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(54) Title: ENTPD2 ANTIBODIES, COMBINATION THERAPIES, AND METHODS OF USING THE ANTIBODIES AND COMBINATION THERAPIES

(57) Abstract: Provided herein are antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to ENTPD2 (e.g., human ENTPD2 protein), and methods of using these antibodies or antigen-binding fragments. The present invention also relates to combination therapies comprising an anti-human ENTPD2 antibody or antigen binding fragment and at least one additional therapeutic agent, and methods of using these combination therapies.

FIG. 1A

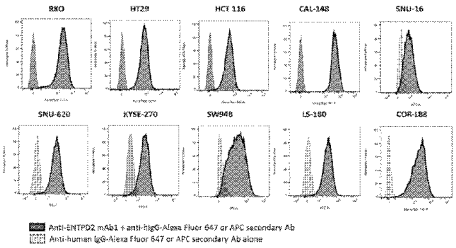

FIG. 1B

Table 20: ENTPD2 expression density across representative cancer cell lines

Cell Line	Source	Indication	Receptor Density
CAL-148	DSMZ (Germany)	Breast Adenocarcinoma	111,726
COR-L88	ECACC (UK)	Small Cell Lung Cancer	90,000
RKO	ATCC (Manassas, VA)	Colorectal Cancer	51,203
LS-180	ATCC (Manassas, VA)	Colorectal Cancer	44,708
SW948	ATCC (Manassas, VA)	Colorectal Cancer	41,576
HT29	ATCC (Manassas, VA)	Colorectal Cancer	28,337
KYSE-270	DSMZ (Germany)	Esophageal Cancer	28,273
SNU-620	KCLB (South Korea)	Stomach Adenocarcinoma	19,646
HCT 116	ATCC (Manassas, VA)	Colorectal Cancer	18,697
SNU-16	ATCC (Manassas, VA)	Gastric Carcinoma	12,763

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[Continued on next page]

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ENTPD2 ANTIBODIES, COMBINATION THERAPIES, AND METHODS OF USING THE ANTIBODIES AND COMBINATION THERAPIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/677,850 filed May 30, 2018, the content of which are hereby incorporated by reference in its entirety.

TECHNICAL FIELD

[0002] The present invention provides antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to the ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2) and methods of using these antibodies or antigen-binding fragments.

[0003] The present invention also relates to combination therapies comprising an anti-human ENTPD2 antibody or antigen-binding fragment thereof and at least one additional therapeutic agent.

SEQUENCE LISTING

[0004] 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 April 5, 2019, is named PAT058145-WO-PCT_SL.txt and is 635,873 bytes in size.

BACKGROUND

[0005] Cellular stress and apoptosis trigger the release of ATP into the extracellular space. Increased ATP concentration promotes rapid inflammation, resulting in amplification of T-cell signaling, inhibiting regulatory T cells (Tregs), and promoting inflammasome activation in dendritic cells and macrophages. The ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2) is part of the family of ecto-nucleosidases that hydrolyze 5'-triphosphates and is an integral membrane protein, which participates in purinergic signaling. ENTPD2 catalyzes the conversion of adenosine triphosphate (ATP) to adenosine diphosphate (ADP) and adenosine monophosphate (AMP). In turn, AMP is catalyzed by Cluster of Differentiation 73 (CD73), also known as ecto-5'-nucleotidase (ecto-5'NT), to adenosine. The molecule AMP interacts with several receptors, including the Adenosine A1, A2A, A2B, and A3 receptors. The A2A receptor has received particular attention due to its

broad expression on immune cells. AMP has pleiotropic effects in the tumor microenvironment, including expansion of regulatory T cells (Tregs), inhibition of effector T cell (Teff) responses mediated by interferon (IFN)-γ, and expansion of myeloid derived suppressor cells (MDSCs). See, e.g., Allard B, et al., Curr Opin Pharmacol 29:7-16 (2016) and Allard D, et al., Immunotherapy 8:145-163 (2016).

[0006] In a mouse model of hepatocellular carcinoma it was shown that ENTPD2 converts extracellular ATP to AMP which prevents the differentiation of monocytic myeloid derived suppressor cells (MDSCs) to dendritic cells, therefore promoting the maintenance of MDSCs in vitro and *in vivo* (Chiu et al., Nat Commun. 8:517-28 (2017).

[0007] ENTPD2 is expressed on cancer cells as described herein. New compositions and methods for regulating ENTPD2 activity and related therapeutic agents are highly desirable.

SUMMARY OF THE INVENTION

[0008] Provided herein are antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen-binding fragments thereof, that specifically bind to the ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2). The ENTPD2 antibodies or antigen-binding fragments thereof are useful for treating ENTPD2-associated diseases, such as cancer.

[0009] In one aspect, provided herein are antibodies or antigen-binding fragments thereof that specifically bind to human ENTPD2 protein, wherein the antibody or antigen binding fragment thereof comprises a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2), a heavy chain complementarity determining region 3 (HCDR3), a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2), and a light chain complementarity determining region 3 (LCDR3) of any antibody or antigen binding fragment provided in Table 1. In some embodiments, the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of such antibodies or antigen binding fragments are selected from the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences provided in Table 1. In some embodiments, such antibodies or antigen binding fragments comprise a heavy chain variable region (VH) provided in Table 1. In some embodiments, such antibodies or antigen binding fragments comprise a light chain variable region (VL) provided in Table 1.

[0010] In another aspect, provided herein are antibodies or antigen binding fragments selected from any one of the following:

1) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 2,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 14,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 16;

2) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 5,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;

3) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 8,
an HCDR3 sequence comprising SEQ ID NO: 9,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 16;

4) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 50,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

5) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 53,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

6) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 45,
an LCDR1 sequence comprising SEQ ID NO: 56,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

7) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

8) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

9) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 45,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

10) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 50,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

11) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 53,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

12) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 69,
an LCDR1 sequence comprising SEQ ID NO: 56,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

13) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 82,
an HCDR2 sequence comprising SEQ ID NO: 83,

an HCDR3 sequence comprising SEQ ID NO: 84,
an LCDR1 sequence comprising SEQ ID NO: 95,
an LCDR2 sequence comprising SEQ ID NO: 96, and
an LCDR3 sequence comprising SEQ ID NO: 97;

14) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 85,
an HCDR2 sequence comprising SEQ ID NO: 86,
an HCDR3 sequence comprising SEQ ID NO: 84,
an LCDR1 sequence comprising SEQ ID NO: 98,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 100;

15) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 88,
an HCDR2 sequence comprising SEQ ID NO: 89,
an HCDR3 sequence comprising SEQ ID NO: 90,
an LCDR1 sequence comprising SEQ ID NO: 101,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 97;

16) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 106,
an HCDR2 sequence comprising SEQ ID NO: 107,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 119,
an LCDR2 sequence comprising SEQ ID NO: 120, and
an LCDR3 sequence comprising SEQ ID NO: 121;

17) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 109,
an HCDR2 sequence comprising SEQ ID NO: 110,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 122,

an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 123;

18) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 112,
an HCDR2 sequence comprising SEQ ID NO: 113,
an HCDR3 sequence comprising SEQ ID NO: 114,
an LCDR1 sequence comprising SEQ ID NO: 124,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 121;

19) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 106,
an HCDR2 sequence comprising SEQ ID NO: 129,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 119,
an LCDR2 sequence comprising SEQ ID NO: 120, and
an LCDR3 sequence comprising SEQ ID NO: 121;

20) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 109,
an HCDR2 sequence comprising SEQ ID NO: 130,
an HCDR3 sequence comprising SEQ ID NO: 108
an LCDR1 sequence comprising SEQ ID NO: 122,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 123;

21) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 112,
an HCDR2 sequence comprising SEQ ID NO: 131,
an HCDR3 sequence comprising SEQ ID NO: 114,
an LCDR1 sequence comprising SEQ ID NO: 124,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 121;

22) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 136,
an HCDR2 sequence comprising SEQ ID NO: 137,
an HCDR3 sequence comprising SEQ ID NO: 138,
an LCDR1 sequence comprising SEQ ID NO: 149,
an LCDR2 sequence comprising SEQ ID NO: 150, and
an LCDR3 sequence comprising SEQ ID NO: 151;

23) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 139,
an HCDR2 sequence comprising SEQ ID NO: 140,
an HCDR3 sequence comprising SEQ ID NO: 138,
an LCDR1 sequence comprising SEQ ID NO: 152,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 154;

24) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 142,
an HCDR2 sequence comprising SEQ ID NO: 143,
an HCDR3 sequence comprising SEQ ID NO: 144,
an LCDR1 sequence comprising SEQ ID NO: 155,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 151;

25) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 160,
an HCDR2 sequence comprising SEQ ID NO: 161,
an HCDR3 sequence comprising SEQ ID NO: 162,
an LCDR1 sequence comprising SEQ ID NO: 173,
an LCDR2 sequence comprising SEQ ID NO: 150, and
an LCDR3 sequence comprising SEQ ID NO: 174;

26) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 163,
an HCDR2 sequence comprising SEQ ID NO: 164,
an HCDR3 sequence comprising SEQ ID NO: 162,
an LCDR1 sequence comprising SEQ ID NO: 175,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 176;

27) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 166,
an HCDR2 sequence comprising SEQ ID NO: 167,
an HCDR3 sequence comprising SEQ ID NO: 168,
an LCDR1 sequence comprising SEQ ID NO: 177,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 174;

28) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 220,
an HCDR3 sequence comprising SEQ ID NO: 221,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

29) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 222,
an HCDR3 sequence comprising SEQ ID NO: 221,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

30) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 223,

an HCDR3 sequence comprising SEQ ID NO: 224,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

31) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 220,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

32) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 222,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

33) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 223,
an HCDR3 sequence comprising SEQ ID NO: 69,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

34) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 245,
an HCDR3 sequence comprising SEQ ID NO: 246,
an LCDR1 sequence comprising SEQ ID NO: 254,

an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 255;

35) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 247,
an HCDR3 sequence comprising SEQ ID NO: 246,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 256;

36) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 248,
an HCDR3 sequence comprising SEQ ID NO: 249,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 255;

37) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 261,
an HCDR3 sequence comprising SEQ ID NO: 262,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 16;

38) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 247,
an HCDR3 sequence comprising SEQ ID NO: 262,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;

39) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 248,
an HCDR3 sequence comprising SEQ ID NO: 263,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 16;

40) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 272,
an HCDR2 sequence comprising SEQ ID NO: 273,
an HCDR3 sequence comprising SEQ ID NO: 274,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 285, and
an LCDR3 sequence comprising SEQ ID NO: 16;

41) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 275,
an HCDR2 sequence comprising SEQ ID NO: 276,
an HCDR3 sequence comprising SEQ ID NO: 274,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 286, and
an LCDR3 sequence comprising SEQ ID NO: 19;

42) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 278,
an HCDR2 sequence comprising SEQ ID NO: 279,
an HCDR3 sequence comprising SEQ ID NO: 280,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 286, and
an LCDR3 sequence comprising SEQ ID NO: 16.

[0011] In another aspect, provided herein are antibodies or antigen binding fragments selected from any one of the following:

1) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 10 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 21 or a sequence at least about 95% or more identical thereto;

2) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

3) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 33 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

4) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 46 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 57 or a sequence at least about 95% or more identical thereto;

5) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 46 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 64 or a sequence at least about 95% or more identical thereto;

6) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 70 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 74 or a sequence at least about 95% or more identical thereto;

7) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 78 or a sequence at least about 95% or more identical thereto;

8) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 91 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 102 or a sequence at least about 95% or more identical thereto;

9) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 115 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 125 or a sequence at least about 95% or more identical thereto;

10) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 132 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 125 or a sequence at least about 95% or more identical thereto;

11) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 145 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 156 or a sequence at least about 95% or more identical thereto;

12) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 169 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 178 or a sequence at least about 95% or more identical thereto;

13) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 225 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 229 or a sequence at least about 95% or more identical thereto;

14) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 233 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 237 or a sequence at least about 95% or more identical thereto;

15) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 241 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 229 or a sequence at least about 95% or more identical thereto;

16) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 250 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 257 or a sequence at least about 95% or more identical thereto;

17) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 264 or a sequence at least about 95% or more

identical thereto, and a VL comprising SEQ ID NO: 268 or a sequence at least about 95% or more identical thereto; or

18) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 281 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 287 or a sequence at least about 95% or more identical thereto.

[0012] In another aspect, provided herein are antibodies or antigen binding fragments selected from any one of the following:

1) an antibody comprising a heavy chain comprising SEQ ID NO: 12 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 23 or a sequence at least about 95% or more identical thereto;

2) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;

3) an antibody comprising a heavy chain comprising SEQ ID NO: 35 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;

4) an antibody comprising a heavy chain comprising SEQ ID NO: 48 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 59 or a sequence at least about 95% or more identical thereto;

5) an antibody comprising a heavy chain comprising SEQ ID NO: 48 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 66 or a sequence at least about 95% or more identical thereto;

6) an antibody comprising a heavy chain comprising SEQ ID NO: 72 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 76 or a sequence at least about 95% or more identical thereto;

7) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 80 or a sequence at least about 95% or more identical thereto;

8) an antibody comprising a heavy chain comprising SEQ ID NO: 93 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 104 or a sequence at least about 95% or more identical thereto;

9) an antibody comprising a heavy chain comprising SEQ ID NO: 117 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 127 or a sequence at least about 95% or more identical thereto;

10) an antibody comprising a heavy chain comprising SEQ ID NO: 134 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 127 or a sequence at least about 95% or more identical thereto;

11) an antibody comprising a heavy chain comprising SEQ ID NO: 147 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 158 or a sequence at least about 95% or more identical thereto;

12) an antibody comprising a heavy chain comprising SEQ ID NO: 171 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 180 or a sequence at least about 95% or more identical thereto;

13) an antibody comprising a heavy chain comprising SEQ ID NO: 227 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto;

14) an antibody comprising a heavy chain comprising SEQ ID NO: 235 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 239 or a sequence at least about 95% or more identical thereto;

15) an antibody comprising a heavy chain comprising SEQ ID NO: 243 or a sequence at least about 95% or more identical thereto, and a light chain

comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto;

16) an antibody comprising a heavy chain comprising SEQ ID NO: 252 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 259 or a sequence at least about 95% or more identical thereto;

17) an antibody comprising a heavy chain comprising SEQ ID NO: 266 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 270 or a sequence at least about 95% or more identical thereto; or

18) an antibody comprising a heavy chain comprising SEQ ID NO: 283 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 289 or a sequence at least about 95% or more identical thereto.

[0013] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: His50, Asp76, Pro78, Gly79, Gly80, Tyr85, Asp87, Asn88, Gly91, Gln94, Ser95, Gly98, Glu101, Gln102, Gln105, Asp106, Arg245, Thr272, Gln273, Leu275, Asp278, Arg298, Ala347, Ala350, Thr351, Arg392, Ala393, Arg394, or Tyr398.

[0014] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: Gly79, Gln250, Leu253, Trp266, Arg268, Gly269, Phe270, Ser271, Thr272, Gln273, Val274, Leu275, Asp278, Arg298, Ser300, Ser302, Gly303, Thr380, Trp381, Ala382, Gly390, Gln391, Arg392, Ala393, Arg394, or Asp397.

[0015] In some embodiments, the antibodies or antigen binding fragments thereof described herein have an IgG1, IgG2, IgG3 or IgG4 isotype. In some embodiments, the antibodies or antigen binding fragments thereof described herein have an IgG1 isotype. In some embodiments, the antibodies or antigen binding fragments thereof described herein

comprise an Fc region selected from an IgG1 Fc region, an IgG2 Fc region, an IgG4 Fc region, or an IgG2/IgG4 hybrid Fc region. . In some embodiments, the antibodies or antigen binding fragments thereof described herein comprise an Fc region selected from an IgG1 Fc region. In some embodiments, the antibodies or antigen binding fragments thereof described herein comprise a modified Fc region. In some embodiments, the antibodies or antigen binding fragments thereof described herein comprise a modified Fc region having reduced antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) activity compared to the parent antibody.

