ser Asp His Thr Pro Cys Gly Arg Pro Lys Met Pro Ile		
385	390	395
400		
Val His Arg Asp Leu Lys Ser Ser Asn Ile Leu Val Lys Asn Asp Leu		
405	410	415
Thr Cys Cys Leu Cys Asp Phe Gly Leu Ser Leu Arg Leu Asp Pro Thr		
420	425	430
Leu Ser Val Asp Asp Leu Ala Asn Ser Gly Gln Val Gly Thr Ala Arg		
435	440	445
Tyr Met Ala Pro Glu Val Leu Glu Ser Arg Met Asn Leu Glu Asn Val		
450	455	460
Glu Ser Phe Lys Gln Thr Asp Val Tyr Ser Met Ala Leu Val Leu Trp		
465	470	475
480		
Glu Met Thr Ser Arg Cys Asn Ala Val Gly Glu Val Lys Asp Tyr Glu		
485	490	495
Pro Pro Phe Gly Ser Lys Val Arg Glu His Pro Cys Val Glu Ser Met		
500	505	510
Lys Asp Asn Val Leu Arg Asp Arg Gly Arg Pro Glu Ile Pro Ser Phe		
515	520	525
Trp Leu Asn His Gln Gly Ile Gln Met Val Cys Glu Thr Leu Thr Glu		
530	535	540
Cys Trp Asp His Asp Pro Glu Ala Arg Leu Thr Ala Gln Cys Val Ala		
545	550	555
560		
Glu Arg Phe Ser Glu Leu Glu His Leu Asp Arg Leu Ser Gly Arg Ser		
565	570	575
Cys Ser Glu Glu Lys Ile Pro Glu Asp Gly Ser Leu Asn Thr Thr Lys		
580	585	590

<210> SEQ ID NO 3100

<211> LENGTH: 137

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3100

US 12,384,842 B2

683**684**

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Thr Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val
 1 5 10 15

Thr Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys
 20 25 30

Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn
 35 40 45

Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala
 50 55 60

Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His
 65 70 75 80

Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser
 85 90 95

Pro Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe
 100 105 110

Met Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser
 115 120 125

Glu Glu Tyr Asn Thr Ser Asn Pro Asp
 130 135

<210> SEQ ID NO 3101
 <211> LENGTH: 136
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3101

Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
 1 5 10 15

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
 20 25 30

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
 35 40 45

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
 50 55 60

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
 65 70 75 80

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
 85 90 95

Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe Met
 100 105 110

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
 115 120 125

Glu Tyr Asn Thr Ser Asn Pro Asp
 130 135

<210> SEQ ID NO 3102
 <211> LENGTH: 162
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3102

Thr Ile Pro Pro His Val Gln Lys Ser Asp Val Glu Met Glu Ala Gln
 1 5 10 15

Lys Asp Glu Ile Ile Cys Pro Ser Cys Asn Arg Thr Ala His Pro Leu
 20 25 30

Arg His Ile Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val
 35 40 45

US 12,384,842 B2

685**686**

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Lys	Phe	Pro	Gln	Leu	Cys	Lys	Phe	Cys	Asp	Val	Arg	Phe	Ser	Thr	Cys
50						55					60				

Asp	Asn	Gln	Lys	Ser	Cys	Met	Ser	Asn	Cys	Ser	Ile	Thr	Ser	Ile	Cys
65						70					75				80

Glu	Lys	Pro	Gln	Glu	Val	Cys	Val	Ala	Val	Trp	Arg	Lys	Asn	Asp	Glu
						85				90				95	

Asn	Ile	Thr	Leu	Glu	Thr	Val	Cys	His	Asp	Pro	Lys	Leu	Pro	Tyr	His
						100			105			110			

Asp	Phe	Ile	Leu	Glu	Asp	Ala	Ala	Ser	Pro	Lys	Cys	Ile	Met	Lys	Glu
						115			120			125			

Lys	Lys	Lys	Pro	Gly	Glu	Thr	Phe	Phe	Met	Cys	Ser	Cys	Ser	Ser	Asp
						130			135			140			

Glu	Cys	Asn	Asp	Asn	Ile	Ile	Phe	Ser	Glu	Glu	Tyr	Asn	Thr	Ser	Asn
						145			150			155			160

Pro Asp

<210> SEQ ID NO 3103

<211> LENGTH: 101

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3103

Gln	Leu	Cys	Lys	Phe	Cys	Asp	Val	Arg	Phe	Ser	Thr	Cys	Asp	Asn	Gln
1							5		10			15			

Lys	Ser	Cys	Met	Ser	Asn	Cys	Ser	Ile	Thr	Ser	Ile	Cys	Glu	Lys	Pro
							20		25			30			

Gln	Glu	Val	Cys	Val	Ala	Val	Trp	Arg	Lys	Asn	Asp	Glu	Asn	Ile	Thr
						35		40			45				

Leu	Glu	Thr	Val	Cys	His	Asp	Pro	Lys	Leu	Pro	Tyr	His	Asp	Phe	Ile
						50		55			60				

Leu	Glu	Asp	Ala	Ala	Ser	Pro	Lys	Cys	Ile	Met	Lys	Glu	Lys	Lys	Asn
						65		70		75		80			

Pro	Gly	Glu	Thr	Phe	Phe	Met	Cys	Ser	Cys	Ser	Ser	Asp	Glu	Cys	Asn
						85		90			95				

Asp	Asn	Ile	Ile	Phe
		100		

<210> SEQ ID NO 3104

<211> LENGTH: 93

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3104

Leu	Gln	Cys	Phe	Cys	His	Leu	Cys	Thr	Lys	Asp	Asn	Phe	Thr	Cys	Val
1							5		10			15			

Thr	Asp	Gly	Leu	Cys	Phe	Val	Ser	Val	Thr	Glu	Thr	Thr	Asp	Lys	Val
						20		25			30				

Ile	His	Asn	Ser	Met	Cys	Ile	Ala	Glu	Ile	Asp	Leu	Ile	Pro	Arg	Asp
						35		40			45				

Arg	Pro	Phe	Val	Cys	Ala	Pro	Ser	Ser	Lys	Thr	Gly	Ser	Val	Thr	Thr
						50		55			60				

Thr	Tyr	Cys	Cys	Asn	Gln	Asp	His	Cys	Asn	Lys	Ile	Glu	Leu	Pro	Thr
						65		70		75		80			

Thr	Val	Lys	Ser	Ser	Pro	Gly	Leu	Gly	Pro	Val	Glu	Leu
						85		90				

US 12,384,842 B2

687

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<210> SEQ ID NO 3105

<211> LENGTH: 79

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3105

Ala	Leu	Gln	Cys	Phe	Cys	His	Leu	Cys	Thr	Lys	Asp	Asn	Phe	Thr	Cys
1				5					10				15		

Val	Thr	Asp	Gly	Leu	Cys	Phe	Val	Ser	Val	Thr	Glu	Thr	Thr	Asp	Lys
	20				25					30					

Val	Ile	His	Asn	Ser	Met	Cys	Ile	Ala	Glu	Ile	Asp	Leu	Ile	Pro	Arg
	35				40				45						

Asp	Arg	Pro	Phe	Val	Cys	Ala	Pro	Ser	Ser	Lys	Thr	Gly	Ser	Val	Thr
	50				55					60					

Thr	Thr	Tyr	Cys	Cys	Asn	Gln	Asp	His	Cys	Asn	Lys	Ile	Glu	Leu
	65				70				75					

<210> SEQ ID NO 3106

<211> LENGTH: 851

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3106

Met	Thr	Ser	His	Tyr	Val	Ile	Ala	Ile	Phe	Ala	Leu	Met	Ser	Ser	Cys
1					5				10			15			

Leu	Ala	Thr	Ala	Gly	Pro	Glu	Pro	Gly	Ala	Leu	Cys	Glu	Leu	Ser	Pro
	20				25				30						

Val	Ser	Ala	Ser	His	Pro	Val	Gln	Ala	Leu	Met	Glu	Ser	Phe	Thr	Val
	35				40				45						

Leu	Ser	Gly	Cys	Ala	Ser	Arg	Gly	Thr	Thr	Gly	Leu	Pro	Gln	Glu	Val
	50				55				60						

His	Val	Leu	Asn	Leu	Arg	Thr	Ala	Gly	Gln	Gly	Pro	Gly	Gln	Leu	Gln
	65				70				75				80		

Arg	Glu	Val	Thr	Leu	His	Leu	Asn	Pro	Ile	Ser	Ser	Val	His	Ile	His
	85				90					95					

His	Lys	Ser	Val	Val	Phe	Leu	Leu	Asn	Ser	Pro	His	Pro	Leu	Val	Trp
	100				105					110					

His	Leu	Lys	Thr	Glu	Arg	Leu	Ala	Thr	Gly	Val	Ser	Arg	Leu	Phe	Leu
	115				120				125						

Val	Ser	Glu	Gly	Ser	Val	Val	Gln	Phe	Ser	Ser	Ala	Asn	Phe	Ser	Leu
	130				135				140						

Thr	Ala	Glu	Thr	Glu	Glu	Arg	Asn	Phe	Pro	His	Gly	Asn	Glu	His	Leu
	145				150				155				160		

Leu	Asn	Trp	Ala	Arg	Lys	Glu	Tyr	Ala	Val	Thr	Ser	Phe	Thr	Glu	
	165				170					175					

Leu	Lys	Ile	Ala	Arg	Asn	Ile	Tyr	Ile	Lys	Val	Gly	Glu	Asp	Gln	Val
	180				185				190						

Phe	Pro	Pro	Lys	Cys	Asn	Ile	Gly	Lys	Asn	Phe	Leu	Ser	Leu	Asn	Tyr
	195				200					205					

Leu	Ala	Glu	Tyr	Leu	Gln	Pro	Lys	Ala	Ala	Glu	Gly	Cys	Val	Met	Ser
	210				215					220					

Ser	Gln	Pro	Gln	Asn	Glu	Glu	Val	His	Ile	Ile	Glu	Leu	Ile	Thr	Pro
	225				230				235				240		

Asn	Ser	Asn	Pro	Tyr	Ser	Ala	Phe	Gln	Val	Asp	Ile	Thr	Ile	Asp	Ile
	245				250					255					

Arg	Pro	Ser	Gln	Glu	Asp	Leu	Glu	Val	Val	Lys	Asn	Leu	Ile	Leu	Ile
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688

US 12,384,842 B2

689**690**

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260

265

270

Leu Lys Cys Lys Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val
275 280 285

Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys
290 295 300

Glu Ser Glu Arg Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile
305 310 315 320

Pro Ser Thr Gln Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr
325 330 335

Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His
340 345 350

Leu Arg Leu Glu Asn Asn Ala Glu Glu Met Gly Asp Glu Glu Val His
355 360 365

Thr Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro
370 375 380

Ala Leu Gln Asn Pro Pro Ile Arg Gly Glu Gly Gln Asn Gly Gly
385 390 395 400

Leu Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu
405 410 415

Gly Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile
420 425 430

Gln Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val
435 440 445

Asp Ile Ala Leu Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala
450 455 460

Val Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val
465 470 475 480

Thr Leu Leu Asp Pro Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe
485 490 495

Val Leu Glu Ser Pro Leu Asn Gly Cys Gly Thr Arg Pro Arg Trp Ser
500 505 510

Ala Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro
515 520 525

Ala Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu
530 535 540

Ser Gly Asp Asn Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser
545 550 555 560

Leu Phe Thr Arg Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln
565 570 575

Val Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro His Gly Asn Ile Thr
580 585 590

Phe Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln
595 600 605

Gly Val Phe Ser Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser
610 615 620

Val Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe
625 630 635 640

Ile Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile
645 650 655

Glu Asn Ile Cys Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys
660 665 670

Arg Val His Phe Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe
675 680 685

US 12,384,842 B2

691**692**

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Ser Phe Val Phe Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln
 690 695 700

Cys Glu Leu Thr Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu
 705 710 715 720

Pro Lys Cys Val Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser
 725 730 735

Ile Ile Trp Ala Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu
 740 745 750

Ala Val Ile His His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met
 755 760 765

Lys Glu Pro Asn Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr
 770 775 780

Leu Thr Val Met Gly Ile Ala Phe Ala Ala Phe Val Ile Gly Ala Leu
 785 790 795 800

Leu Thr Gly Ala Leu Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala
 805 810 815

Gly Arg Gln Gln Val Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser
 820 825 830

Ala Ala His Ser Ile Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser
 835 840 845

Ser Thr Ala
 850

<210> SEQ ID NO 3107
 <211> LENGTH: 850
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3107

Met Thr Ser His Tyr Val Ile Ala Ile Phe Ala Leu Met Ser Ser Cys
 1 5 10 15

Leu Ala Thr Ala Gly Pro Glu Pro Gly Ala Leu Cys Glu Leu Ser Pro
 20 25 30

Val Ser Ala Ser His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val
 35 40 45

Leu Ser Gly Cys Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val
 50 55 60

His Val Leu Asn Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln
 65 70 75 80

Arg Glu Val Thr Leu His Leu Asn Pro Ile Ser Ser Val His Ile His
 85 90 95

His Lys Ser Val Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp
 100 105 110

His Leu Lys Thr Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu
 115 120 125

Val Ser Glu Gly Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu
 130 135 140

Thr Ala Glu Thr Glu Glu Arg Asn Phe Pro His Gly Asn Glu His Leu
 145 150 155 160

Leu Asn Trp Ala Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr Glu
 165 170 175

Leu Lys Ile Ala Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln Val
 180 185 190

Phe Pro Pro Lys Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn Tyr

US 12,384,842 B2

693**694**

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195 200 205

Leu Ala Glu Tyr Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met Ser
 210 215 220

Ser Gln Pro Gln Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr Pro
 225 230 235 240

Asn Ser Asn Pro Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp Ile
 245 250 255

Arg Pro Ser Gln Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu Ile
 260 265 270

Leu Lys Cys Lys Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val
 275 280 285

Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys
 290 295 300

Glu Ser Glu Arg Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile
 305 310 315 320

Pro Ser Thr Gln Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr
 325 330 335

Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His
 340 345 350

Leu Arg Leu Glu Asn Asn Glu Glu Met Gly Asp Glu Glu Val His Thr
 355 360 365

Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro Ala
 370 375 380

Leu Gln Asn Pro Pro Ile Arg Gly Gly Glu Gln Asn Gly Gly Leu
 385 390 395 400

Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu Gly
 405 410 415

Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile Gln
 420 425 430

Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val Asp
 435 440 445

Ile Ala Leu Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala Val
 450 455 460

Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val Thr
 465 470 475 480

Leu Leu Asp Pro Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe Val
 485 490 495

Leu Glu Ser Pro Leu Asn Gly Cys Gly Thr Arg Pro Arg Trp Ser Ala
 500 505 510

Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro Ala
 515 520 525

Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu Ser
 530 535 540

Gly Asp Asn Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser Leu
 545 550 555 560

Phe Thr Arg Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln Val
 565 570 575

Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro His Gly Asn Ile Thr Phe
 580 585 590

Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln Gly
 595 600 605

Val Phe Ser Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser Val
 610 615 620

US 12,384,842 B2

695**696**

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Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe Ile
 625 630 635 640
 Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile Glu
 645 650 655
 Asn Ile Cys Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys Arg
 660 665 670
 Val His Phe Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe Ser
 675 680 685
 Phe Val Phe Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln Cys
 690 695 700
 Glu Leu Thr Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu Pro
 705 710 715 720
 Lys Cys Val Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser Ile
 725 730 735
 Ile Trp Ala Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu Ala
 740 745 750
 Val Ile His His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met Lys
 755 760 765
 Glu Pro Asn Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr Leu
 770 775 780
 Thr Val Met Gly Ile Ala Ala Phe Val Ile Gly Ala Leu Leu
 785 790 795 800
 Thr Gly Ala Leu Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala Gly
 805 810 815
 Arg Gln Gln Val Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser Ala
 820 825 830
 Ala His Ser Ile Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser Ser
 835 840 845
 Thr Ala
 850

<210> SEQ ID NO 3108
 <211> LENGTH: 767
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3108

Gly Pro Glu Pro Gly Ala Leu Cys Glu Leu Ser Pro Val Ser Ala Ser
 1 5 10 15
 His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val Leu Ser Gly Cys
 20 25 30
 Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val His Val Leu Asn
 35 40 45
 Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln Arg Glu Val Thr
 50 55 60
 Leu His Leu Asn Pro Ile Ser Ser Val His Ile His His Lys Ser Val
 65 70 75 80
 Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp His Leu Lys Thr
 85 90 95
 Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu Val Ser Glu Gly
 100 105 110
 Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu Thr Ala Glu Thr
 115 120 125
 Glu Glu Arg Asn Phe Pro His Gly Asn Glu His Leu Leu Asn Trp Ala

US 12,384,842 B2

697**698**

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130	135	140
Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr	Glu Leu Lys Ile Ala	
145 150 155 160		
Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln	Val Phe Pro Pro Lys	
165 170 175		
Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn	Tyr Leu Ala Glu Tyr	
180 185 190		
Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met	Ser Ser Gln Pro Gln	
195 200 205		
Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr	Pro Asn Ser Asn Pro	
210 215 220		
Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp	Ile Arg Pro Ser Gln	
225 230 235 240		
Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu	Ile Lys Cys Lys	
245 250 255		
Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp	Val Lys Gly Ser Leu	
260 265 270		
Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly	Lys Glu Ser Glu Arg	
275 280 285		
Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp	Ile Pro Ser Thr Gln	
290 295 300		
Gly Asn Leu Val Lys Trp Ala Leu Asp Asn	Gly Tyr Ser Pro Ile Thr	
305 310 315 320		
Ser Tyr Thr Met Ala Pro Val Ala Asn Arg	Phe His Leu Arg Leu Glu	
325 330 335		
Asn Asn Ala Glu Glu Met Gly Asp Glu Glu Val	His Thr Ile Pro Pro	
340 345 350		
Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala	Leu Pro Ala Leu Gln Asn	
355 360 365		
Pro Pro Ile Arg Gly Glu Gly Gln Asn Gly	Gly Leu Pro Phe Pro	
370 375 380		
Phe Pro Asp Ile Ser Arg Arg Val Trp Asn	Glu Glu Gly Asp Gly	
385 390 395 400		
Leu Pro Arg Pro Lys Asp Pro Val Ile Pro	Ser Ile Gln Leu Phe Pro	
405 410 415		
Gly Leu Arg Glu Pro Glu Glu Val Gln	Gly Ser Val Asp Ile Ala Leu	
420 425 430		
Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val	Ala Val Glu Lys Asp	
435 440 445		
Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp	Val Thr Leu Leu Asp	
450 455 460		
Pro Thr Cys Lys Ala Lys Met Asn Gly Thr	His Phe Val Leu Glu Ser	
465 470 475 480		
Pro Leu Asn Gly Cys Gly Thr Arg Pro Arg	Trp Ser Ala Leu Asp Gly	
485 490 495		
Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val	Pro Ala Leu Gly Asp	
500 505 510		
Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu	Glu Ser Gly Asp Asn	
515 520 525		
Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala	Ser Leu Phe Thr Arg	
530 535 540		
Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln	Gln Val Arg Asn Pro	
545 550 555 560		

US 12,384,842 B2

699**700**

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Ser Ser Phe Gln Gln Pro His Gly Asn Ile Thr Phe Asn Met Glu
 565 570 575

Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln Gly Val Phe Ser
 580 585 590

Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser Val Thr Lys Ala
 595 600 605

Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe Ile Ser Pro Tyr
 610 615 620

Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile Glu Asn Ile Cys
 625 630 635 640

Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys Arg Val His Phe
 645 650 655

Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe Ser Phe Val Phe
 660 665 670

Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln Cys Glu Leu Thr
 675 680 685

Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu Pro Lys Cys Val
 690 695 700

Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser Ile Ile Trp Ala
 705 710 715 720

Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu Ala Val Ile His
 725 730 735

His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met Lys Glu Pro Asn
 740 745 750

Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr Leu Thr Val
 755 760 765

<210> SEQ ID NO 3109

<400> SEQUENCE: 3109

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<210> SEQ ID NO 3110

<400> SEQUENCE: 3110

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<210> SEQ ID NO 3111

<400> SEQUENCE: 3111

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<210> SEQ ID NO 3112

<400> SEQUENCE: 3112

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<210> SEQ ID NO 3113

<400> SEQUENCE: 3113

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<210> SEQ ID NO 3114

<400> SEQUENCE: 3114

US 12,384,842 B2

701

702

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<210> SEQ ID NO 3115

<400> SEQUENCE: 3115

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<210> SEQ ID NO 3116

<400> SEQUENCE: 3116

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<210> SEQ ID NO 3117

<211> LENGTH: 361

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3117

Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg			
1	5	10	15

Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser		
20	25	30

Pro Pro Ser Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val		
35	40	45

Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala		
50	55	60

Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr			
65	70	75	80

Arg Val Leu Met Val Glu Thr His Asn Glu Ile Tyr Asp Lys Phe Lys		
85	90	95

Gln Ser Thr His Ser Ile Tyr Met Phe Phe Asn Thr Ser Glu Leu Arg		
100	105	110

Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu		
115	120	125

Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys		
130	135	140

Tyr Ser Asn Asn Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro			
145	150	155	160

Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg		
165	170	175

Gln Trp Leu Ser Arg Gly Gly Glu Ile Glu Gly Phe Arg Leu Ser Ala		
180	185	190

His Cys Ser Cys Asp Ser Arg Asp Asn Thr Leu Gln Val Asp Ile Asn		
195	200	205

Gly Phe Thr Thr Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met		
210	215	220

Asn Arg Pro Phe Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln			
225	230	235	240

His Leu Gln Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys		
245	250	255

Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp		
260	265	270

Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr		
275	280	285

US 12,384,842 B2

703

704

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His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp
 290 295 300

Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly
 305 310 315 320

Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro
 325 330 335

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

Met Ile Val Arg Ser Cys Lys Cys Ser
 355 360

<210> SEQ ID NO 3118

<211> LENGTH: 394

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3118

Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe Met Arg Lys Arg
 1 5 10 15

Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Lys Leu Thr Ser
 20 25 30

Pro Pro Glu Asp Tyr Pro Glu Pro Glu Val Pro Pro Glu Val Ile
 35 40 45

Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu Lys Ala Ser Arg
 50 55 60

Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu Glu Tyr Tyr Ala
 65 70 75 80

Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe Pro Ser Glu Asn
 85 90 95

Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg Ile Val Arg Phe
 100 105 110

Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu Val Lys Ala Glu
 115 120 125

Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg Val Pro Glu Gln
 130 135 140

Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp Leu Thr Ser Pro
 145 150 155 160

Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr Arg Ala Glu Gly
 165 170 175

Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His Glu Trp Leu His
 180 185 190

His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu His Cys Pro Cys
 195 200 205

Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro Asn Lys Ser Glu
 210 215 220

Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr Ser Thr Tyr Thr
 225 230 235 240

Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys Lys Asn Ser Gly
 245 250 255

Lys Thr Pro His Leu Leu Met Leu Leu Pro Ser Tyr Arg Leu Glu
 260 265 270

Ser Gln Gln Thr Asn Arg Arg Lys Lys Arg Ala Leu Asp Ala Ala Tyr
 275 280 285

Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr Ile
 290 295 300

US 12,384,842 B2

705**706**

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Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly
305 310 315 320

Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser Ser
325 330 335

Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn Thr Ile Asn Pro
340 345 350

Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro Leu
355 360 365

Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro Lys Ile Glu Gln Leu Ser
370 375 380

Asn Met Ile Val Lys Ser Cys Lys Cys Ser
385 390

<210> SEQ ID NO 3119

<211> LENGTH: 389

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3119

Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His Ile Lys Lys Lys Arg
1 5 10 15

Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Thr Ser
20 25 30

Pro Pro Glu Pro Thr Val Met Thr His Val Pro Tyr Gln Val Leu Ala
35 40 45

Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu Met His Gly Glu Arg
50 55 60

Glu Glu Gly Cys Thr Gln Glu Asn Thr Glu Ser Glu Tyr Tyr Ala Lys
65 70 75 80

Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu Ala Glu His Asn Glu
85 90 95

Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys Val Phe Arg Phe Asn
100 105 110

Val Ser Ser Val Glu Lys Asn Arg Thr Asn Leu Phe Arg Ala Glu Phe
115 120 125

Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys Arg Asn Glu Gln Arg
130 135 140

Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu His Ile Ala Lys Gln
145 150 155 160

Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg Gly Thr Ala Glu Trp
165 170 175

Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu Trp Leu Leu Arg Arg
180 185 190

Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His Cys Pro Cys His Thr
195 200 205

Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Ile His Glu Val Met Glu
210 215 220

Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp His Gly Arg Gly Asp
225 230 235 240

Leu Gly Arg Leu Lys Lys Gln Lys Asp His His Asn Pro His Leu Ile
245 250 255

Leu Met Met Ile Pro Pro His Arg Leu Asp Asn Pro Gly Gln Gly Gly
260 265 270

Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Tyr Cys Phe Arg Asn Leu

US 12,384,842 B2

707

708

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275

280

285

Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp Phe Arg Gln Asp
 290 295 300

Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr Tyr Ala Asn Phe
 305 310 315 320

Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser
 325 330 335

Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser
 340 345 350

Pro Cys Cys Val Pro Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr
 355 360 365

Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn Met Val Val Lys
 370 375 380

Ser Cys Lys Cys Ser
 385

<210> SEQ ID NO 3120

<211> LENGTH: 470

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3120

Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys Val
 1 5 10 15

Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys Val
 20 25 30

Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg Asp
 35 40 45

Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr Thr
 50 55 60

Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro Thr
 65 70 75 80

Thr Val Lys Ser Ser Pro Gly Leu Gly Pro Val Glu Leu Ala Ala Val
 85 90 95

Ile Ala Gly Pro Val Cys Phe Val Cys Ile Ser Leu Met Leu Met Val
 100 105 110

Tyr Ile Cys His Asn Arg Thr Val Ile His His Arg Val Pro Asn Glu
 115 120 125

Glu Asp Pro Ser Leu Asp Arg Pro Phe Ile Ser Glu Gly Thr Thr Leu
 130 135 140

Lys Asp Leu Ile Tyr Asp Met Thr Thr Ser Gly Ser Gly Ser Gly Leu
 145 150 155 160

Pro Leu Leu Val Gln Arg Thr Ile Ala Arg Thr Ile Val Leu Gln Glu
 165 170 175

Ser Ile Gly Lys Gly Arg Phe Gly Glu Val Trp Arg Gly Lys Trp Arg
 180 185 190

Gly Glu Glu Val Ala Val Lys Ile Phe Ser Ser Arg Glu Glu Arg Ser
 195 200 205

Trp Phe Arg Glu Ala Glu Ile Tyr Gln Thr Val Met Leu Arg His Glu
 210 215 220

Asn Ile Leu Gly Phe Ile Ala Ala Asp Asn Lys Asp Asn Gly Thr Trp
 225 230 235 240

Thr Gln Leu Trp Leu Val Ser Asp Tyr His Glu His Gly Ser Leu Phe
 245 250 255

US 12,384,842 B2

709**710**

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Asp Tyr Leu Asn Arg Tyr Thr Val Thr Val Glu Gly Met Ile Lys Leu
260 265 270

Ala Leu Ser Thr Ala Ser Gly Leu Ala His Leu His Met Glu Ile Val
275 280 285

Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser Lys
290 295 300

Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys Ile Ala Asp Leu Gly
305 310 315 320

Leu Ala Val Arg His Asp Ser Ala Thr Asp Thr Ile Asp Ile Ala Pro
325 330 335

Asn His Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu Asp
340 345 350

Asp Ser Ile Asn Met Lys His Phe Glu Ser Phe Lys Arg Ala Asp Ile
355 360 365

Tyr Ala Met Gly Leu Val Phe Trp Glu Ile Ala Arg Arg Cys Ser Ile
370 375 380

Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr Tyr Asp Leu Val Pro
385 390 395 400

Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val Val Cys Glu Gln Lys
405 410 415

Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser Cys Glu Ala Leu Arg
420 425 430

Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr Ala Asn Gly Ala Ala
435 440 445

Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ser Gln Leu Ser Gln
450 455 460

Gln Glu Gly Ile Lys Met
465 470

<210> SEQ ID NO 3121
<211> LENGTH: 474
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3121

Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys Val
1 5 10 15

Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys Val
20 25 30

Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg Asp
35 40 45

Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr Thr
50 55 60

Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro Thr
65 70 75 80

Thr Gly Pro Phe Ser Val Lys Ser Ser Pro Gly Leu Gly Pro Val Glu
85 90 95

Leu Ala Ala Val Ile Ala Gly Pro Val Cys Phe Val Cys Ile Ser Leu
100 105 110

Met Leu Met Val Tyr Ile Cys His Asn Arg Thr Val Ile His His Arg
115 120 125

Val Pro Asn Glu Glu Asp Pro Ser Leu Asp Arg Pro Phe Ile Ser Glu
130 135 140

Gly Thr Thr Leu Lys Asp Leu Ile Tyr Asp Met Thr Thr Ser Gly Ser
145 150 155 160

US 12,384,842 B2

711

712

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Gly Ser Gly Leu Pro Leu Leu Val Gln Arg Thr Ile Ala Arg Thr Ile
165 170 175