[0016] In another aspect, provided herein are antibodies or antigen binding fragments thereof that compete with any antibody or antigen binding fragment provided in Table 1 for binding to human ENTPD2 protein.

[0017] In another aspect, provided herein are antibodies or antigen binding fragments thereof that bind essentially the same ENTPD2 epitope as any antibody or antigen binding fragment provided in Table 1.

[0018] In some embodiments, the antibodies or antigen binding fragments thereof described herein bind to human ENTPD2 protein with a dissociation constant (KD) of less than 10nM, e.g., with a KD of less than 5nM, or with a KD of less than 3nM, e.g., as measured by Biacore. In some embodiments, the dissociation constant of the antibodies or antigen binding fragments thereof described herein to human ENTPD2 is measured by Biacore at 25 °C.

[0019] In some embodiments, the antibodies or antigen binding fragments thereof described herein inhibit human ENTPD2 enzymatic activity by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In some embodiments, the enzymatic activity of human ENTPD2 is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0020] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein inhibit ENTPD2's ability of hydrolysis of adenosine triphosphate (ATP). In some embodiments, ENTPD2's ability of hydrolysis of ATP is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0021] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein interfere with ATP binding to ENTPD2 or trap ATP within the catalytic domain of ENTPD2. In some embodiments, ENTPD2's ability of

hydrolysis of ATP is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0022] In some embodiments, the antibodies or antigen binding fragments thereof described herein are human or humanized antibodies or fragments thereof.

[0023] In another aspect, provided herein are nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein. Such nucleic acids can encode polypeptides comprising segments or domains of the ENTPD2 antibodies or antigen binding fragments thereof described herein.

[0024] Also provided are vectors comprising such nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein. In some embodiments, the vector is selected from a DNA vector, a RNA vector, a plasmid, a cosmid, or a viral vector. In some embodiments, the vector is a viral vector based on any one of the following viruses: lentivirus, adenovirus, adeno-associated virus (AAV), Herpes Simplex Virus (HSV), parvovirus, retrovirus, vaccinia virus, Sinbis virus, influenza virus, reovirus, Newcastle disease virus (NDV), measles virus, vesicular stomatitis virus (VSV), poliovirus, poxvirus, Seneca Valley virus, coxsackievirus, enterovirus, myxoma virus, or maraba virus. In some embodiments, the vector is an AAV vector. In some embodiments, the vector is a lentiviral vector. In some embodiments, the vector further comprises a promoter, e.g., a tissue-specific promoter. In some embodiments, the vector further comprises a detectable marker.

[0025] Also provided herein are cells comprising a nucleic acid or set of nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein or a vector comprising such a nucleic acid or set of nucleic acids.

[0026] In another aspect, provided herein are pharmaceutical compositions comprising an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein, a nucleic acid encoding such an antibody or antigen binding fragment, a vector comprising such a nucleic acid or set of nucleic acids, or a cell comprising a nucleic acid or sets of nucleic acids or vector described herein, and a pharmaceutically acceptable carrier.

[0027] In another aspect, provided herein are methods of producing an anti-human ENTPD2 antibody or antigen binding fragment thereof by culturing a cell comprising a nucleic acid or sets of nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof or a vector comprising such a nucleic acid or sets of nucleic acids, and collecting the antibody or antigen binding fragment thereof from the culture medium.

[0028] In another aspect, provided herein are methods of treating a cancer in a subject in need thereof by administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody or antigen binding fragment described herein, a nucleic acid or sets of nucleic acids encoding such an antibody or antigen binding fragment, a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, a cell comprising such a nucleic acid or sets of nucleic acids or vector, or a pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid or sets of nucleic acids, vector or cell. In some embodiments, the antibody or antigen binding fragment thereof, the nucleic acid or sets of nucleic acids, the vector, the cell, or the pharmaceutical composition, is administered to the subject through an intravenous, intratumoralor subcutaneous route.

[0029] In another aspect, provided herein are methods of stimulating an immune response in a subject by administering to the subject an anti-human ENTPD2 antibody or antigen binding fragment described herein, a nucleic acid or sets of nucleic acids encoding such an antibody or antigen binding fragment, a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, a cell comprising such a nucleic acid or sets of nucleic acids or vector, or a pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid or sets of nucleic acids, vector or cell, in an amount effective to stimulate the immune response.

[0030] In some embodiments, such methods can further include administration of at least one additional therapeutic agent to the subject.

[0031] In some embodiments, such methods can further include administration of at least two additional therapeutic agents to the subject.

[0032] In another aspect, provided herein is an antibody or antigen binding fragment thereof described herein, the nucleic acid or set of nucleic acids encoding such an antibody or antigen binding fragment thereof, a vector or a cell comprising such a nucleic acid or set of nucleic acids, or a pharmaceutical composition comprising such an antibody or antigen binding fragment thereof, nucleic acid or set of nucleic acids, vector, or cell, for use as a medicament.

[0033] In another aspect, provided herein is an antibody or antigen binding fragment thereof described herein, the nucleic acid encoding such an antibody or antigen binding fragment thereof, a vector or a cell comprising such a nucleic acid or set of nucleic acids, or a pharmaceutical composition comprising such an antibody or antigen binding fragment thereof, nucleic acid or set of nucleic acids, vector, or cell, for use in treatment of a cancer.

[0034] In another aspect, provided herein is a pharmaceutical composition comprising an antibody or antigen binding fragment thereof described herein, and at least one additional therapeutic agent or procedure.

[0035] In some embodiments, the at least one additional therapeutic agent or procedure is selected from one or more of chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a cell therapy.

[0036] In some embodiments, the at least one additional therapeutic agent is a PD-1 inhibitor, e.g., a PD-1 antibody. In some embodiments, the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

[0037] In some embodiments, the at least one additional therapeutic agent is a PD-L1 inhibitor, e.g., a PD-L1 antibody. In some embodiments, the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

[0038] In some embodiments, the at least one additional therapeutic agent is an A2AR antagonist. In some embodiments, the A2AR antagonist is selected from:

i. an anti-CD73 antibody molecule, or antigen-binding fragment thereof, optionally wherein the anti-CD73 antibody is selected from:

a. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 295 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 296, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 295 or 296.;

b. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 299 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 300, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 299 or 300;

c. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 302 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 303, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 302 or 303;

d. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 304 and a light chain

variable region comprising the amino acid sequence of SEQ ID NO: 305, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 304 or 305;

e. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 306 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 307, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 306 or 307; or

f. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 308 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 309, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 308 or 309; or

ii. PBF509/NIR178, CPI444/V81444, AZD4635/HTL-1071, Vipadenant, GBV-2034, AB928, Theophylline, Istradefylline, Tozadenant/SYN-115, KW-6356, ST-4206, and Preladenant/SCH 420814; or

iii. 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine, or a pharmaceutically acceptable salt thereof; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof, or a pharmaceutically acceptable salt thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine, or a pharmaceutically acceptable salt thereof.

[0039] In some embodiments, the at least one additional therapeutic agent is selected from:

i. a CTLA-4 inhibitor, optionally wherein the CTLA-4 inhibitor is selected from Ipilimumab or Tremelimumab;

ii. a TIM-3 inhibitor, optionally wherein the TIM-3 inhibitor is selected from MBG453, TSR-022, or LY3321367;

iii. a LAG-3 inhibitor, optionally wherein the LAG-3 inhibitor is selected from LAG525, BMS-986016, TSR-033, MK-4280 or REGN3767;

iv. a GITR agonist, optionally wherein the GITR agonist is selected from GWN323, BMS-986156, MK-4166, MK-1248, TRX518, INCAGN1876, AMG 228, or INBRX-110;

v. an anti-CD3 multispecific antibody molecule, optionally wherein the anti-CD3 multispecific antibody molecule is an anti-CD3 x anti-CD123 bispecific antibody molecule (e.g., XENP14045), or an anti-CD3 x anti-CD20 bispecific antibody molecule (e.g., XENP13676);

vi. a cytokine molecule, optionally wherein the cytokine molecule is IL-15 complexed with a soluble form of IL-15 receptor alpha (IL-15Ra);

vii. a macrophage colony-stimulating factor (M-CSF) inhibitor, optionally wherein the M-CSF inhibitor is MCS110;

viii. a CSF-1R inhibitor, optionally wherein the CSF-1R inhibitor is BLZ945;

ix. an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO);

x. a TGF-β inhibitor;

xi. an oncolytic virus;

xii. a chimeric antigen receptor (CAR) T-cell therapy.

[0040] In some embodiments, the at least one additional therapeutic agent is selected from: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (e.g., a CYP17 inhibitor or a 17alpha-Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, e.g., an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 (e.g., FLK2/STK1) or PKC; 18) an inhibitor of one or more of VEGFR-2 (e.g., FLK-1/KDR), PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an

inhibitor of CYP11B2; 27) a HDM2 inhibitor, e.g., an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11β-hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, e.g., BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; 39) an inhibitor of a lipid kinase; or one or more agents as provided in Table 16.

[0041] In some embodiments, the antibody or antigen binding fragment, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition is administered concurrently with, prior to, or subsequent to, the at least one additional therapeutic agent.

[0042] In some embodiments, administering the antibody or antigen binding fragment of, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition has one or more of the following effects:

(a) increased number of CD45+ CD4- CD8+ CD69+ CD25+ cells in a tumor or lesion site in the subject;

(b) increased number of CD45+ CD8- CD4+ FOXP3- CD69+ CD25+ cells in a tumor or lesion site in the subject;

(c) descreased plasma MCP1 or IL-1β level in the subject; or

(d) increased MCP1 level in a tumor or lesion site in the subject.

[0043] In another aspect, provided herein are use of an antibody or antigen binding fragment thereof described herein, the nucleic acid encoding such an antibody or antigen binding fragment thereof, a vector or a cell comprising such a nucleic acid, or a pharmaceutical composition comprising such an antibody or antigen binding fragment thereof, nucleic acid, vector, or cell, in the manufacture of a medicament for treatment of a cancer.

[0044] In another aspect, provided herein are methods of treating cancer in a subject in need thereof, such method comprising administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody or antigen binding fragment described herein, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

[0045] In another aspect, provided herein are methods of stimulating an immune response in a subject, such method comprising administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody or antigen binding fragment described

herein, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

[0046] In another aspect, provided herein are compositions comprising an anti-human ENTPD2 antibody or antigen binding fragment described herein for use, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor, in the treatment of cancer in a subject.

[0047] In another aspect, provided herein are compositions comprising an anti-human ENTPD2 antibody or antigen binding fragment described herein, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor, for use in the treatment of cancer in a subject.

[0048] In some embodiments, the PD-1 inhibitor is a PD-1 antibody. In some embodiments, the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

[0049] In some embodiments, the PD-L1 inhibitor is a PD-L1 antibody. In some embodiments, the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

[0050] In some embodiments, the cancer is an ENTPD2+ cancer. In some embodiments, the cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

[0051] 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.

BRIEF DESCRIPTION OF THE DRAWINGS

[0052] **FIG. 1A** depicts ENTPD2 expression across representative cancer cell lines as determined by flow cytometry. **FIG. 1B** is table (Table 20) showing ENTPD2 receptor density across representative cancer cell lines.

[0053] **FIG. 2** depicts representative IHC staining images of ENTPD2 in formalin-fixed paraffin-embedded primary colorectal, esophageal and ovarian tumor tissues.

[0054] **FIG. 3A** shows the amino acid sequence of anti-human ENTPD2 FAb22 heavy chain (SEQ ID NO: 330) and light chain (SEQ ID NO: 334) with the CDRs underlined

(as defined by Kabat), and residues located at the antibody-antigen interface labeled for each Fab as (*). **FIG. 3B** shows the amino acid sequence of anti-human ENTPD2 FAb23 heavy chain (SEQ ID NO: 336) and light chains (SEQ ID NO: 239) with the CDRs underlined (as defined by Kabat), and residues located at the antibody-antigen interface labeled with (*). **FIG. 3C** shows the amino acid sequence of the anti-mouse ENTPD2 FAb24 heavy chain (SEQ ID NO: 338) and light chains (SEQ ID NO: 340) with the CDRs underlined (as defined by Kabat), and residues located at the antibody-antigen interface labeled with (*).

[0055] **FIG. 4A** shows the amino acid sequence of recombinant human ENTPD2 (residues 29-462, Y350A mutant) used in crystallographic studies (SEQ ID NO: 1014), with the secondary structure elements shown below the amino acid sequence. Bars represent α-helices and arrows represent β-strands. Unlabeled arrows and bars from sequence formatting breaks are contiguous to preceding structural elements labeled. Unstructured regions are unmarked. Soluble extracellular domain of human ENTPD2 spans residues 29-462. The construct utilizes an N-terminal GP67 secretion signal peptide (first 38 residues highlighted in gray) with the signal peptide cleavage site after last residue, and a C-terminal hexahistidine (SEQ ID NO: 1010) metal affinity tag to facilitate purification. Asn129, Asn294, Asn378 and Asn443 are predicted N-linked glycosylation sites for which glycosylation is observed in crystal structures and shown in italics. Asn64 is also a predicted N-linked glycosylation site not observed in these crystal structures. Residues located at the antigen-Fab interface for the FAb22 and FAb23 complexes are indicated by (*) and (:) symbols, respectively, below the amino acid sequence. **FIG. 4B** shows the amino acid sequence of recombinant murine ENTPD2 (residues 29-462) used in crystallography studies (SEQ ID NO: 1015), with the secondary structure elements shown below the amino acid sequence. The bars represent α-helices and arrows represent β-strands. Unlabeled arrows and bars from line breaks are contiguous to preceding structural elements labeled. Unstructured regions are unmarked. Mature murine ENTPD2 starts from Thr29. The construct utilizes an N-terminal GP67 secretion signal peptide (residues 1-38), with the signal peptide cleavage site after residue 38, and a C-terminal hexahistidine (SEQ ID NO: 1010) metal affinity tag to facilitate purification. Asn129, Asn294, Asn378 and Asn443 are potential N-linked glycosylation sites shown in italics. Residues positioned at the antigen-FAb24 interface are indicated by (#) symbol beneath the amino acid sequence.

[0056] **FIG. 5A** shows a cartoon depiction of the human ENTPD2 ectodomain apo crystal structure with residues 33-453 shown. Two views are rotated by 90 degrees.

Consecutive secondary structural elements are labeled. Disulfides are shown as sticks. The amino- and carboxy- termini are labeled NT and CT, respectively. The membrane proximal lobe contains both N- and C-termini (subdomain1: Pro36-Ser161 and Lys427-Phe461) and is shaded darker than the membrane distal lobe (subdomain 2: Gly162-Gln426). Substrate ATP binds deep within the interlobe cleft. The location of the ATP binding site is illustrated in **FIG. 5B**. Shown is the ATP analog AMP-PNP superposed in the human ENTPD2 active site from the rat ENTPD2 co-structure (PDB 3CJA).

[0057] **FIG. 6** illustrates an overview of anti-human ENTPD2 FAb22 in complex with human ENTPD2. Two views are shown 90 degrees apart. AMP-PNP is modeled in the ENTPD2 active site based upon superposition with the rat ENTPD2 co-structure PDB 3CJA. The heavy chain of the Fab is shaded darker.