Val Leu Gln Glu Ser Ile Gly Lys Gly Arg Phe Gly Glu Val Trp Arg
180 185 190

Gly Lys Trp Arg Gly Glu Glu Val Ala Val Lys Ile Phe Ser Ser Arg
195 200 205

Glu Glu Arg Ser Trp Phe Arg Glu Ala Glu Ile Tyr Gln Thr Val Met
210 215 220

Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ala Asp Asn Lys Asp
225 230 235 240

Asn Gly Thr Trp Thr Gln Leu Trp Leu Val Ser Asp Tyr His Glu His
245 250 255

Gly Ser Leu Phe Asp Tyr Leu Asn Arg Tyr Thr Val Thr Val Glu Gly
260 265 270

Met Ile Lys Leu Ala Leu Ser Thr Ala Ser Gly Leu Ala His Leu His
275 280 285

Met Glu Ile Val Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp
290 295 300

Leu Lys Ser Lys Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys Ile
305 310 315 320

Ala Asp Leu Gly Leu Ala Val Arg His Asp Ser Ala Thr Asp Thr Ile
325 330 335

Asp Ile Ala Pro Asn His Arg Val Gly Thr Lys Arg Tyr Met Ala Pro
340 345 350

Glu Val Leu Asp Asp Ser Ile Asn Met Lys His Phe Glu Ser Phe Lys
355 360 365

Arg Ala Asp Ile Tyr Ala Met Gly Leu Val Phe Trp Glu Ile Ala Arg
370 375 380

Arg Cys Ser Ile Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr Tyr
385 390 395 400

Asp Leu Val Pro Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val Val
405 410 415

Cys Glu Gln Lys Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser Cys
420 425 430

Glu Ala Leu Arg Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr Ala
435 440 445

Asn Gly Ala Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ser
450 455 460

Gln Leu Ser Gln Gln Glu Gly Ile Lys Met
465 470

<210> SEQ ID NO 3122

<211> LENGTH: 393

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3122

Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys Val
1 5 10 15

Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys Val
20 25 30

Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg Asp
35 40 45

Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr Thr

US 12,384,842 B2

713

714

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

<210> SEQ ID NO 3123

<211> LENGTH: 545

<212> TYPE: PRT

<213> ORGANISM: *Homo sapiens*

<400> SEQUENCE: 3123

Thr	Ile	Pro	Pro	His	Val	Gln	Lys	Ser	Val	Asn	Asn	Asp	Met	Ile	Val
1				5					10					15	
Thr	Asp	Asn	Asn	Gly	Ala	Val	Lys	Phe	Pro	Gln	Leu	Cys	Lys	Phe	Cys
	20						25						30		

US 12,384,842 B2

715**716**

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Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn
 35 40 45
 Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala
 50 55 60
 Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His
 65 70 75 80
 Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser
 85 90 95
 Pro Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe
 100 105 110
 Met Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser
 115 120 125
 Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln
 130 135 140
 Val Thr Gly Ile Ser Leu Leu Pro Pro Leu Gly Val Ala Ile Ser Val
 145 150 155 160
 Ile Ile Ile Phe Tyr Cys Tyr Arg Val Asn Arg Gln Gln Lys Leu Ser
 165 170 175
 Ser Thr Trp Glu Thr Gly Lys Thr Arg Lys Leu Met Glu Phe Ser Glu
 180 185 190
 His Cys Ala Ile Ile Leu Glu Asp Asp Arg Ser Asp Ile Ser Ser Thr
 195 200 205
 Cys Ala Asn Asn Ile Asn His Asn Thr Glu Leu Leu Pro Ile Glu Leu
 210 215 220
 Asp Thr Leu Val Gly Lys Gly Arg Phe Ala Glu Val Tyr Lys Ala Lys
 225 230 235 240
 Leu Lys Gln Asn Thr Ser Glu Gln Phe Glu Thr Val Ala Val Lys Ile
 245 250 255
 Phe Pro Tyr Glu Glu Tyr Ala Ser Trp Lys Thr Glu Lys Asp Ile Phe
 260 265 270
 Ser Asp Ile Asn Leu Lys His Glu Asn Ile Leu Gln Phe Leu Thr Ala
 275 280 285
 Glu Glu Arg Lys Thr Glu Leu Gly Lys Gln Tyr Trp Leu Ile Thr Ala
 290 295 300
 Phe His Ala Lys Gly Asn Leu Gln Glu Tyr Leu Thr Arg His Val Ile
 305 310 315 320
 Ser Trp Glu Asp Leu Arg Lys Leu Gly Ser Ser Leu Ala Arg Gly Ile
 325 330 335
 Ala His Leu His Ser Asp His Thr Pro Cys Gly Arg Pro Lys Met Pro
 340 345 350
 Ile Val His Arg Asp Leu Lys Ser Ser Asn Ile Leu Val Lys Asn Asp
 355 360 365
 Leu Thr Cys Cys Leu Cys Asp Phe Gly Leu Ser Leu Arg Leu Asp Pro
 370 375 380
 Thr Leu Ser Val Asp Asp Leu Ala Asn Ser Gly Gln Val Gly Thr Ala
 385 390 395 400
 Arg Tyr Met Ala Pro Glu Val Leu Glu Ser Arg Met Asn Leu Glu Asn
 405 410 415
 Val Glu Ser Phe Lys Gln Thr Asp Val Tyr Ser Met Ala Leu Val Leu
 420 425 430
 Trp Glu Met Thr Ser Arg Cys Asn Ala Val Gly Glu Val Lys Asp Tyr
 435 440 445
 Glu Pro Pro Phe Gly Ser Lys Val Arg Glu His Pro Cys Val Glu Ser

US 12,384,842 B2

717

718

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450 455 460

Met Lys Asp Asn Val Leu Arg Asp Arg Gly Arg Pro Glu Ile Pro Ser
 465 470 475 480

Phe Trp Leu Asn His Gln Gly Ile Gln Met Val Cys Glu Thr Leu Thr
 485 490 495

Glu Cys Trp Asp His Asp Pro Glu Ala Arg Leu Thr Ala Gln Cys Val
 500 505 510

Ala Glu Arg Phe Ser Glu Leu Glu His Leu Asp Arg Leu Ser Gly Arg
 515 520 525

Ser Cys Ser Glu Glu Lys Ile Pro Glu Asp Gly Ser Leu Asn Thr Thr
 530 535 540

Lys
 545

<210> SEQ ID NO 3124

<211> LENGTH: 570

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3124

Thr Ile Pro Pro His Val Gln Lys Ser Asp Val Glu Met Glu Ala Gln
 1 5 10 15

Lys Asp Glu Ile Ile Cys Pro Ser Cys Asn Arg Thr Ala His Pro Leu
 20 25 30

Arg His Ile Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val
 35 40 45

Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys
 50 55 60

Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys
 65 70 75 80

Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu
 85 90 95

Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His
 100 105 110

Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu
 115 120 125

Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp
 130 135 140

Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn
 145 150 155 160

Pro Asp Leu Leu Val Ile Phe Gln Val Thr Gly Ile Ser Leu Leu
 165 170 175

Pro Pro Leu Gly Val Ala Ile Ser Val Ile Ile Ile Phe Tyr Cys Tyr
 180 185 190

Arg Val Asn Arg Gln Gln Lys Leu Ser Ser Thr Trp Glu Thr Gly Lys
 195 200 205

Thr Arg Lys Leu Met Glu Phe Ser Glu His Cys Ala Ile Ile Leu Glu
 210 215 220

Asp Asp Arg Ser Asp Ile Ser Ser Thr Cys Ala Asn Asn Ile Asn His
 225 230 235 240

Asn Thr Glu Leu Leu Pro Ile Glu Leu Asp Thr Leu Val Gly Lys Gly
 245 250 255

Arg Phe Ala Glu Val Tyr Lys Ala Lys Leu Lys Gln Asn Thr Ser Glu
 260 265 270

US 12,384,842 B2

719

720

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Gln Phe Glu Thr Val Ala Val Lys Ile Phe Pro Tyr Glu Glu Tyr Ala
 275 280 285

Ser Trp Lys Thr Glu Lys Asp Ile Phe Ser Asp Ile Asn Leu Lys His
 290 295 300

Glu Asn Ile Leu Gln Phe Leu Thr Ala Glu Glu Arg Lys Thr Glu Leu
 305 310 315 320

Gly Lys Gln Tyr Trp Leu Ile Thr Ala Phe His Ala Lys Gly Asn Leu
 325 330 335

Gln Glu Tyr Leu Thr Arg His Val Ile Ser Trp Glu Asp Leu Arg Lys
 340 345 350

Leu Gly Ser Ser Leu Ala Arg Gly Ile Ala His Leu His Ser Asp His
 355 360 365

Thr Pro Cys Gly Arg Pro Lys Met Pro Ile Val His Arg Asp Leu Lys
 370 375 380

Ser Ser Asn Ile Leu Val Lys Asn Asp Leu Thr Cys Cys Leu Cys Asp
 385 390 395 400

Phe Gly Leu Ser Leu Arg Leu Asp Pro Thr Leu Ser Val Asp Asp Leu
 405 410 415

Ala Asn Ser Gly Gln Val Gly Thr Ala Arg Tyr Met Ala Pro Glu Val
 420 425 430

Leu Glu Ser Arg Met Asn Leu Glu Asn Val Glu Ser Phe Lys Gln Thr
 435 440 445

Asp Val Tyr Ser Met Ala Leu Val Leu Trp Glu Met Thr Ser Arg Cys
 450 455 460

Asn Ala Val Gly Glu Val Lys Asp Tyr Glu Pro Pro Phe Gly Ser Lys
 465 470 475 480

Val Arg Glu His Pro Cys Val Glu Ser Met Lys Asp Asn Val Leu Arg
 485 490 495

Asp Arg Gly Arg Pro Glu Ile Pro Ser Phe Trp Leu Asn His Gln Gly
 500 505 510

Ile Gln Met Val Cys Glu Thr Leu Thr Glu Cys Trp Asp His Asp Pro
 515 520 525

Glu Ala Arg Leu Thr Ala Gln Cys Val Ala Glu Arg Phe Ser Glu Leu
 530 535 540

Glu His Leu Asp Arg Leu Ser Gly Arg Ser Cys Ser Glu Glu Lys Ile
 545 550 555 560

Pro Glu Asp Gly Ser Leu Asn Thr Thr Lys
 565 570

<210> SEQ ID NO 3125

<211> LENGTH: 831

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3125

Gly Pro Glu Pro Gly Ala Leu Cys Glu Leu Ser Pro Val Ser Ala Ser
 1 5 10 15

His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val Leu Ser Gly Cys
 20 25 30

Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val His Val Leu Asn
 35 40 45

Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln Arg Glu Val Thr
 50 55 60

Leu His Leu Asn Pro Ile Ser Ser Val His Ile His His Lys Ser Val
 65 70 75 80

US 12,384,842 B2

721

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Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp His Leu Lys Thr
85 90 95

Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu Val Ser Glu Gly
100 105 110

Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu Thr Ala Glu Thr
115 120 125

Glu Glu Arg Asn Phe Pro His Gly Asn Glu His Leu Leu Asn Trp Ala
130 135 140

Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr Glu Leu Lys Ile Ala
145 150 155 160

Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln Val Phe Pro Pro Lys
165 170 175

Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn Tyr Leu Ala Glu Tyr
180 185 190

Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met Ser Ser Gln Pro Gln
195 200 205

Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr Pro Asn Ser Asn Pro
210 215 220

Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp Ile Arg Pro Ser Gln
225 230 235 240

Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu Ile Leu Lys Cys Lys
245 250 255

Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val Lys Gly Ser Leu
260 265 270

Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys Glu Ser Glu Arg
275 280 285

Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile Pro Ser Thr Gln
290 295 300

Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr Ser Pro Ile Thr
305 310 315 320

Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His Leu Arg Leu Glu
325 330 335

Asn Asn Ala Glu Glu Met Gly Asp Glu Glu Val His Thr Ile Pro Pro
340 345 350

Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro Ala Leu Gln Asn
355 360 365

Pro Pro Ile Arg Gly Gly Glu Gln Asn Gly Gly Leu Pro Phe Pro
370 375 380

Phe Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu Gly Asp Gly
385 390 395 400

Leu Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile Gln Leu Phe Pro
405 410 415

Gly Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val Asp Ile Ala Leu
420 425 430

Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala Val Glu Lys Asp
435 440 445

Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val Thr Leu Leu Asp
450 455 460

Pro Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe Val Leu Glu Ser
465 470 475 480

Pro Leu Asn Gly Cys Gly Thr Arg Pro Arg Trp Ser Ala Leu Asp Gly
485 490 495

722

US 12,384,842 B2

723

724

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Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro Ala Leu Gly Asp
500 505 510

Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu Ser Gly Asp Asn
515 520 525

Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser Leu Phe Thr Arg
530 535 540

Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln Val Arg Asn Pro
545 550 555 560

Ser Ser Phe Gln Gln Pro His Gly Asn Ile Thr Phe Asn Met Glu
565 570 575

Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln Gly Val Phe Ser
580 585 590

Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser Val Thr Lys Ala
595 600 605

Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe Ile Ser Pro Tyr
610 615 620

Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile Glu Asn Ile Cys
625 630 635 640

Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys Arg Val His Phe
645 650 655

Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe Ser Phe Val Phe
660 665 670

Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln Cys Glu Leu Thr
675 680 685

Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu Pro Lys Cys Val
690 695 700

Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser Ile Ile Trp Ala
705 710 715 720

Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu Ala Val Ile His
725 730 735

His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met Lys Glu Pro Asn
740 745 750

Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr Leu Thr Val Met
755 760 765

Gly Ile Ala Phe Ala Ala Phe Val Ile Gly Ala Leu Leu Thr Gly Ala
770 775 780

Leu Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala Gly Arg Gln Gln
785 790 795 800

Val Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser Ala Ala His Ser
805 810 815

Ile Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser Thr Ala
820 825 830

<210> SEQ ID NO 3126

<211> LENGTH: 830

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3126

Gly Pro Glu Pro Gly Ala Leu Cys Glu Leu Ser Pro Val Ser Ala Ser
1 5 10 15

His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val Leu Ser Gly Cys
20 25 30

Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val His Val Leu Asn
35 40 45

US 12,384,842 B2

725**726**

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Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln Arg Glu Val Thr
 50 55 60
 Leu His Leu Asn Pro Ile Ser Ser Val His Ile His His Lys Ser Val
 65 70 75 80
 Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp His Leu Lys Thr
 85 90 95
 Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu Val Ser Glu Gly
 100 105 110
 Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu Thr Ala Glu Thr
 115 120 125
 Glu Glu Arg Asn Phe Pro His Gly Asn Glu His Leu Leu Asn Trp Ala
 130 135 140
 Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr Glu Leu Lys Ile Ala
 145 150 155 160
 Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln Val Phe Pro Pro Lys
 165 170 175
 Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn Tyr Leu Ala Glu Tyr
 180 185 190
 Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met Ser Ser Gln Pro Gln
 195 200 205
 Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr Pro Asn Ser Asn Pro
 210 215 220
 Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp Ile Arg Pro Ser Gln
 225 230 235 240
 Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu Ile Leu Lys Cys Lys
 245 250 255
 Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val Lys Gly Ser Leu
 260 265 270
 Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys Glu Ser Glu Arg
 275 280 285
 Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile Pro Ser Thr Gln
 290 295 300
 Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr Ser Pro Ile Thr
 305 310 315 320
 Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His Leu Arg Leu Glu
 325 330 335
 Asn Asn Glu Glu Met Gly Asp Glu Glu Val His Thr Ile Pro Pro Glu
 340 345 350
 Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro Ala Leu Gln Asn Pro
 355 360 365
 Pro Ile Arg Gly Glu Gly Gln Asn Gly Gly Leu Pro Phe Pro Phe
 370 375 380
 Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu Gly Glu Asp Gly Leu
 385 390 395 400
 Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile Gln Leu Phe Pro Gly
 405 410 415
 Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val Asp Ile Ala Leu Ser
 420 425 430
 Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala Val Glu Lys Asp Ser
 435 440 445
 Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val Thr Leu Leu Asp Pro
 450 455 460

US 12,384,842 B2

727

728

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Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe Val Leu Glu Ser Pro
 465 470 475 480
 Leu Asn Gly Cys Gly Thr Arg Pro Arg Trp Ser Ala Leu Asp Gly Val
 485 490 495
 Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro Ala Leu Gly Asp Ser
 500 505 510
 Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu Ser Gly Asp Asn Gly
 515 520 525
 Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser Leu Phe Thr Arg Pro
 530 535 540
 Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln Val Arg Asn Pro Ser
 545 550 555 560
 Ser Phe Gln Glu Gln Pro His Gly Asn Ile Thr Phe Asn Met Glu Leu
 565 570 575
 Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln Gly Val Phe Ser Val
 580 585 590
 Pro Glu Asn Gly His Val Tyr Val Glu Val Ser Val Thr Lys Ala Glu
 595 600 605
 Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe Ile Ser Pro Tyr Ser
 610 615 620
 Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile Glu Asn Ile Cys Pro
 625 630 635 640
 Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys Arg Val His Phe Pro
 645 650 655
 Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe Ser Phe Val Phe Lys
 660 665 670
 Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln Cys Glu Leu Thr Leu
 675 680 685
 Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu Pro Lys Cys Val Pro
 690 695 700
 Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser Ile Ile Trp Ala Met
 705 710 715 720
 Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu Ala Val Ile His His
 725 730 735
 Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met Lys Glu Pro Asn Pro
 740 745 750
 Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr Leu Thr Val Met Gly
 755 760 765
 Ile Ala Phe Ala Ala Phe Val Ile Gly Ala Leu Leu Thr Gly Ala Leu
 770 775 780
 Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala Gly Arg Gln Gln Val
 785 790 795 800
 Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser Ala Ala His Ser Ile
 805 810 815
 Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser Ser Thr Ala
 820 825 830

<210> SEQ ID NO 3127

<400> SEQUENCE: 3127

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<210> SEQ ID NO 3128

US 12,384,842 B2

729**730**-continued

<400> SEQUENCE: 3128

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<210> SEQ ID NO 3129

<400> SEQUENCE: 3129

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<210> SEQ ID NO 3130

<400> SEQUENCE: 3130

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<210> SEQ ID NO 3131

<400> SEQUENCE: 3131

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<210> SEQ ID NO 3132

<400> SEQUENCE: 3132

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<210> SEQ ID NO 3133

<400> SEQUENCE: 3133

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<210> SEQ ID NO 3134

<400> SEQUENCE: 3134

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<210> SEQ ID NO 3135

<400> SEQUENCE: 3135

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<210> SEQ ID NO 3136

<400> SEQUENCE: 3136

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<210> SEQ ID NO 3137

<400> SEQUENCE: 3137

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<210> SEQ ID NO 3138

<400> SEQUENCE: 3138

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<210> SEQ ID NO 3139

<400> SEQUENCE: 3139

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<210> SEQ ID NO 3140

<400> SEQUENCE: 3140

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<210> SEQ ID NO 3141

<400> SEQUENCE: 3141

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<210> SEQ ID NO 3142

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<210> SEQ ID NO 3143

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<210> SEQ ID NO 3144

<400> SEQUENCE: 3144

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<210> SEQ ID NO 3145

<400> SEQUENCE: 3145

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<210> SEQ ID NO 3146

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<210> SEQ ID NO 3147

<400> SEQUENCE: 3147

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<210> SEQ ID NO 3148

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<210> SEQ ID NO 3149

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<210> SEQ ID NO 3150

<400> SEQUENCE: 3150

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<210> SEQ ID NO 3151

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<210> SEQ ID NO 3152

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<210> SEQ ID NO 3153

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<210> SEQ ID NO 3154

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<210> SEQ ID NO 3155

<400> SEQUENCE: 3155

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<210> SEQ ID NO 3156

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<210> SEQ ID NO 3157

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<210> SEQ ID NO 3158

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<210> SEQ ID NO 3159

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<210> SEQ ID NO 3160

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<210> SEQ ID NO 3161

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<210> SEQ ID NO 3162

<400> SEQUENCE: 3162

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<210> SEQ ID NO 3163

<400> SEQUENCE: 3163

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<210> SEQ ID NO 3164

<400> SEQUENCE: 3164

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<210> SEQ ID NO 3165

<400> SEQUENCE: 3165

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<210> SEQ ID NO 3166

<400> SEQUENCE: 3166

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<210> SEQ ID NO 3167

<400> SEQUENCE: 3167

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<210> SEQ ID NO 3168

<400> SEQUENCE: 3168

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<210> SEQ ID NO 3169

<400> SEQUENCE: 3169

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<210> SEQ ID NO 3170

<400> SEQUENCE: 3170

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<210> SEQ ID NO 3171

<400> SEQUENCE: 3171

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<210> SEQ ID NO 3172

<400> SEQUENCE: 3172

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<210> SEQ ID NO 3173

<400> SEQUENCE: 3173

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<210> SEQ ID NO 3174

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<210> SEQ ID NO 3175

<400> SEQUENCE: 3175

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<210> SEQ ID NO 3176

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<210> SEQ ID NO 3177

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<210> SEQ ID NO 3178

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<210> SEQ ID NO 3179

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<210> SEQ ID NO 3180

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<210> SEQ ID NO 3181

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<210> SEQ ID NO 3182

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<210> SEQ ID NO 3183

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<210> SEQ ID NO 3184

<400> SEQUENCE: 3184

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<210> SEQ ID NO 3185

<400> SEQUENCE: 3185

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<210> SEQ ID NO 3186

<400> SEQUENCE: 3186

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<210> SEQ ID NO 3187

<400> SEQUENCE: 3187

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<210> SEQ ID NO 3188

<400> SEQUENCE: 3188

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<210> SEQ ID NO 3189

<400> SEQUENCE: 3189

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<210> SEQ ID NO 3190

<400> SEQUENCE: 3190

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<210> SEQ ID NO 3191

<400> SEQUENCE: 3191

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<210> SEQ ID NO 3192

<211> LENGTH: 481

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<220> FEATURE:

<221> NAME/KEY: VARIANT

<222> LOCATION: (330)..(330)

<223> OTHER INFORMATION: /replace=" "

<220> FEATURE:

<221> NAME/KEY: SITE

<222> LOCATION: (1)..(481)

<223> OTHER INFORMATION: /note="Variant residues given in the sequence
have no preference with respect to those in the annotations
for variant positions"

<400> SEQUENCE: 3192

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser

US 12,384,842 B2

741**742**

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35	40	45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly		
50	55	60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly		
65	70	75
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys		
85	90	95
Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys		
100	105	110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu		
115	120	125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu		
130	135	140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys		
145	150	155
Phe Asn Trp		160
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys		
165	170	175
Glu Val Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu		
180	185	190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys		
195	200	205
Val Ser Asn Ala Pro Ala Pro Ile Glu Lys Thr Ile Ser		
210	215	220
Lys Lys Ala Lys Pro Arg Glu Pro Gln Val Cys Thr Leu		
225	230	235
Pro Pro Ser Arg Glu Glu		240
Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys		
245	250	255
Gly Phe Tyr		
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln		
260	265	270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly		
275	280	285
Ser Ser Phe Phe		
Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln		
290	295	300
Gln Gln Gly Asn		
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn		
305	310	315
His Tyr Thr		320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly		
325	330	335
Ser Ser Gly Gly Gly Gly Ser Ile Pro Pro His Val Gln		
340	345	350
Lys Asn		
Ser Val Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly		
355	360	365
Ala Val Lys		
Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser		
370	375	380
Thr Cys Asp		
Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser		
385	390	395
Ile Cys Glu		400
Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn		
405	410	415
Asp Glu Asn		
Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro		
420	425	430
Tyr His Asp		
Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met		
435	440	445
Lys Lys Met Lys Glu Lys		
Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser		
450	455	460
Asp Asp Glu		

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Cys	Asn	Asp	Asn	Ile	Ile	Phe	Ser	Glu	Glu	Tyr	Asn	Thr	Ser	Asn	Pro
465				470				475							480

Asp

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<210> SEQ ID NO 3193
<211> LENGTH: 481
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (330)..(330)
<223> OTHER INFORMATION: /replace=" "
<220> FEATURE:
<221> NAME/KEY: SITE
<222> LOCATION: (1)..(481)
<223> OTHER INFORMATION: /note="Variant residues given in the sequence
have no preference with respect to those in the annotations
for variant positions"

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<400> SEQUENCE: 3193

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

Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr
				20				25							30

Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser
				35				40							45

Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser
				50				55							60

Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr
				65				70							80

Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys
				85				90							95

Arg	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys
				100				105							110

Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro
				115				120							125

Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys
				130				135							140

Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp
				145				150							160

Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu
				165				170							175

Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu
				180				185							190

His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn
				195				200							205

Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly
				210				215							220

Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Cys	Arg	Glu	Glu
				225				230							240

Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Trp	Cys	Leu	Val	Lys	Gly	Phe	Tyr
				245				250							255

Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn
				260				265							270

US 12,384,842 B2

745**746**

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Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe
275												280			285

Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn
290												295			300

Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr
305												310			315

Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly	Ser	Gly
								325		330			335	

Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Ile	Pro	Pro	His	Val	Gln	Lys
								340		345			350	

Ser	Val	Asn	Asn	Asp	Met	Ile	Val	Thr	Asp	Asn	Asn	Gly	Ala	Val	Lys
						355		360				365			

Phe	Pro	Gln	Leu	Cys	Lys	Phe	Cys	Asp	Val	Arg	Phe	Ser	Thr	Cys	Asp
						370		375				380			

Asn	Gln	Lys	Ser	Cys	Met	Ser	Asn	Cys	Ser	Ile	Thr	Ser	Ile	Cys	Glu
						385		390			395			400	

Lys	Pro	Gln	Glu	Val	Cys	Val	Ala	Val	Trp	Arg	Lys	Asn	Asp	Glu	Asn
						405		410			415				

Ile	Thr	Leu	Glu	Thr	Val	Cys	His	Asp	Pro	Lys	Leu	Pro	Tyr	His	Asp
						420		425			430				

Phe	Ile	Leu	Glu	Asp	Ala	Ala	Ser	Pro	Lys	Cys	Ile	Met	Lys	Glu	Lys
						435		440			445				

Lys	Lys	Pro	Gly	Glu	Thr	Phe	Phe	Met	Cys	Ser	Cys	Ser	Ser	Asp	Glu
						450		455			460				

Cys	Asn	Asp	Asn	Ile	Ile	Phe	Ser	Glu	Glu	Tyr	Asn	Thr	Ser	Asn	Pro
						465		470			475				480

Asp

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<210> SEQ ID NO 3194
<211> LENGTH: 378
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (227)..(227)
<223> OTHER INFORMATION: /replace=" "
<220> FEATURE:
<221> NAME/KEY: SITE
<222> LOCATION: (1)..(378)
<223> OTHER INFORMATION: /note="Variant residues given in the sequence
have no preference with respect to those in the annotations
for variant positions"

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<400> SEQUENCE: 3194

Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
1						5		10			15				

Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
						20		25			30				

Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His
						35		40			45				

Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val
						50		55			60				

His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Tyr	Asn	Ser	Thr	Tyr	
						65		70			75			80	

Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
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US 12,384,842 B2

747

748

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

<210> SEQ ID NO 3195
<211> LENGTH: 378
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (227)..(227)
<223> OTHER INFORMATION: /replace=""
<220> FEATURE:
<221> NAME/KEY: SITE
<222> LOCATION: (1)..(378)
<223> OTHER INFORMATION: /note="Variant residues given in the sequence
have no preference with respect to those in the annotations
for variant positions"
<400> SEQUENCE: 3195

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Gly

US 12,384,842 B2

749**750**

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1	5	10	15
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met			
20	25		30
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His			
35	40		45
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val			
50	55		60
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr			
65	70		75
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly			
85	90		95
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile			
100	105		110
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val			
115	120		125
Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser			
130	135		140
Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu			
145	150		155
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro			
165	170		175
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val			
180	185		190
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met			
195	200		205
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser			
210	215		220
Pro Gly Lys Gly Gly Ser Gly Gly Ser Gly Gly Gly			
225	230		235
Gly Ser Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile			
245	250		255
Val Thr Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe			
260	265		270
Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser			
275	280		285
Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val			
290	295		300
Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys			
305	310		315
His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala			
325	330		335
Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe			
340	345		350
Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe			
355	360		365
Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp			
370	375		

<210> SEQ ID NO 3196
 <211> LENGTH: 481
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence"