[0058] **FIG. 7** illustrates an overview of anti-human ENTPD2 FAb23 in complex with human ENTPD2. Two views are shown 90 degrees apart. AMP-PNP is modeled in the ENTPD2 active site based upon superposition with the rat ENTPD2 co-structure PDB 3CJA. The heavy chain of the Fab is shaded darker.

[0059] **FIG. 8** illustrates an overview of anti-murine ENTPD2 FAb24 in complex with mouse ENTPD2. AMP-PNP is modeled in the ENTPD2 active site based upon superposition with the rat ENTPD2 co-structure PDB 3CJA. The heavy chain of the Fab is shaded darker.

[0060] **FIG. 9** is a plot illustrating long-term efficacy with anti-mouse ENTPD2 mAb13 in combination with anti-PD-1 Ab in the syngeneic B16LM3 tumor model.

[0061] **FIGs. 10A-10C** are graphs illustrating efficacy with anti-mouse ENTPD2 mAb13 in combination with anti-PD-1 Ab in the syngeneic B16F10 tumor model, associated with increased influx of activated CD8 and CD4 T helper cells at the tumor site on day 8 post treatment.

[0062] **FIGs. 11A-11B** depict characterization of the human ENTPD2 engineered model B16LM3 clone B5, illustrating expression of human ENTPD2 by FACS *in vitro* and sustainability of human ENTPD2 expression in tumors *in vivo* by IHC with the Novus anti-human CD39L1 Ab (1:40 dilution).

[0063] **FIGs. 12A-12B** are graphs illustrating dose response efficacy of anti-human ENTPD2 mAb1 and mAb6 in combination with anti-PD-1 Ab in the human ENTPD2 engineered B16LM3 clone B5 model.

[0064] **FIGs. 13A-13B** are dot plots showing plasma IL-1b (FIG. 13A) and MCP-1 (FIG. 13B) levels after treatment with anti-human ENTPD2 mAb1 or an isotype control in the human ENTPD2 engineered B16LM3 clone B5 xenograft model in C57BL/6 mice. **FIGs. 13C-13D** are dot plots showing IL-1β (FIG. 13C) and MCP-1 (FIG. 13D) levels in tumor after treatment with anti-human ENTPD2 mAb1 or an isotype control in the human ENTPD2 engineered B16LM3 clone B5 xenograft model in C57BL/6 mice.

[0065] **FIG. 14** is a graph showing *in vivo* efficacy of anti-ENTPD2 mAb1 in combination with A2AR antagonist NIR178 in the human ENTPD2 engineered B16LM3 xenograft model in C57BL/6 mice.

[0066] **FIG. 15** is a graph showing representative activity of anti-ENTPD2 Abs in the biochemical human ENTPD2 functional assay. Anti-human ENTPD2 mAb1, mAb17, mAb19, and mAb21 potently inhibit the catalytic activity of the recombinant human ENTPD2.

[0067] **FIGs. 16A-16B** depicts representative activity of anti-human ENTPD2 Abs in the human or cyno ENTPD2 NIH/3T3 or RKO cell-based functional assay.

[0068] **FIG. 17** depicts graph illustrating in vitro functional activity of anti-mouse ENTPD2 mAb13, mAb14, mAb15 in the mouse ENTPD2 NIH/3T3 cell-based functional assay.

DETAILED DESCRIPTION

[0069] Provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to the ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (e.g., human ENTPD2 protein). The ENTPD2 antibodies or antigen binding fragments thereof are useful for treating ENTPD2-associated diseases, such as a cancer.

Definitions

[0070] As used in the specification and claims, the singular form “a”, “an” and “the” include plural references unless the context clearly dictates otherwise. For example, the term “a cell” includes a plurality of cells, including mixtures thereof.

[0071] Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and

"comprising", are used herein in their open-ended and non-limiting sense unless otherwise noted.

[0072] When used herein "consisting of" excludes any element, step, or ingredient not specified in the aspect, embodiment and/or claim element. When used herein, "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the aspect, embodiment and/or claim.

[0073] In each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms.

[0074] All numerical designations, e.g., pH, temperature, time, concentration, and molecular weight, including ranges, are approximations which are varied (+) or (-) by increments of 0.1. It is to be understood, although not always explicitly stated that all numerical designations are preceded by the term "about". It also is to be understood, although not always explicitly stated, that the reagents described herein are merely examples and that equivalents of such are known in the art.

[0075] As used herein, ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2) (also known as CD39 Antigen-Like 1, CD39-like-1, CD39L1, Ecto-ATP Diphosphohydrolase 2, ecto-ATPase, Ecto-ATPase 2, Ecto-ATPDase 2, NTPDase-2, NTPDase 2) refers to the type 2 enzyme of the ecto-nucleoside triphosphate diphosphohydrolase family (E-NTPDase), which are a family of ecto-nucleosidases that hydrolyze 5'-triphosphates. The ENTPD2 enzyme is encoded by the gene *ENTPD2*. The human *ENTPD2* gene is mapped to chromosomal location 9q34.3, and the genomic sequence of human *ENTPD2* gene can be found in GenBank at NC_000009.12. The mRNA and protein sequences of the *ENTPD2* human transcript variants can be found in GenBank with the following Accession Nos:

Isoform1: NM_203468.2 (mRNA) → NP_982293.1 (protein with 495 aa);

Isoform2: NM_001246.3 (mRNA) → NP_001237.1 (protein with 472 aa);

Ectonucleoside triphosphate diphosphohydrolase 2 isoform 1 [Homo sapiens, NP_982293.1]

MAGKVRSLLPPLLLAAAGLAGLLLLCVPTRDVREPPALKYGIVLDAGSSH
TSMFIYKWPADKENDTGIVGQHSSCDVPGGGISSYADNPSGASQSLVGCL
EQALQDVPKERHAGTPLYLGATAGMRLLNLTNPEASTSVLMAVTHTLTQY
PFDFRGARILSGQEEGVFGWVTANYLLENFIKYGWVGRWFRPRKGTLGAM
DLGGASTQITFETTSPAEDRASEVQLHLYGQHYRVYTHSFLCYGRDQVLQ
RLLASALQTHGFHPCWPRGFSTQVLLGDVYQSPCTMAQRPQNFNSSARVS

LSGSSDPHLCRDLVSGLFSFSSCPFSRCSFNGVFQPPVAGNFVAFSAFFY
TVDFLRTSMGLPVATLQQLEAAAVNVCNQTWAQLQARVPGQRARLADYCA
GAMFVQQLLSRGYGFDERAFGGVIFQKKAADTAVGWALGYMLNLTNLIPA
DPPGLRKGTDFSSWVVLLLLFASALLAALVLLLRQVHSAKLPSTI (SEQ ID NO: 291)

Homo sapiens ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2), transcript variant 1, mRNA [NM_203468.2]

1 ggctccccgc actctccggg tccacgcatc gtcctcccgc gcgcccgccc gcccatggcc
61 gggaaggtgc ggtcactgct gccgccgctg ctgctggccg ccgcgggcct cgccggcctc
121 ctactgctgt gcgtccccac ccgcgacgtc cgggagccgc ccgccctcaa gtatggcatc
181 gtcctggacg ctggttcttc acacacgtcc atgtttatct acaagtggcc ggcagacaag
241 gagaacgaca caggcattgt gggccagcac agctcctgtg atgttccagg tgggggcatc
301 tccagctatg cagacaaccc ttctggggcc agccagagtc ttgttggatg cctcgaacag
361 gcgcttcagg atgtgcccaa agagagacac gcgggcacac ccctctacct gggagccaca
421 gcgggtatgc gcctgctcaa cctgaccaat ccagaggcct cgaccagtgt gctcatggca
481 gtgactcaca cactgaccca gtaccccttt gacttccggg gtgcacgcat cctctcgggc
541 caggaagagg gggtgtttgg ctgggtgact gccaactacc tgctggagaa cttcatcaag
601 tacggctggg tgggccggtg gttccggcca cggaagggga cactgggggc catggacctg
661 gggggtgcct ctacccagat cacttttgag acaaccagtc cagctgagga cagagccagc
721 gaggtccagc tgcatctcta cggccagcac taccgagtct acacccacag cttcctctgc
781 tatggccgtg accaggtcct ccagaggctg ctggccagcg ccctccagac ccacggcttc
841 cacccctgct ggccgagggg cttttccacc caagtgctgc tcggggatgt gtaccagtca
901 ccatgcacca tggcccagcg gccccagaac ttcaacagca gtgccagggt cagcctgtca
961 gggagcagtg acccccacct ctgccgagat ctggtttctg ggctcttcag cttctcctcc
1021 tgccccttct cccgatgctc tttcaatggg gtcttccagc ccccagtggc tgggaacttt
1081 gtggccttct ctgccttctt ctacactgtg gacttttgc ggacttcgat ggggctgccc
1141 gtggccaccc tgcagcagct ggaggcagcc gcagtgaatg tctgcaacca gacctgggct
1201 cagctgcaag ctcgggtgcc agggcaacgg gcccgcctgg ccgactactg cgccggggcc
1261 atgttcgtgc agcagctgct gagtcgcggc tacggcttcg acgagcgcgc cttcggcggc
1321 gtgatcttcc agaagaaggc cgcggacact gcagtgggct gggcgctcgg ctacatgctg
1381 aacctgacca acctgatccc cgccgacccg ccggggctgc gcaagggcac agacttcagc
1441 tcctgggtcg tcctcctgct gctcttcgcc tccgcgctcc tggctgcgct tgtcctgctg
1501 ctgcgtcagg tgcactccgc caagctgcca agcaccattt aggggccgac gggggcagct
1561 gccccatccc tcccccaacc cctgtatccc caccccgtac tcccaccct cccacaaccc
1621 ctgtacctcc caccctgta tccccacccc tccacccacc cctctcccaa cctctctccc
1681 cgcccctgta tcctgcattc ctccacccac cctctatccc ccaccgctcc accccaccac
1741 tgtcttctcc atccttccac cccaccctca gcgtctctgc ccctaaggca gcccaggaaa
1801 taggaactga gactctggta cccacaggag cctgggtggg caaagagcgc tcaatccagc
1861 tccttgaacc cctccagccc gcttcagcct gggcatcact gcaggccccg tgctcctcct
1921 cctcctcctc agggctgggt ctccagagag tggggccttg gtcctgagaa tcagccctta
1981 gaggctcctt ctgtgtagtc tgggtctgta ctggggaggg tcacagccca cgggctggca
2041 gccagcccag cacctacttg taaaaatttt gtaataaaaa gtttttccta gagacgtgaa

2101 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa (SEQ ID NO: 292)

Ectonucleoside triphosphate diphosphohydrolase 2 isoform 2 [Homo sapiens, NP_001237.1]

MAGKVRSLLPPLLLAAAGLAGLLLLCVPTRDVREPPALKYGIVLDAGSSH
TSMFIYKWPADKENDTGIVGQHSSCDVPGGGISSYADNPSGASQSLVGCL
EQALQDVPKERHAGTPLYLGATAGMRLLNLTNPEASTSVLMAVTHTLTQY
PFDFRGARILSGQEEGVFGWVTANYLLENFIKYGWVGRWFRPRKGTLGAM
DLGGASTQITFETTSPAEDRASEVQLHLYGQHYRVYTHSFLCYGRDQVLQ
RLLASALQTHGFHPCWPRGFSTQVLLGDVYQSPCTMAQRPQNFNSSARVS
LSGSSDPHLCRDLVSGLFSFSSCPFSRCSFNGVFQPPVAGNFVAFSAFFY
TVDFLRTSMGLPVATLQQLEAAAVNVCNQTWAQQLLSRGYGFDERAFGGV
IFQKKAADTAVGWALGYMLNLTNLIPADPPGLRKGTDFSSWVVLLLLFAS
ALLAALVLLLRQVHSAKLPSTI (SEQ ID NO: 293)

Homo sapiens ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2), transcript variant 2, mRNA [NM_001246.3]

1 ggctccccgc actctccggg tccacgcatc gtcctcccgc gcgcccgccc gcccatggcc
61 gggaaggtgc ggtcactgct gccgccgctg ctgctggccg ccgcgggcct cgccggcctc
121 ctactgctgt gcgtccccac ccgcgacgtc cgggagccgc ccgccctcaa gtatggcatc
181 gtcctggacg ctggttcttc acacacgtcc atgtttatct acaagtggcc ggcagacaag
241 gagaacgaca caggcattgt gggccagcac agctcctgtg atgttccagg tgggggcatc
301 tccagctatg cagacaaccc ttctggggcc agccagagtc ttgttggatg cctcgaacag
361 gcgcttcagg atgtgcccaa agagagacac gcgggcacac ccctctacct gggagccaca
421 gcgggtatgc gcctgctcaa cctgaccaat ccagaggcct cgaccagtgt gctcatggca
481 gtgactcaca cactgaccca gtaccccttt gacttccggg gtgcacgcat cctctcgggc
541 caggaagagg gggtgtttgg ctgggtgact gccaactacc tgctggagaa cttcatcaag
601 tacggctggg tgggccggtg gttccggcca cggaagggga cactgggggc catggacctg
661 gggggtgcct ctacccagat cacttttgag acaaccagtc cagctgagga cagagccagc
721 gaggtccagc tgcatctcta cggccagcac taccgagtct acacccacag cttcctctgc
781 tatggccgtg accaggtcct ccagaggctg ctggccagcg ccctccagac ccacggcttc
841 caccctgct ggccgagggg cttttccacc caagtgctgc tcggggatgt gtaccagtca
901 ccatgcacca tggcccagcg gccccagaac ttcaacagca gtgccagggt cagcctgtca
961 gggagcagtg acccccacct ctgccgagat ctggtttctg ggctcttcag cttctcctcc
1021 tgccccttct cccgatgctc tttcaatggg gtcttccagc ccccagtggc tgggaacttt
1081 gtggccttct ctgccttctt ctacactgtg gacttttgc ggacttcgat ggggctgccc
1141 gtggccaccc tgcagcagct ggaggcagcc gcagtgaatg tctgcaacca gacctgggct
1201 cagcagctgc tgagtcgcgg ctacggcttc gacgagcgcg ccttcggcgg cgtgatcttc
1261 cagaagaagg ccgcggacac tgcagtgggc tgggcgctcg gctacatgct gaacctgacc
1321 aacctgatcc ccgccgaccc gccggggctg cgcaagggca cagacttcag ctcctgggtc
1381 gtcctcctgc tgctcttcgc ctccgcgctc ctggctgcgc ttgtcctgct gctgcgtcag
1441 gtgcactccg ccaagctgcc aagcaccatt taggggccga cgggggcagc tgccccatcc

1501 ctcccccaac ccctgtatcc ccaccccgta ctcccacccc tcccacaacc cctgtacctc
1561 ccacccctgt atccccaccc ctccacccac ccctctccca acctctctcc ccgcccctgt
1621 atcctgcatt cctccaccca ccctctatcc cccaccgctc caccccacca ctgtcttctc
1681 catccttcca ccccaccctc agcgtctctg cccctaaggc agcccaggaa ataggaactg
1741 agactctggt acccacagga gcctgggtgg gcaaagagcg ctcaatccag ctccttgaac
1801 ccctccagcc cgcttcagcc tgggcatcac tgcaggcccc gtgctcctcc tcctcctcct
1861 cagggctggg tctccagaga gtggggcctt ggtcctgaga atcagccctt agaggctcct
1921 tctgtgtagt ctgggtctgt actggggagg gtcacagccc acgggctggc agccagccca
1981 gcacctactt gtaaaaattt tgtaataaaa agtttttcct agagacgtga aaaaaaaaaa
2041 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa (SEQ ID NO: 294)

[0076] As used herein, human ENTPD2 protein also encompasses proteins that have over its full length at least about 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity with any one of the ENTPD2 isoforms. The sequences of murine, Cynomolgus monkey, and other animal ENTPD2 proteins are known in the art.