US 12,384,842 B2

751**752**

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Synthetic polypeptide"
 <220> FEATURE:
 <221> NAME/KEY: VARIANT
 <222> LOCATION: (481)..(481)
 <223> OTHER INFORMATION: /replace=""
 <220> FEATURE:
 <221> NAME/KEY: SITE
 <222> LOCATION: (1)..(481)
 <223> OTHER INFORMATION: /note="Variant residues given in the sequence
 have no preference with respect to those in the annotations
 for variant positions"

<400> SEQUENCE: 3196

Ile	Pro	Pro	His	Val	Gln	Lys	Ser	Val	Asn	Asn	Asp	Met	Ile	Val	Thr
1				5				10				15			

Asp	Asn	Asn	Gly	Ala	Val	Lys	Phe	Pro	Gln	Leu	Cys	Lys	Phe	Cys	Asp
				20			25				30				

Val	Arg	Phe	Ser	Thr	Cys	Asp	Asn	Gln	Lys	Ser	Cys	Met	Ser	Asn	Cys
	35				40						45				

Ser	Ile	Thr	Ser	Ile	Cys	Glu	Lys	Pro	Gln	Glu	Val	Cys	Val	Ala	Val
50					55						60				

Trp	Arg	Lys	Asn	Asp	Glu	Asn	Ile	Thr	Leu	Glu	Thr	Val	Cys	His	Asp
65					70			75			80				

Pro	Lys	Leu	Pro	Tyr	His	Asp	Phe	Ile	Leu	Glu	Asp	Ala	Ala	Ser	Pro
	85				90						95				

Lys	Cys	Ile	Met	Lys	Glu	Lys	Lys	Pro	Gly	Glu	Thr	Phe	Phe	Met
		100				105					110			

Cys	Ser	Cys	Ser	Ser	Asp	Glu	Cys	Asn	Asp	Asn	Ile	Ile	Phe	Ser	Glu
	115				120						125				

Glu	Tyr	Asn	Thr	Ser	Asn	Pro	Asp	Gly	Gly	Gly	Ser	Gly	Gly	Gly	
	130				135						140				

Gly	Ser	Gly	Gly	Gly	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	
145					150			155			160				

Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu
	165					170						175			

Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp
		180				185						190			

Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu
	195				200						205				

Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser
	210				215						220				

Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro
225					230			235			240				

Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys
	245				250						255				

Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro
	260					265						270			

Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
	275				280						285				

Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp
	290				295						300				

Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
	305				310			315			320				

Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val
	325				330			335			335				

Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
	340				345						350				

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Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 355 360 365

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr
 370 375 380

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser
 385 390 395 400

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 405 410 415

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 420 425 430

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
 435 440 445

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 450 455 460

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 465 470 475 480

Lys

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<210> SEQ ID NO 3197
<211> LENGTH: 481
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (481)..(481)
<223> OTHER INFORMATION: /replace=" "
<220> FEATURE:
<221> NAME/KEY: SITE
<222> LOCATION: (1)..(481)
<223> OTHER INFORMATION: /note="Variant residues given in the sequence
have no preference with respect to those in the annotations
for variant positions"

<400> SEQUENCE: 3197

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Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
 1 5 10 15

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
 20 25 30

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
 35 40 45

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
 50 55 60

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
 65 70 75 80

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
 85 90 95

Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe Met
 100 105 110

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
 115 120 125

Glu Tyr Asn Thr Ser Asn Pro Asp Gly Gly Ser Gly Gly Gly
 130 135 140

Gly Ser Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 145 150 155 160

US 12,384,842 B2

755**756**

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Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
165 170 175

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
180 185 190

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
195 200 205

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
210 215 220

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
225 230 235 240

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
245 250 255

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
260 265 270

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
275 280 285

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
290 295 300

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
305 310 315 320

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
325 330 335

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
340 345 350

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
355 360 365

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
370 375 380

Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
385 390 395 400

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
405 410 415

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
420 425 430

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
435 440 445

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
450 455 460

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
465 470 475 480

Lys

<210> SEQ ID NO 3198
<211> LENGTH: 257
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 3198

Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
1 5 10 15

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
20 25 30

US 12,384,842 B2

757

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Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
 35 40 45

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
 50 55 60

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
 65 70 75 80

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
 85 90 95

Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe Met
 100 105 110

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
 115 120 125

Glu Tyr Asn Thr Ser Asn Pro Asp Gly Gly Gly Ser Gly Gly Gly
 130 135 140

Gly Ser Gly Gly Gly Ser Gly Gln Pro Lys Ala Asn Pro Thr Val
 145 150 155 160

Thr Leu Phe Pro Pro Ser Ser Glu Leu Gln Ala Asn Lys Ala Thr
 165 170 175

Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala
 180 185 190

Trp Lys Ala Asp Gly Ser Pro Val Lys Ala Gly Val Glu Thr Thr Lys
 195 200 205

Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser
 210 215 220

Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val
 225 230 235 240

Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys
 245 250 255

Ser

<210> SEQ ID NO 3199
 <211> LENGTH: 258
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 3199

Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
 1 5 10 15

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
 20 25 30

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
 35 40 45

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
 50 55 60

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
 65 70 75 80

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
 85 90 95

Lys Cys Ile Met Lys Glu Lys Lys Pro Gly Glu Thr Phe Phe Met
 100 105 110

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu

758

US 12,384,842 B2

759**760**

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115 120 125

Glu Tyr Asn Thr Ser Asn Pro Asp Gly Gly Gly Ser Gly Gly Gly
 130 135 140

Gly Ser Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe
 145 150 155 160

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
 165 170 175

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
 180 185 190

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
 195 200 205

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
 210 215 220

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
 225 230 235 240

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
 245 250 255

Glu Cys

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US 12,384,842 B2

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US 12,384,842 B2

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US 12,384,842 B2

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<220> FEATURE:

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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<400> SEQUENCE: 6000

Thr Gly Gly Tyr His Trp Asn
1 5

<210> SEQ ID NO 6001

<211> LENGTH: 16

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 6002

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6002

Gly Asn Trp His Tyr Phe Asp Phe

US 12,384,842 B2

1259**1260**

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Thr Gly Gly Tyr His Trp Asn
1 5

<210> SEQ ID NO 6008
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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Tyr Ile Tyr Ser Ser Gly Thr Thr Arg Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 6009
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Gly Asn Trp His Tyr Phe Asp Tyr
1 5

<210> SEQ ID NO 6010
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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Gln Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Phe Ser Ile Asn
20 25 30

<210> SEQ ID NO 6011
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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<400> SEQUENCE: 6011

Trp Ile Arg Gln Phe Pro Gly Lys Lys Leu Glu Trp Met Gly
1 5 10

<210> SEQ ID NO 6012
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6012

US 12,384,842 B2

1261**1262**

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Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln			
1	5	10	15

Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Thr Tyr Tyr Cys Thr Arg			
20	25	30	

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Trp Gly Gln Gly Thr Leu Val Ala Val Ser Ser			
1	5	10	

<210> SEQ ID NO 6014
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<212> TYPE: PRT
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6014

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn			
20	25	30	

<210> SEQ ID NO 6015
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 6015

Trp Ile Arg Gln Pro Ala Gly Lys Gly Leu Glu Trp Ile Gly			
1	5	10	

<210> SEQ ID NO 6016
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

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Arg Val Thr Met Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys			
1	5	10	15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg			
20	25	30	

<210> SEQ ID NO 6017
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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1263**1264**

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6017

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 6018

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<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6018

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn
20 25 30

<210> SEQ ID NO 6019

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6019

Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 6020

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6020

Leu Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> SEQ ID NO 6021

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6021

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 6022

<211> LENGTH: 30

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

US 12,384,842 B2

1265**1266**

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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6022

Glu	Ile	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Ley	Val	Gln	Pro	Gly	Gly
1					5					10			15	
Ser Ley Arg Ley Ser Cys Ala Val Ser Gly Phe Ser Ile Asn														
20 25 30														

<210> SEQ ID NO 6023
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

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Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Ley	Glu	Trp	Val	Gly
1					5				10				

<210> SEQ ID NO 6024
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6024

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Thr	Ser	Lys	Asn	Thr	Phe	Tyr	Ley	Gln
1					5			10			15				

Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg
					20			25			30				

<210> SEQ ID NO 6025
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<213> ORGANISM: Artificial Sequence
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Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser
1					5			10		

<210> SEQ ID NO 6026
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6026

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

Ser	Val	Lys	Val	Ser	Cys	Lys	Val	Ser	Gly	Phe	Ser	Ile	Asn	
					20			25			30			

US 12,384,842 B2

1267**1268**

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<210> SEQ ID NO 6027
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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```
Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
1           5             10
```

<210> SEQ ID NO 6028
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6028

```
Arg Val Thr Ile Thr Arg Asp Thr Ser Thr Asn Thr Phe Tyr Met Glu
1           5           10           15
```

```
Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20          25           30
```

<210> SEQ ID NO 6029
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6029

```
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1           5           10
```

<210> SEQ ID NO 6030
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6030

```
Glu Ile Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
1           5           10           15
```

```
Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ser Ile Asn
20          25           30
```

<210> SEQ ID NO 6031

<400> SEQUENCE: 6031

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<210> SEQ ID NO 6032
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<212> TYPE: PRT
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US 12,384,842 B2

1269**1270**

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<221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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<400> SEQUENCE: 6032

Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Gly
1	5								10				

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 Synthetic polypeptide"

<400> SEQUENCE: 6033

Arg	Phe	Thr	Ile	Ser	Arg	Asp	Thr	Ala	Lys	Asn	Ser	Phe	Tyr	Leu	Gln
1	5							10				15			

Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg
	20							25				30			

<210> SEQ ID NO 6034
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6034

Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser
1	5							10		

<210> SEQ ID NO 6035
 <211> LENGTH: 30
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6035

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

Ser	Val	Lys	Val	Ser	Cys	Lys	Val	Ser	Gly	Phe	Ser	Ile	Asn
	20							25			30		

<210> SEQ ID NO 6036
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6036

Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly
1	5							10					

<210> SEQ ID NO 6037
 <211> LENGTH: 32
 <212> TYPE: PRT

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<210> SEQ ID NO 6042
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6042

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 6043
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6043

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn
20 25 30

<210> SEQ ID NO 6044
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6044

Trp Ile Arg Gln Pro Ala Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 6045
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6045

Arg Val Thr Met Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> SEQ ID NO 6046
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6046

US 12,384,842 B2

1275**1276**

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```
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1           5           10
```

<210> SEQ ID NO 6047
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6047

```
Glu Ile Gln Leu Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
1           5           10           15
```

```
Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ser Ile Asn
20          25          30
```

<210> SEQ ID NO 6048
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6048

```
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly
1           5           10
```

<210> SEQ ID NO 6049
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6049

```
Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Phe Tyr Leu Gln
1           5           10           15
```

```
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20          25          30
```

<210> SEQ ID NO 6050
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6050

```
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1           5           10
```

<210> SEQ ID NO 6051
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

US 12,384,842 B2

1277

1278

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<400> SEQUENCE: 6051

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

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ser Ile Asn
 20 25 30

<210> SEQ ID NO 6052

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6052

Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly
 1 5 10

<210> SEQ ID NO 6053

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6053

Arg Phe Thr Ile Ser Arg Asp Thr Ala Lys Asn Ser Phe Tyr Leu Gln
 1 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 20 25 30

<210> SEQ ID NO 6054

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6054

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 1 5 10

<210> SEQ ID NO 6055

<211> LENGTH: 30

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6055

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Phe Ser Ile Asn
 20 25 30

<210> SEQ ID NO 6056

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

US 12,384,842 B2

1279**1280**

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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6056

Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly
1													
													10

<210> SEQ ID NO 6057
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6057

Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Thr	Asn	Thr	Phe	Tyr	Met	Glu
1															
															15

Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg
															30
20															25

<210> SEQ ID NO 6058
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6058

Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
1										
										10

<210> SEQ ID NO 6059
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6059

Glu	Ile	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1															
															15

Thr	Val	Lys	Ile	Ser	Cys	Lys	Val	Ser	Gly	Phe	Ser	Ile	Asn	
20														30

<210> SEQ ID NO 6060
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6060

Trp	Val	Gln	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Met	Gly	
1														
														10

<210> SEQ ID NO 6061
<211> LENGTH: 32

US 12,384,842 B2

1281**1282**

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6061

Arg Val Thr Ile Thr Arg Asp Thr Ser Thr Asn Thr Phe Tyr Met Glu		
1	5	10
		15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg		
20	25	30

<210> SEQ ID NO 6062
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6062

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser		
1	5	10

<210> SEQ ID NO 6063
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6063

Ser Gly Glu Arg Leu Ser Asp Lys Tyr Val His		
1	5	10

<210> SEQ ID NO 6064
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6064

Glu Asn Asp Lys Arg Pro Ser		
1	5	

<210> SEQ ID NO 6065
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6065

Gln Ala Gly Tyr Glu Ala Asp Tyr Tyr Cys		
1	5	10

<210> SEQ ID NO 6066
<211> LENGTH: 22
<212> TYPE: PRT

1283**1284**

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6066

Ser	Tyr	Thr	Leu	Thr	Gln	Pro	Pro	Leu	Leu	Ser	Val	Ala	Leu	Gly	His
1				5				10					15		

Lys Ala Thr Ile Thr Cys
20

<210> SEQ ID NO 6067
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6067

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Arg	Ala	Pro	Val	Met	Val	Ile	Tyr
1				5				10				15		

<210> SEQ ID NO 6068
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6068

Gly	Ile	Pro	Asp	Gln	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Ile	Ala	Thr
1				5			10				15				

Leu Thr Ile Ser Lys Ala
20

<210> SEQ ID NO 6069
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6069

Phe	Gly	Ser	Gly	Thr	Gln	Leu	Thr	Val	Leu
1				5			10		

<210> SEQ ID NO 6070
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6070

Ser	Gly	Glu	Asn	Leu	Ser	Asp	Lys	Tyr	Val	His
1				5			10			

<210> SEQ ID NO 6071

US 12,384,842 B2

1285

1286

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<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6071

Glu	Asn	Glu	Lys	Arg	Pro	Ser
1					5	

<210> SEQ ID NO 6072
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6072

His	Tyr	Trp	Glu	Ser	Ile	Asn	Ser	Val	Val
1					5			10	

<210> SEQ ID NO 6073
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6073

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

Lys	Ala	Thr	Ile	Ile	Cys
	20				

<210> SEQ ID NO 6074
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6074

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Arg	Ala	Pro	Val	Met	Val	Ile	Tyr
1					5			10			15			