[0077] The term "antibody", as used herein, refers to a protein, or polypeptide sequence derived from an immunoglobulin molecule that specifically binds to an antigen. Antibodies can be polyclonal or monoclonal, multiple or single chain, or intact immunoglobulins, and may be derived from natural sources or from recombinant sources. For example, a naturally occurring IgG antibody can be a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the

first component (C1q) of the classical complement system. An antibody can be a monoclonal antibody, human antibody, humanized antibody, camelised antibody, or chimeric antibody. The antibodies can be of any isotype (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass.

[0078] The term "antibody fragment" or "antigen-binding fragment" refers to at least one portion of an antibody, that retains the ability to specifically interact with (e.g., by binding, steric hinderance, stabilizing/destabilizing, spatial distribution) an epitope of an antigen. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')2, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), camelid VHH domains, multi-specific antibodies formed from antibody fragments such as a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region, and an isolated CDR or other epitope binding fragments of an antibody. An antigen binding fragment can also be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, Nature Biotechnology 23:1126-1136, 2005). Antigen binding fragments can also be grafted into scaffolds based on polypeptides such as a fibronectin type III (Fn3) (see U.S. Patent No.: 6,703,199, which describes fibronectin polypeptide minibodies). The term "scFv" refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked, e.g., via a synthetic linker, e.g., a short flexible polypeptide linker, and capable of being expressed as a single chain polypeptide, and wherein the scFv retains the specificity of the intact antibody from which it is derived. Unless specified, as used herein an scFv may have the VL and VH variable regions in either order, e.g., with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

[0079] The terms "complementarity determining region" or "CDR", as used herein, refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. For example, in general, there are three CDRs in each heavy chain variable region (e.g., HCDR1, HCDR2, and HCDR3) and three CDRs in each light chain variable region (e.g., LCDR1, LCDR2, and LCDR3). The precise amino acid sequence boundaries of a given CDR can be determined using any one of a number of well-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), or a combination thereof, and ImMunoGenTics (IMGT) numbering (Lefranc, M.-P., The Immunologist, 7, 132-136 (1999); Lefranc, M.-P. et al., Dev. Comp. Immunol., 27, 55-77 (2003) ("IMGT" numbering scheme). In a combined Kabat and Chothia numbering scheme for a given CDR region (for example, HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2 or LC CDR3), in some embodiments, the CDRs correspond to the amino acid residues that are defined as part of the Kabat CDR, together with the amino acid residues that are defined as part of the Chothia CDR. As used herein, the CDRs defined according to the "Chothia" number scheme are also sometimes referred to as "hypervariable loops."

[0080] For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1) (e.g., insertion(s) after position 35), 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) (e.g., insertion(s) after position 27), 50-56 (LCDR2), and 89-97 (LCDR3). As another example, under Chothia, the CDR amino acids in the VH are numbered 26-32 (HCDR1) (e.g., insertion(s) after position 31), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1) (e.g., insertion(s) after position 30), 50-52 (LCDR2), and 91-96 (LCDR3). By combining the CDR definitions of both Kabat and Chothia, the CDRs comprise or consist of, e.g., amino acid residues 26-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3) in human VH and amino acid residues 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3) in human VL. Under IMGT, the CDR amino acid residues in the VH are numbered approximately 26-35 (CDR1), 51-57 (CDR2) and 93-102 (CDR3), and the CDR amino acid residues in the VL are numbered approximately 27-32 (CDR1), 50-52 (CDR2), and 89-97 (CDR3) (numbering according to "Kabat"). Under IMGT, the CDR regions of an antibody can be determined using the program IMGT/DomainGap Align. Generally, unless specifically indicated, the antibody molecules can include any combination of one or more Kabat CDRs and/or Chothia CDRs.

[0081] The term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or otherwise interacting with a molecule. Epitopic determinants generally consist of chemically active surface groupings of molecules such as

amino acids or carbohydrate or sugar side chains and can have specific three-dimensional structural characteristics, as well as specific charge characteristics. An epitope may be "linear" or "conformational." Conformational and linear epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[0082] The term "monovalent antibody" as used herein, refers to an antibody that binds to a single epitope on a target molecule.

[0083] The term "bivalent antibody" as used herein, refers to an antibody that binds to two epitopes on at least two identical target molecules. The bivalent antibody may also crosslink the target molecules to one another. A "bivalent antibody" also refers to an antibody that binds to two different epitopes on at least two identical target molecules.

[0084] The term "multivalent antibody" refers to a single binding molecule with more than one valency, where "valency" is described as the number of antigen-binding moieties present per molecule of an antibody construct. As such, the single binding molecule can bind to more than one binding site on a target molecule. Examples of multivalent antibodies include, but are not limited to, bivalent antibodies, trivalent antibodies, tetravalent antibodies, pentavalent antibodies, and the like, as well as bispecific antibodies and biparatopic antibodies. For example, for ENTPD2, the multivalent antibody (e.g., a ENTPD2 biparatopic antibody) has a binding moiety for two domains of ENTPD2, respectively.

[0085] The term "multivalent antibody" also refers to a single binding molecule that has more than one antigen-binding moiety for two separate target molecules. For example, an antibody that binds to ENTPD2 (e.g., human ENTPD2 protein) and a second target molecule that is not ENTPD2. In one embodiment, a multivalent antibody is a tetravalent antibody that has four epitope binding domains. A tetravalent molecule may be bispecific and bivalent for each binding site on that target molecule.

[0086] The term "bispecific antibody" as used herein, refers to an antibody that binds to two or more different epitopes. In some embodiments, a bispecific antibody binds to two different targets. In some embodiments, a bispecific antibody binds to two different epitopes on a single target molecule. An antibody that binds to two different epitopes on a single target molecule is also known as a "biparatopic antibody."

[0087] The phrases "monoclonal antibody" or "monoclonal antibody composition" as used herein refers to polypeptides, including antibodies, bispecific antibodies, etc., that have substantially identical amino acid sequence or are derived from the same genetic source. This

term also includes preparations of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope.

[0088] The phrase "human antibody," as used herein, includes antibodies having variable regions in which both the framework and CDR regions are derived from sequences of human origin. Furthermore, if the antibody contains a constant region, the constant region is also derived from such human sequences, e.g., human germline sequences, or mutated versions of human germline sequences or antibody containing consensus framework sequences derived from human framework sequences analysis, for example, as described in Knappik, et al. (2000. J Mol Biol 296, 57-86). The structures and locations of immunoglobulin variable domains, e.g., CDRs, may be defined using well known numbering schemes, e.g., the Kabat numbering scheme, the Chothia numbering scheme, or a combination of Kabat and Chothia, and ImMunoGenTics (IMGT) numbering (see, e.g., Sequences of Proteins of Immunological Interest, U.S. Department of Health and Human Services (1991), eds. Kabat et al.; Al Lazikani et al., (1997) J. Mol. Bio. 273:927 948); Kabat et al., (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services; Chothia et al., (1987) J. Mol. Biol. 196:901-917; Chothia et al., (1989) Nature 342:877-883; Al-Lazikani et al., (1997) J. Mal. Biol. 273:927-948 and Lefranc, M.-P., The Immunologist, 7, 132-136 (1999); Lefranc, M.-P. et al., Dev. Comp. Immunol., 27, 55-77 (2003)).

[0089] The human antibodies of the invention may include amino acid residues not encoded by human sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation *in vivo*, or a conservative substitution to promote stability or manufacturing). However, the term "human antibody" as used herein, is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

[0090] The phrase "recombinant human antibody" as used herein, includes all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom, antibodies isolated from a host cell transformed to express the human antibody, e.g., from a transfectoma, antibodies isolated from a recombinant, combinatorial human antibody library, and antibodies prepared, expressed, created or isolated by any other means that involve splicing of all or a portion of a

human immunoglobulin gene, sequences to other DNA sequences. Such recombinant human antibodies have variable regions in which the framework and CDR regions are derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies can be subjected to in vitro mutagenesis (or, when an animal transgenic for human Ig sequences is used, *in vivo* somatic mutagenesis) and thus the amino acid sequences of the VH and VL regions of the recombinant antibodies are sequences that, while derived from and related to human germline VH and VL sequences, may not naturally exist within the human antibody germline repertoire *in vivo*.