<210> SEQ ID NO 6075
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6075

Gly	Ile	Pro	Asp	Gln	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Ile	Ala	Thr
1					5			10			15				

Leu	Thr	Ile	Ser	Lys	Ala	Gln	Pro	Gly	Ser	Glu	Ala	Asp	Tyr	Tyr	Cys
					20			25				30			

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<210> SEQ ID NO 6076
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6076

Phe	Gly	Ser	Gly	Thr	His	Leu	Thr	Val	Leu
1									
									10

<210> SEQ ID NO 6077
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6077

Gln	Ser	Val	Thr	Thr	Gln	Pro	Pro	Ser	Val	Ser	Gly	Ala	Pro	Gly	Gln
1															
															15

Arg	Val	Thr	Ile	Ser	Cys
					20

<210> SEQ ID NO 6078
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6078

Trp	Tyr	Gln	Gln	Leu	Pro	Gly	Thr	Ala	Pro	Lys	Met	Leu	Ile	Tyr
1														
														15

<210> SEQ ID NO 6079
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6079

Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Ser	Ala	Ser
1															
															15

Leu	Ala	Ile	Thr	Gly	Leu	Gln	Ala	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys
															20
															25
															30

<210> SEQ ID NO 6080
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6080

Phe	Gly	Gly	Gly	Thr	Gln	Leu	Thr	Val	Leu
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

US 12,384,842 B2

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1 5

1

10

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<210> SEQ ID NO 6081
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

Gln Ser Val Thr Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys
20

```
<210> SEQ ID NO 6082
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

<400> SEQUENCE: 6082

Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
1 5 10 15

```
<210> SEQ ID NO 6083
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
```

<400> SEQUENCE: 6083

Gly Val Pro Asp Arg Phe Ser Gly Ser Asn Ser Gly Asn Ser Ala Ser
 1 5 10 15

Leu Ala Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys
20 25 30

```
<210> SEQ ID NO 6084
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

<400> SEQUENCE: 6084

Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
1 5 10

```
<210> SEQ ID NO 6085
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

<400> SEQUENCE: 6085

1291**1292**

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Gln Ser Val Thr Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
 1 5 10 15

Arg Val Thr Ile Ser Cys
 20

<210> SEQ ID NO 6086
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6086

Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
 1 5 10 15

<210> SEQ ID NO 6087
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6087

Gly Val Pro Asp Arg Phe Ser Gly Ser Asn Ser Gly Asn Ser Ala Ser
 1 5 10 15

Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys
 20 25 30

<210> SEQ ID NO 6088
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6088

Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
 1 5 10

<210> SEQ ID NO 6089
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6089

Ser Ser Glu Thr Thr Gln Pro His Ser Val Ser Val Ala Thr Ala Gln
 1 5 10 15

Met Ala Arg Ile Thr Cys
 20

<210> SEQ ID NO 6090
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6090

Trp Tyr Gln Gln Lys Pro Gly Gln Asp Pro Val Met Val Ile Tyr
 1 5 10 15

<210> SEQ ID NO 6091
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6091

Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Pro Gly Asn Thr Ala Thr
 1 5 10 15

Leu Thr Ile Ser Arg Ile Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys
 20 25 30

<210> SEQ ID NO 6092
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6092

Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
 1 5 10

<210> SEQ ID NO 6093
 <211> LENGTH: 23
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6093

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

Asp Arg Val Thr Ile Thr Cys
 20

<210> SEQ ID NO 6094
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6094

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Met Leu Ile Tyr
 1 5 10 15

<210> SEQ ID NO 6095
 <211> LENGTH: 32
 <212> TYPE: PRT

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<210> SEQ ID NO 6100
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6100

Phe	Gly	Glu	Gly	Thr	Glu	Leu	Thr	Val	Leu
1				5				10	

<210> SEQ ID NO 6101
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6101

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

Arg	Val	Thr	Ile	Ser	Cys
20					

<210> SEQ ID NO 6102
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6102

Trp	Tyr	Gln	Gln	Leu	Pro	Gly	Thr	Ala	Pro	Lys	Met	Leu	Ile	Tyr
1					5			10		15				

<210> SEQ ID NO 6103
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6103

Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Ser	Ala	Ser
1					5			10		15					

Leu	Ala	Ile	Ser	Gly	Leu	Arg	Ser	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys
20					25				30						

<210> SEQ ID NO 6104
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6104

US 12,384,842 B2

1299**1300**

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Phe	Gly	Glu	Gly	Thr	Glu	Leu	Thr	Val	Leu
1				5			10		

<210> SEQ ID NO 6105
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6105

Ser	Tyr	Glu	Leu	Thr	Gln	Pro	Pro	Ser	Val	Ser	Val	Pro	Gly	Gln
1				5			10			15				

Thr	Ala	Ser	Ile	Thr	Cys
			20		

<210> SEQ ID NO 6106
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6106

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Val	Met	Val	Ile	Tyr
1				5			10			15				

<210> SEQ ID NO 6107
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6107

Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Thr	Ala	Thr
1				5			10			15					

Leu	Thr	Ile	Ser	Gly	Thr	Gln	Ala	Met	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys
		20			25					30					

<210> SEQ ID NO 6108
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6108

Phe	Gly	Glu	Gly	Thr	Glu	Leu	Thr	Val	Leu
1				5			10		

<210> SEQ ID NO 6109
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

US 12,384,842 B2

1301**1302**

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<400> SEQUENCE: 6109

Asp	Tyr	Val	Leu	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Pro	Gly
1															15

Glu	Pro	Ala	Ser	Ile	Ser	Cys
						20

<210> SEQ ID NO 6110

<211> LENGTH: 15

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6110

Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Gln	Met	Leu	Ile	Tyr
1														15

<210> SEQ ID NO 6111

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6111

Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Asp	Ala	Thr
1															15

Leu	Lys	Ile	Ser	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Val	Tyr	Tyr	Cys
															30

<210> SEQ ID NO 6112

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6112

Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys
1									

5 10

<210> SEQ ID NO 6113

<211> LENGTH: 23

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6113

Ala	Tyr	Gln	Leu	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1															15

Asp	Arg	Val	Thr	Ile	Thr	Cys
						20

<210> SEQ ID NO 6114

<211> LENGTH: 15

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

US 12,384,842 B2

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<220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6114

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Met	Leu	Ile	Tyr
				5				10			15			

<210> SEQ ID NO 6115
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6115

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Asp	Ala	Thr
1					5			10			15				

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
					20			25			30				

<210> SEQ ID NO 6116
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6116

Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys
1					5			10	

<210> SEQ ID NO 6117
 <211> LENGTH: 23
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6117

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

Glu	Arg	Ala	Thr	Leu	Ser	Cys
				20		

<210> SEQ ID NO 6118
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 6118

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

<210> SEQ ID NO 6119
 <211> LENGTH: 32

US 12,384,842 B2

1305**1306**

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6119

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

<210> SEQ ID NO 6120
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 6120

Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys
1					5			10	

<210> SEQ ID NO 6121
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6121

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

Ser	Leu	Ser	Leu	Thr	Cys	Ser	Val	Thr	Gly	Phe	Ser	Ile	Asn	Thr	Gly
					20			25				30			

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

Trp	Met	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Ser	Thr	Ser	Tyr	Asn	Pro	Ser
	50				55				60						

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

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

Cys	Ala	Arg	Gly	Asn	Trp	His	Tyr	Phe	Asp	Phe	Trp	Gly	Gln	Gly	Thr
					100			105			110				

Met	Val	Thr	Val	Ser	Ser
				115	

<210> SEQ ID NO 6122
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6122

Gln	Ile	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

US 12,384,842 B2

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<210> SEQ ID NO 6123
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
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<400> SEQUENCE: 6123

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn Thr Gly
20 25 30

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

Trp Ile Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Met Ser Arg Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser

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<210> SEQ ID NO 6124
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
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<400> SEQUENCE: 6124
Gln Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn Thr Gly

Gly Tyr His Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
25 10 45

US 12,384,842 B2

1309**1310**

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Trp Ile Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Leu Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser
 115

<210> SEQ ID NO 6125
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6125

Glu Ile Gln Leu Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

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

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35 40 45

Trp Val Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Phe
 65 70 75 80

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

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser
 115

<210> SEQ ID NO 6126
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6126

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Phe Ser Ile Asn Thr Gly
 20 25 30

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu
 35 40 45

Trp Met Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Ile Thr Arg Asp Thr Ser Thr Asn Thr Phe
 65 70 75 80

US 12,384,842 B2

1311**1312**

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

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser
 115

<210> SEQ ID NO 6127
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6127

Glu Ile Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

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

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35 40 45

Trp Val Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Phe Thr Ile Ser Arg Asp Thr Ala Lys Asn Ser Phe
 65 70 75 80

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

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser
 115

<210> SEQ ID NO 6128
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6128

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Phe Ser Ile Asn Thr Gly
 20 25 30

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu
 35 40 45

Trp Met Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Phe
 65 70 75 80

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

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser

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115

<210> SEQ ID NO 6129
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6129

Gln	Ile	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
1															
															15

Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Ile	Asn	Thr	Gly
															30
20															

Gly	Tyr	His	Trp	Asn	Trp	Ile	Arg	Gln	His	Pro	Gly	Lys	Gly	Leu	Glu
															45
35															

Trp	Ile	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Thr	Thr	Arg	Tyr	Asn	Pro	Ser
															60
50															

Leu	Lys	Ser	Leu	Val	Thr	Ile	Ser	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe
															80
65															

Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr
															95
85															

Cys	Ala	Arg	Gly	Asn	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
															110
100															

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 6130
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6130

Gln	Ile	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Glu
1															
															15

Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Ile	Asn	Thr	Gly
															30
20															

Gly	Tyr	His	Trp	Asn	Trp	Ile	Arg	Gln	Pro	Ala	Gly	Lys	Gly	Leu	Glu
															45
35															

Trp	Ile	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Thr	Thr	Arg	Tyr	Asn	Pro	Ser
															60
50															

Leu	Lys	Ser	Arg	Val	Thr	Met	Ser	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe
															80
65															

Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr
															95
85															

Cys	Ala	Arg	Gly	Asn	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
															110
100															

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 6131
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

US 12,384,842 B2

1315**1316**

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<220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6131

Glu	Ile	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1															
							5				10				15

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

Gly	Tyr	His	Trp	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu
								35		40		45			

Trp	Val	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Thr	Thr	Arg	Tyr	Asn	Pro	Ser
				50		55			60						

Leu	Lys	Ser	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Thr	Ser	Lys	Asn	Thr	Phe
							65		70		75		80		

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

Cys	Ala	Arg	Gly	Asn	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
							100		105		110				

Leu	Val	Thr	Val	Ser	Ser										
						115									

<210> SEQ ID NO 6132
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6132

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

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

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

Trp	Val	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Thr	Thr	Arg	Tyr	Asn	Pro	Ser
				50		55			60						

Leu	Lys	Ser	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Thr	Ala	Lys	Asn	Ser	Phe
							65		70		75		80		

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

Cys	Ala	Arg	Gly	Asn	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
							100		105		110				

Leu	Val	Thr	Val	Ser	Ser										
						115									

<210> SEQ ID NO 6133
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6133

US 12,384,842 B2

1317**1318**

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

<210> SEQ ID NO 6134
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6134

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

<210> SEQ ID NO 6135
<211> LENGTH: 97
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6135

Ser Tyr Thr Leu Thr Gln Pro Pro Leu Leu Ser Val Ala Leu Gly His
 1 5 10 15
 Lys Ala Thr Ile Thr Cys Ser Gly Glu Arg Leu Ser Asp Lys Tyr Val
 20 25 30
 His Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Val Met Val Ile Tyr

US 12,384,842 B2

1319**1320**

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35 40 45

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

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

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

Leu

<210> SEQ ID NO 6136

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6136

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

Lys Ala Thr Ile Ile Cys Ser Gly Glu Asn Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Val Met Val Ile Tyr
 35 40 45

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

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

Ser Glu Ala Asp Tyr Tyr Cys His Tyr Trp Glu Ser Ile Asn Ser Val
 85 90 95

Val Phe Gly Ser Gly Thr His Leu Thr Val Leu
 100 105

<210> SEQ ID NO 6137

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6137

Gln Ser Val Thr Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
 1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Glu Arg Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
 35 40 45

Glu Asn Asp Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
 50 55 60

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

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

Val Phe Gly Gly Thr Gln Leu Thr Val Leu
 100 105

US 12,384,842 B2

1321

1322

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<210> SEQ ID NO 6138
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
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<400> SEQUENCE: 6138
Gln Ser Val Thr Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln

Arg Val Thr Ile Ser Cys Ser Gly Glu Arg Leu Ser Asp Lys Tyr Val

His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
35 40 45

Glu Asn Asp Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
50 55 60

Asn	Ser	Gly	Asn	Ser	Ala	Ser	Leu	Ala	Ile	Ser	Gly	Leu	Gln	Ser	Glut
65				70					75						80

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

Val Phe Gly Gly Gly Thr Gin Leu Thr Val Leu
100 105

```
<210> SEQ ID NO: 6139
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
```

<400> SEQUENCE: 6139

Gln Ser Val Thr Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Glu Arg Leu Ser Asp Lys Tyr Val
20 25 30

His Trp Tyr Gin Gin Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
35 40 45

50 55 60

65 70 75 80

Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu

```
<210> SEQ_ID NO 6140
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
```

<400> SEQUENCE: 6140

Ser Ser Glu Thr Thr Gln Pro His Ser Val Ser Val Ala Thr Ala Gln

US 12,384,842 B2

1323

1324

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

<210> SEQ ID NO 6141
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6141

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

<210> SEQ ID NO 6142
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6142

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

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Asp Glu Ala Asp Tyr Tyr Cys His Tyr Trp Glu Ser Ile Asn Ser Val
 85 90 95

Val Phe Gly Glu Gly Thr Glu Leu Thr Val Leu
 100 105

<210> SEQ ID NO 6143
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6143

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

Arg Val Thr Ile Ser Cys Ser Gly Glu Asn Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
 35 40 45

Glu Asn Glu Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
 50 55 60

Asn Ser Gly Asn Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu
 65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys His Tyr Trp Glu Ser Ile Asn Ser Val
 85 90 95

Val Phe Gly Glu Gly Thr Glu Leu Thr Val Leu
 100 105

<210> SEQ ID NO 6144
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6144

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Pro Gly Gln
 1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Glu Asn Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Val Met Val Ile Tyr
 35 40 45

Glu Asn Glu 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 Gln Ala Met
 65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys His Tyr Trp Glu Ser Ile Asn Ser Val
 85 90 95

Val Phe Gly Glu Gly Thr Glu Leu Thr Val Leu
 100 105

<210> SEQ ID NO 6145
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

US 12,384,842 B2

1327

1328

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<221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6145

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

<210> SEQ ID NO 6146
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6146

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

<210> SEQ ID NO 6147
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6147

Glu	Tyr	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Val	Ser	Pro	Gly
1									5		10			15	
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Ser	Gly	Glu	Asn	Leu	Ser	Asp	Lys	Tyr
				20				25			30				
Val	His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Met	Leu	Ile

US 12,384,842 B2

1329**1330**

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35	40	45
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Tyr Glu Asn Glu Lys Arg Pro Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

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

Glu Asp Phe Ala Val Tyr Tyr Cys His Tyr Trp Glu Ser Ile Asn Ser
85 90 95

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

<210> SEQ ID NO 6148

<211> LENGTH: 448

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6148

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

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Phe Ser Ile Asn Thr Gly
20 25 30

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

Trp Met Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
50 55 60

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

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

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
100 105 110

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

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

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

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

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

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

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

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

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

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

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

US 12,384,842 B2

1331**1332**

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

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

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

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

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

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

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

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

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

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

<210> SEQ ID NO 6149
 <211> LENGTH: 448
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6149

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

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Phe Ser Ile Asn Thr Gly
 20 25 30

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

Trp Met Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

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

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

Cys Ala Arg Gly Asn Trp His Tyr Phe Asp Phe Trp Gly Gln Gly Thr
 100 105 110

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

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

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

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

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

US 12,384,842 B2

1333

1334

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> SEQ ID NO 6150
 <211> LENGTH: 213
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 6150

Ser Tyr Thr Leu Thr Gln Pro Pro Leu Leu Ser Val Ala Leu Gly His
1 5 10 15

Lys Ala Thr Ile Thr Cys Ser Gly Glu Arg Leu Ser Asp Lys Tyr Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Val Met Val Ile Tyr
35 40 45

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

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

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

Val Phe Gly Ser Gly Thr Gln Leu Thr Val Leu Gly Gln Pro Lys Ala

US 12,384,842 B2

1335**1336**

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

<210> SEQ ID NO 6151
<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6151

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

US 12,384,842 B2

1337**1338**

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

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

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

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

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

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

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

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

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

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

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

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

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

<210> SEQ ID NO 6152
<211> LENGTH: 448
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 6152

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

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Phe Ser Ile Asn Thr Gly
20 25 30

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

Trp Met Gly Tyr Ile Tyr Ser Ser Gly Thr Thr Arg Tyr Asn Pro Ser
50 55 60

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

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

Cys Thr Arg Gly Asn Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

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

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

US 12,384,842 B2

1339**1340**

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
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Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
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Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
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Lys Ala Thr Ile Ile Cys Ser Gly Glu Asn Leu Ser Asp Lys Tyr Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Val Met Val Ile Tyr
35 40 45

Glu Asn Glu Lys Arg Pro Ser Gly Ile Pro Asp Gln Phe Ser Gly Ser

US 12,384,842 B2

1341**1342**

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50 55 60

Asn Ser Gly Asn Ile Ala Thr Leu Thr Ile Ser Lys Ala Gln Pro Gly
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Ser Glu Ala Asp Tyr Tyr Cys His Tyr Trp Glu Ser Ile Asn Ser Val
 85 90 95

Val Phe Gly Ser Gly Thr His Leu Thr Val Leu Gly Gln Pro Lys Ala
 100 105 110

Asn Pro Thr Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala
 115 120 125

Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala
 130 135 140

Val Thr Val Ala Trp Lys Ala Asp Gly Ser Pro Val Lys Ala Gly Val
 145 150 155 160

Glu Thr Thr Lys Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser
 165 170 175

Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser Tyr
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Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala
 195 200 205

Pro Thr Glu Cys Ser
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 Ala Ala Lys' repeating units"

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Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys
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Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala
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US 12,384,842 B2

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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Gly Ile Pro Asp Gln Phe Ser Gly Ser Asn Ser Gly Asn Ile Ala Thr
1 5 10 15Leu Thr Ile Ser Lys Ala Gln Ala Gly Tyr Glu Ala Asp Tyr Tyr Cys
20 25 30

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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Synthetic peptide"

<400> SEQUENCE: 7293

Gln Ser Trp Asp Ser Thr Asn Ser Ala Val
1 5 10

<210> SEQ ID NO 7294

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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Synthetic polypeptide"

<400> SEQUENCE: 7294

US 12,384,842 B2

1545**1546**

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

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<212> TYPE: PRT
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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7295

Gln Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Ser Leu Ser Leu Ser Cys Ser Val Thr Gly Phe Ser Ile Asn Thr Gly
 20 25 30
 Gly Tyr His Trp Asn Trp Ile Arg Gln Phe Pro Gly Lys Lys Val Glu
 35 40 45
 Trp Met Gly Tyr Ile Tyr Ser Ser Gly Thr Thr Lys Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Phe Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr
 85 90 95
 Cys Ala Arg Gly Asp Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110
 Met Val Ala Val Ser Ser
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<210> SEQ ID NO 7296
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<400> SEQUENCE: 7296

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

US 12,384,842 B2

1547**1548**

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Glu	Asn	Asp	Lys	Arg	Pro	Ser	Gly	Ile	Pro	Asp	Gln	Phe	Ser	Gly	Ser
50															
															60

Asn	Ser	Gly	Asn	Ile	Ala	Thr	Leu	Thr	Ile	Ser	Lys	Ala	Gln	Ala	Gly
65															
															80

Tyr	Glu	Ala	Asp	Tyr	Tyr	Cys	His	Cys	Trp	Asp	Ser	Thr	Asn	Ser	Ala
85															95

Val	Phe	Gly	Ser	Gly	Thr	His	Leu	Thr	Val	Leu					
100															105

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Synthetic polypeptide"

<400> SEQUENCE: 7297

Gln	Ile	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
1															
															15

Ser	Leu	Ser	Leu	Thr	Cys	Ser	Val	Thr	Gly	Phe	Ser	Ile	Asn	Thr	Gly
20															30

Gly	Tyr	His	Trp	Asn	Trp	Ile	Arg	Gln	Phe	Pro	Gly	Lys	Lys	Leu	Glu
35															45

Trp	Met	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Ser	Thr	Arg	Tyr	Asn	Pro	Ser
50															60

Leu	Lys	Ser	Arg	Phe	Ser	Ile	Thr	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe
65															80

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

Cys	Thr	Arg	Gly	Asn	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
100															110

Leu	Val	Ala	Val	Ser	Ser										
															115

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1															15

Ser	Leu	Ser	Leu	Ser	Cys	Ser	Val	Thr	Gly	Phe	Ser	Ile	Thr	Thr	Thr
20															30

Gly	Tyr	His	Trp	Asn	Trp	Ile	Arg	Gln	Phe	Pro	Gly	Lys	Lys	Leu	Glu
35															45

Trp	Met	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Ser	Thr	Ser	Tyr	Asn	Pro	Ser
50															60

Leu	Lys	Ser	Arg	Phe	Ser	Ile	Thr	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe
65															80

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

Cys	Ala	Arg	Gly	Asp	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Pro	Gly	Thr
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US 12,384,842 B2

1549**1550**

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Met Val Thr Val Ser Ser
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7299

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

Val Ala Thr Ile Thr Cys Ser Gly Glu Lys Leu Ser Asp Lys Tyr Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Val Met Val Ile Tyr
35 40 45

Glu Asn Asp Arg Arg Pro Ser Gly Ile Pro Asp Gln Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Phe Cys Gln Phe Trp Asp Ser Thr Asn Ser Ala
85 90 95

Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
100 105

<210> SEQ ID NO 7300
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7300

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Thr Thr Thr
20 25 30

Gly Tyr His Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Leu Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Gly Asp Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> SEQ ID NO 7301
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

US 12,384,842 B2

1551**1552**

-continued

<220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7301

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

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Phe	Ser	Ile	Thr	Thr	Thr
								20	25		30				

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

Trp	Val	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Ser	Thr	Ser	Tyr	Asn	Pro	Ser
								50	55		60				

Leu	Lys	Ser	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Thr	Ala	Lys	Asn	Ser	Phe
								65	70		75		80		

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

Cys	Ala	Arg	Gly	Asp	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
								100	105		110				

Met	Val	Thr	Val	Ser	Ser										
								115							

<210> SEQ ID NO 7302
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7302

Glu	Ile	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Ley	Val	Gln	Pro	Gly	Gly	
1															
								5	10		15				

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Phe	Ser	Ile	Thr	Thr	Thr
								20	25		30				

Gly	Tyr	His	Trp	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu
								35	40		45				

Trp	Val	Gly	Tyr	Ile	Tyr	Ser	Ser	Gly	Ser	Thr	Ser	Tyr	Asn	Pro	Ser
								50	55		60				

Leu	Lys	Ser	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Thr	Ser	Lys	Asn	Thr	Phe
								65	70		75		80		

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

Cys	Ala	Arg	Gly	Asp	Trp	His	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr
								100	105		110				

Met	Val	Thr	Val	Ser	Ser										
								115							

<210> SEQ ID NO 7303
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7303

US 12,384,842 B2

1553**1554**

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Glu Ile Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ser Ile Thr Thr Thr
 20 25 30

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35 40 45

Trp Val Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Phe Thr Ile Ser Arg Asp Thr Ala Lys Asn Ser Phe
 65 70 75 80

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

Cys Ala Arg Gly Asp Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser
 115

<210> SEQ ID NO 7304
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7304

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Phe Ser Ile Thr Thr Thr
 20 25 30

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu
 35 40 45

Trp Met Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Phe
 65 70 75 80

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

Cys Ala Arg Gly Asp Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser
 115

<210> SEQ ID NO 7305
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7305

Ser Ser Glu Thr Thr Gln Pro Pro Ser Val Ser Val Pro Gly Gln
 1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Glu Lys Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Val Met Val Ile Tyr

US 12,384,842 B2

1555**1556**

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35 40 45

Glu Asn Asp Arg 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 Gln Ala Met
 65 70 75 80

Asp Glu Ala Asp Tyr Phe Cys Gln Phe Trp Asp Ser Thr Asn Ser Ala
 85 90 95

Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
 100 105

<210> SEQ ID NO 7306
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7306

Ser Ser Glu Thr Thr Gln Pro His Ser Val Ser Val Ala Thr Ala Gln
 1 5 10 15

Met Ala Arg Ile Thr Cys Ser Gly Glu Lys Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Asp Pro Val Met Val Ile Tyr
 35 40 45

Glu Asn Asp Arg Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
 50 55 60

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

Asp Glu Ala Asp Tyr Phe Cys Gln Phe Trp Asp Ser Thr Asn Ser Ala
 85 90 95

Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
 100 105

<210> SEQ ID NO 7307
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7307

Gln Ser Val Thr Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
 1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Glu Lys Leu Ser Asp Lys Tyr Val
 20 25 30

His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Met Leu Ile Tyr
 35 40 45

Glu Asn Asp Arg Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
 50 55 60

Asn Ser Gly Asn Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu
 65 70 75 80

Asp Glu Ala Asp Tyr Phe Cys Gln Phe Trp Asp Ser Thr Asn Ser Ala
 85 90 95

Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu
 100 105

US 12,384,842 B2

1557**1558**

-continued

<210> SEQ ID NO 7308
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7308

Gln	Ser	Val	Thr	Thr	Gln	Pro	Pro	Ser	Val	Ser	Gly	Ala	Pro	Gly	Gln
1					5			10				15			

Arg	Val	Thr	Ile	Ser	Cys	Ser	Gly	Glu	Lys	Leu	Ser	Asp	Lys	Tyr	Val
	20					25					30				

His	Trp	Tyr	Gln	Gln	Leu	Pro	Gly	Thr	Ala	Pro	Lys	Met	Leu	Ile	Tyr
	35					40			45						

Glu	Asn	Asp	Arg	Arg	Pro	Ser	Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser
	50				55			60							

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

Asp	Glu	Ala	Asp	Tyr	Phe	Cys	Gln	Phe	Trp	Asp	Ser	Thr	Asn	Ser	Ala
	85					90				95					

Val	Phe	Gly	Gly	Gly	Thr	Gln	Leu	Thr	Val	Leu					
	100					105									

<210> SEQ ID NO 7309
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7309

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

Gln	Pro	Ala	Ser	Ile	Ser	Cys	Ser	Gly	Glu	Lys	Leu	Ser	Asp	Lys	Tyr
	20					25			30						

Val	His	Trp	Tyr	Gln	Gln	Arg	Pro	Gly	Gln	Ser	Pro	Arg	Met	Leu	Ile
	35					40			45						

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

Ser	Asn	Ser	Gly	Asn	Asp	Ala	Thr	Leu	Lys	Ile	Ser	Arg	Val	Glu	Ala
	65						70		75		80				

Glu	Asp	Val	Gly	Val	Tyr	Phe	Cys	Gln	Phe	Trp	Asp	Ser	Thr	Asn	Ser
	85					90			95						

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

<210> SEQ ID NO 7310
<211> LENGTH: 245
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7310

US 12,384,842 B2

1559**1560**

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Glu Ile Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ser Ile Thr Thr Thr
 20 25 30

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35 40 45

Trp Val Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Phe
 65 70 75 80

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

Cys Ala Arg Gly Asp Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Met Val Thr Val Ser Ser Gly Gly Ser Gly Gly Ser Gly Ser
 115 120 125

Gly Gly Gly Ser Gly Gly Ser Ser Ser Gly Thr Thr Gln
 130 135 140

Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile Thr Cys
 145 150 155 160

Ser Gly Glu Lys Leu Ser Asp Lys Tyr Val His Trp Tyr Gln Gln Lys
 165 170 175

Pro Gly Gln Ser Pro Val Met Val Ile Tyr Glu Asn Asp Arg Arg Pro
 180 185 190

Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala
 195 200 205

Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Phe
 210 215 220

Cys Gln Phe Trp Asp Ser Thr Asn Ser Ala Val Phe Gly Gly Thr
 225 230 235 240

Gln Leu Thr Val Leu
 245

<210> SEQ ID NO 7311
 <211> LENGTH: 246
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <221> NAME/KEY: source
 <223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7311

Glu Ile Gln Leu Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ser Ile Thr Thr Thr
 20 25 30

Gly Tyr His Trp Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35 40 45

Trp Val Gly Tyr Ile Tyr Ser Ser Gly Ser Thr Ser Tyr Asn Pro Ser
 50 55 60

Leu Lys Ser Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Phe
 65 70 75 80

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

Cys Ala Arg Gly Asp Trp His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr

US 12,384,842 B2

1561**1562**

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100	105	110	
Met Val Thr Val Ser Ser Gly	Gly Gly Ser Gly	Gly Ser	
115	120	125	
Gly Gly Gly Ser Gly	Gly Gly Ser Asp	Ser Val Thr Thr Gln	
130	135	140	
Ser Pro Leu Ser Leu Pro Val	Thr Leu Gly Gln	Pro Ala Ser Ile Ser	
145	150	155	160
Cys Ser Gly Glu Lys Leu Ser Asp	Lys Tyr Val His Trp	Tyr Gln Gln	
165	170	175	
Arg Pro Gly Gln Ser Pro Arg Met	Leu Ile Tyr Glu Asn	Asp Arg Arg	
180	185	190	
Pro Ser Gly Val Pro Asp Arg Phe	Ser Gly Ser Asn	Ser Gly Asn Asp	
195	200	205	
Ala Thr Leu Lys Ile Ser Arg Val	Glu Ala Glu Asp Val	Gly Val Tyr	
210	215	220	
Phe Cys Gln Phe Trp Asp Ser Thr Asn Ser Ala Val	Phe Gly Gln	Gly	
225	230	235	240
Thr Lys Val Glu Ile Lys			
245			

<210> SEQ ID NO 7312
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7312
Gln Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15
Ser Leu Ser Leu Ser Cys Ser Val Thr Gly Phe Ser Ile Asn Thr Gly
20 25 30

<210> SEQ ID NO 7313
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7313

Gly Tyr His Trp Asn
1 5

<210> SEQ ID NO 7314
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7314

Trp Ile Arg Gln Phe Pro Gly Lys Lys Val Glu Trp Met Gly
1 5 10

<210> SEQ ID NO 7315

1563**1564**

-continued

<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7315

Gly Asp Trp His Tyr Phe Asp Tyr
1 5

<210> SEQ ID NO 7316
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7316

Trp Gly Gln Gly Thr Met Val Ala Val Ser Ser
1 5 10

<210> SEQ ID NO 7317
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7317

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

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Phe Ser Ile Asn Thr Gly
20 25 30

<210> SEQ ID NO 7318
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7318

Tyr Ile Tyr Ser Ser Gly Ser Thr Arg Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> SEQ ID NO 7319
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7319

Arg Phe Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln
1 5 10 15

Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Thr Arg
20 25 30

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<210> SEQ ID NO 7320
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7320

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

Lys Ala Thr Ile Ile Cys
20

<210> SEQ ID NO 7321
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7321

His	Cys	Trp	Asp	Ser	Thr	Asn	Ser	Ala	Val
1				5					10

<210> SEQ ID NO 7322
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7322

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

Ser Leu Ser Leu Ser Cys Ser Val Thr Gly Phe Ser Ile Thr Thr Thr
20 25 30

<210> SEQ ID NO 7323
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7323

Arg	Phe	Ser	Ile	Thr	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Phe	Leu	Gln
1				5				10				15			

Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

<210> SEQ ID NO 7324
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

US 12,384,842 B2

1567**1568**

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<400> SEQUENCE: 7324

```
Trp Gly Pro Gly Thr Met Val Thr Val Ser Ser
1           5           10
```

```
<210> SEQ ID NO 7325
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

<400> SEQUENCE: 7325

```
Ser Phe Thr Leu Thr Gln Pro Pro Leu Val Ser Val Ala Val Gly Gln
1           5           10           15
```

```
Val Ala Thr Ile Thr Cys
20
```

```
<210> SEQ ID NO 7326
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

<400> SEQUENCE: 7326

```
Ser Gly Glu Lys Leu Ser Asp Lys Tyr Val His
1           5           10
```

```
<210> SEQ ID NO 7327
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
```

<400> SEQUENCE: 7327

```
Glu Asn Asp Arg Arg Pro Ser
1           5
```

```
<210> SEQ ID NO 7328
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
```

<400> SEQUENCE: 7328

```
Gly Ile Pro Asp Gln Phe Ser Gly Ser Asn Ser Gly Asn Ile Ala Ser
1           5           10           15
```

```
Leu Thr Ile Ser Lys Ala Gln Ala Gly Asp Glu Ala Asp Tyr Phe Cys
20          25          30
```

```
<210> SEQ ID NO 7329
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
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1569**1570**

-continued

Synthetic peptide"

<400> SEQUENCE: 7329

Gln	Phe	Trp	Asp	Ser	Thr	Asn	Ser	Ala	Val
1				5				10	

<210> SEQ ID NO 7330
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7330

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

Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Ile	Thr	Thr	Thr
				20			25					30			

<210> SEQ ID NO 7331
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7331

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

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Phe	Ser	Ile	Thr	Thr	Thr
			20				25					30			

<210> SEQ ID NO 7332
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7332

Glu	Ile	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1					5			10				15			

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Phe	Ser	Ile	Thr	Thr	Thr
			20				25					30			

<210> SEQ ID NO 7333
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7333

Glu	Ile	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1					5			10				15			

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Phe	Ser	Ile	Thr	Thr	Thr
			20				25					30			

1571

1572

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<210> SEQ ID NO 7334
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
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Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Val Ser Gly Phe Ser Ile Thr Thr Thr
20 25 30

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<210> SEQ ID NO 7335
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"
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<400> SEQUENCE: 7335

Ser Ser Glu Thr Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
 1 5 10 15

Thr Ala Ser Ile Thr Cys
20

```
<210> SEQ ID NO 7336
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
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<400> SEQUENCE: 7336

Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Phe Cys
20 25 30

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<210> SEQ ID NO 7337
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"
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<400> SEQUENCE: 7337

Leu Thr Ile Ser Arg Ile Glu Ala Gly Asp Glu Ala Asp Tyr Phe Cys
20 25 30

```
<210> SEQ ID NO 7338
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
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US 12,384,842 B2

1573**1574**

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7338

Gly Val Pro Asp Arg Phe Ser Gly Ser Asn Ser Gly Asn Ser Ala Ser			
1	5	10	15
Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Phe Cys			
20	25	30	

<210> SEQ ID NO 7339

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7339

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

<210> SEQ ID NO 7340

<211> LENGTH: 23

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7340

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

Gln Pro Ala Ser Ile Ser Cys		
20		

<210> SEQ ID NO 7341

<211> LENGTH: 15

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 7341

Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro Arg Met Leu Ile Tyr			
1	5	10	15

<210> SEQ ID NO 7342

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7342

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

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<210> SEQ ID NO 7343

<400> SEQUENCE: 7343

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<210> SEQ ID NO 7344

<400> SEQUENCE: 7344

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<210> SEQ ID NO 7345

<400> SEQUENCE: 7345

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<210> SEQ ID NO 7346

<400> SEQUENCE: 7346

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<210> SEQ ID NO 7347

<400> SEQUENCE: 7347

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<210> SEQ ID NO 7348

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<210> SEQ ID NO 7349

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<210> SEQ ID NO 7350

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<210> SEQ ID NO 7351

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<210> SEQ ID NO 7352

<400> SEQUENCE: 7352

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<210> SEQ ID NO 7353

<400> SEQUENCE: 7353

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<210> SEQ ID NO 7354

<400> SEQUENCE: 7354

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<210> SEQ ID NO 7355

<400> SEQUENCE: 7355

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<210> SEQ ID NO 7356

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<210> SEQ ID NO 7357

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<210> SEQ ID NO 7359

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<210> SEQ ID NO 7360

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<210> SEQ ID NO 7361

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<210> SEQ ID NO 7362

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<210> SEQ ID NO 7363

<400> SEQUENCE: 7363

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<210> SEQ ID NO 7364

<400> SEQUENCE: 7364

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<210> SEQ ID NO 7365

US 12,384,842 B2

1579**1580**

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<400> SEQUENCE: 7365

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<210> SEQ ID NO 7366

<400> SEQUENCE: 7366

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<210> SEQ ID NO 7367

<400> SEQUENCE: 7367

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<210> SEQ ID NO 7368

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<210> SEQ ID NO 7369

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<210> SEQ ID NO 7370

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<210> SEQ ID NO 7371

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7371

Gln Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn Thr Gly
20 25 30

<210> SEQ ID NO 7372

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7372

Gln Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Ile Asn Thr Gly
20 25 30

<210> SEQ ID NO 7373

<211> LENGTH: 32

<212> TYPE: PRT

US 12,384,842 B2

1581**1582**

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7373

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

<210> SEQ ID NO 7374
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7374

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

<210> SEQ ID NO 7375
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7375

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

<210> SEQ ID NO 7376
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7376

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

<210> SEQ ID NO 7377
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 7377

US 12,384,842 B2

1583**1584**

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

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

<210> SEQ ID NO 7378
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic polypeptide"

<400> SEQUENCE: 7378

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

Thr Val Lys Ile Ser Cys Lys Val Ser Gly Phe Ser Ile Asn Thr Gly
 20 25 30

<210> SEQ ID NO 7379

<400> SEQUENCE: 7379

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<210> SEQ ID NO 7380

<400> SEQUENCE: 7380

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<210> SEQ ID NO 7381

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<210> SEQ ID NO 7383

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<210> SEQ ID NO 7384

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<210> SEQ ID NO 7385

<211> LENGTH: 16

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<221> NAME/KEY: source

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
 Synthetic peptide"

<400> SEQUENCE: 7385

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Tyr	Ile	Tyr	Ser	Ser	Gly	Thr	Thr	Lys	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1															
														10	
															15

What is claimed is:

1. An antibody or an antigen-binding portion thereof that binds to NKp30 comprising:

- (a) a heavy chain variable region (VH) comprising
 - (i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313,
 - (ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and
 - (iii) a VHCDR3 amino acid sequence of SEQ ID NO: 7315; and
- (b) a light chain variable region (VL) comprising
 - (i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326,
 - (ii) a VLCDR2 amino acid sequence of SEQ ID NO: 7327, and
 - (iii) a VLCDR3 amino acid sequence of SEQ ID NO: 7329.

2. The antibody or an antigen-binding portion thereof of claim 1, wherein

- (a) the VH comprises an amino acid sequence with at least 75% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 7298 and 7300-7304; and
- (b) the VL comprises an amino acid sequence with at least 75% sequence identity to a sequence selected from the group consisting of SEQ ID NOS: 7299 and 7305-7309.

3. The antibody or an antigen-binding portion thereof of claim 2, wherein

- (a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7302; and
- (b) the VL comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7305.

4. The antibody or an antigen-binding portion thereof of claim 2, wherein

- (a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7302; and
- (b) the VL comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NOS: 7305 or SEQ ID NO: 7309.

5. The antibody or antigen-binding portion thereof of claim 4, wherein

- (a) the VH comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 7302; and
- (b) the VL comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 7305 or SEQ ID NO: 7309.

6. The antibody or antigen-binding portion thereof of claim 5, wherein

- (a) the VH comprises the amino acid sequence of SEQ ID No: 7302; and
- (b) the VL comprises the amino acid sequence of SEQ ID No: 7305.

7. The antibody or antigen-binding portion thereof of claim 5, wherein

- (a) the VH comprises the amino acid sequence of SEQ ID No: 7302; and
- (b) the VL comprises the amino acid sequence of SEQ ID No: 7309.

8. The antibody or an antigen-binding portion thereof of claim 2, wherein the antibody or an antigen-binding portion thereof comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7310 or SEQ ID NO: 7311.

9. A multispecific molecule comprising the antibody or an antigen-binding portion thereof of claim 2.

10. The multispecific molecule of claim 9, wherein the multispecific molecule further comprises

- (a) a tumor targeting moiety;
- (b) a cytokine molecule;
- (c) a T cell engager;
- (d) a stromal modifying moiety; or
- (e) any combination thereof.

11. The multispecific molecule of claim 9, wherein the multispecific molecule further comprises

- (a) a T cell engager that binds to an antigen present on the surface of an autoreactive T cell that is associated with an inflammatory or autoimmune disorder, or
- (b) a binding moiety that binds to an antigen present on the surface of a cell infected by a virus or a bacteria.

12. The multispecific molecule of claim 10, wherein the multispecific molecule comprises a linker between one or more of:

- (a) the targeting moiety and the cytokine molecule or the stromal modifying moiety,
- (b) the targeting moiety and the immune cell engager,
- (c) the cytokine molecule or the stromal modifying moiety,
- (d) the immune cell engager, the cytokine molecule or the stromal modifying moiety and the immunoglobulin chain constant region,
- (e) the targeting moiety and the immunoglobulin chain constant region, and
- (f) the immune cell engager and the immunoglobulin chain constant region.

13. The antibody or the antigen-binding portion thereof of claim 1, wherein the antibody or the antigen-binding portion thereof comprises an immunoglobulin chain constant region.

14. The antibody or the antigen-binding portion thereof of claim 13, wherein the immunoglobulin chain constant region is an IgG1 chain constant region that comprises an amino acid substitution at a position selected from the group consisting of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, 409, and any combination thereof.

15. The antibody or the antigen-binding portion thereof of claim 14, wherein the IgG1 chain constant region comprises an amino acid substitution at a position selected from the group consisting of T366S, L368A, Y407V, T366W, and any combination thereof.

16. A polynucleotide comprising a sequence encoding the antibody or an antigen-binding portion thereof of claim 2.

17. A host cell comprising the polynucleotide of claim 16.

18. An expression vector comprising a polynucleotide sequence encoding the antibody or an antigen-binding portion thereof of claim 2.

19. A host cell comprising the expression vector of claim 18.

20. A method of making the antibody or an antigen-binding portion thereof of claim 2, comprising culturing the

1587

host cell of claim 17 under suitable conditions for gene expression and/or homo- or heterodimerization.

21. A pharmaceutical composition comprising the antibody or an antigen-binding portion thereof of claim 2; and a pharmaceutically acceptable carrier, excipient, or stabilizer. 5

22. A method of treating a disease or condition, wherein the disease or condition is cancer, an autoimmune or inflammatory disorder, an infectious disorder, or a hyperproliferative disorder, comprising administering to a subject in need 10 thereof the antibody or an antigen-binding portion thereof of claim 2, wherein the antibody or antigen-binding portion thereof is administered in an amount effective to treat the disease or condition.

23. The method of claim 22, wherein the disease or 15 condition is cancer, an autoimmune or inflammatory disorder, or an infectious disorder.

1588

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