[0091] The term "Fc region" as used herein refers to a polypeptide comprising the CH3, CH2 and at least a portion of the hinge region of a constant domain of an antibody. Optionally, an Fc region may include a CH4 domain, present in some antibody classes. An Fc region, may comprise the entire hinge region of a constant domain of an antibody. In one embodiment, the invention comprises an Fc region and a CH1 region of an antibody. In one embodiment, the invention comprises an Fc region CH3 region of an antibody. In another embodiment, the invention comprises an Fc region, a CH1 region and a Ckappa/lambda region from the constant domain of an antibody. In one embodiment, a binding molecule of the invention comprises a constant region, e.g., a heavy chain constant region. In one embodiment, such a constant region is modified compared to a wild-type constant region. That is, the polypeptides of the invention disclosed herein may comprise alterations or modifications to one or more of the three heavy chain constant domains (CH1, CH2 or CH3) and/or to the light chain constant region domain (CL). Example modifications include additions, deletions or substitutions of one or more amino acids in one or more domains. Such changes may be included to optimize effector function, half-life, etc.

[0092] As used herein, the term "affinity" refers to the strength of interaction between antibody and antigen at single antigenic sites. Within each antigenic site, the variable region of the antibody "arm" interacts through weak non-covalent forces with the antigen at numerous sites; the more interactions, the stronger the affinity. As used herein, the term "high affinity" for an IgG antibody or fragment thereof (e.g., a Fab fragment) refers to an antibody having a knock down of 10^{-8} M or less, 10^{-9} M or less, or 10^{-10} M, or 10^{-11} M or less, or 10^{-12} M or less, or 10^{-13} M or less for a target antigen. However, high affinity binding can vary for other antibody isotypes. For example, high affinity binding for an IgM isotype refers to an antibody having a knock down of 10^{-7} M or less, or 10^{-8} M or less.

[0093] As used herein, the term "avidity" refers to an informative measure of the overall stability or strength of the antibody-antigen complex. It is controlled by three major factors: antibody epitope affinity; the valency of both the antigen and antibody; and the structural arrangement of the interacting parts. Ultimately these factors define the specificity of the antibody, that is, the likelihood that the particular antibody is binding to a precise antigen epitope.

[0094] The term "binding specificity" as used herein refers to the ability of an individual antibody combining site to react with one antigenic determinant and not with a different antigenic determinant. The combining site of the antibody is located in the Fab portion of the molecule and is constructed from the hypervariable regions of the heavy and light chains. Binding affinity of an antibody is the strength of the reaction between a single antigenic determinant and a single combining site on the antibody. It is the sum of the attractive and repulsive forces operating between the antigenic determinant and the combining site of the antibody.

[0095] The term "treat" and "treatment" refer to both therapeutic treatment and prophylactic or preventive measures, wherein the object is to prevent or slow down an undesired physiological change or disorder. For purpose of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (i.e., not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. "Treatment" can also mean prolonging survival as compared to expected survival if not receiving treatment. In other embodiments the terms "treat", "treatment" and "treating" refer to the inhibition of the progression of a proliferative disorder, either physically by, *e.g.,* stabilization of a discernible symptom, physiologically by, *e.g.,* stabilization of a physical parameter, or both. In other embodiments the terms "treat", "treatment" and "treating" refer to the reduction or stabilization of tumor size or cancerous cell count.

[0096] The term "subject" refers to an animal, human or non-human, to whom treatment according to the methods of the present invention is provided. Veterinary and non-veterinary applications are contemplated. The term includes, but is not limited to, mammals, e.g., humans, other primates, pigs, rodents such as mice and rats, rabbits, guinea pigs, hamsters, cows, horses, cats, dogs, sheep and goats. Typical subjects include humans, farm

animals, and domestic pets such as cats and dogs. In some embodiments, the subject is a human.

[0097] An "effective amount" refers to an amount sufficient to effect beneficial or desired results. For example, a therapeutic amount is one that achieves the desired therapeutic effect. This amount can be the same or different from a prophylactically effective amount, which is an amount necessary to prevent onset of disease or disease symptoms. An effective amount can be administered in one or more administrations, applications or dosages. A "therapeutically effective amount" of a therapeutic compound (i.e., an effective dosage) depends on the therapeutic compounds selected. The compositions can be administered from one or more times per day to one or more times per week. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of the therapeutic compounds described herein can include a single treatment or a series of treatments.

[0098] The term "nucleic acid" or "polynucleotide" refers to deoxyribonucleic acids (DNA) or ribonucleic acids (RNA) and polymers thereof in either single- or double-stranded form. The term "set of nucleic acids" may, for example, include separate isolated nucleic acids encoding a light chain and a heavy chain of an antibody or domains of a bi-specific or multispecific antibody. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19:5081 (1991); Ohtsuka et al., J. Biol. Chem. 260:2605-2608 (1985); and Rossolini et al., Mol. Cell. Probes 8:91-98 (1994)).

[0099] The terms "peptide", "polypeptide", and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed

on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

[0100] The term "conservative sequence modifications" refers to amino acid modifications that do not significantly affect or alter the binding characteristics of the antibody or antibody fragment containing the amino acid sequence. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into an antibody or antibody fragment of the invention by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis. Conservative amino acid substitutions are ones 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, tryptophan), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

[0101] The term "homologous" or "identity" refers to the subunit sequence identity between two polymeric molecules, e.g., between two nucleic acid molecules, such as, two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a subunit position in both of the two molecules is occupied by the same monomeric subunit; e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous or identical at that position. The homology between two sequences is a direct function of the number of matching or homologous positions; e.g., if half (e.g., five positions in a polymer ten subunits in length) of the positions in two sequences are homologous, the two sequences are 50% homologous; if 90% of the positions (e.g., 9 of 10), are matched or

homologous, the two sequences are 90% homologous. Percentage of "sequence identity" can be determined by comparing two optimally aligned sequences over a comparison window, where the fragment of the amino acid sequence in the comparison window may comprise additions or deletions (e.g., gaps or overhangs) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage can be calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison, and multiplying the result by 100 to yield the percentage of sequence identity. The output is the percent identity of the subject sequence with respect to the query sequence.

[0102] The term "isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell. An isolated antibody is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds ENTPD2 is substantially free of antibodies that specifically bind antigens other than ENTPD2). An isolated antibody that specifically binds a target molecule may, however, have cross-reactivity to the same antigens from other species, e.g., an isolated antibody that specifically binds ENTPD2 may bind ENTPD2 molecules from other species. Moreover, an isolated antibody may be substantially free of other cellular material and/or chemicals.

[0103] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and materials similar or equivalent to those described herein can be used to practice the invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

[0104] The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

Antibodies and Antigen-Binding Fragments Thereof That Specifically Bind To Human ENTPD2

[0105] In one aspect, provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to ENTPD2 protein ("ENTPD2 antibodies or antigen binding fragments" or "anti-ENTPD2 antibodies or antigen binding fragments"). In some embodiments, provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to human ENTPD2 protein ("human ENTPD2 antibodies or antigen binding fragments" or "anti-human ENTPD2 antibodies or antigen binding fragments").

[0106] In some embodiments, the anti-ENTPD2 antibodies or antigen-binding fragments thereof (e.g., anti-human ENTPD2 antibodies or antigen binding fragments) provided herein include a heavy chain CDR1 (HCDR1), a heavy chain CDR2 (HCDR2), a heavy chain CDR3 (HCDR3), and a light chain CDR1 (LCDR1), a light chain CDR2 (LCDR2), and a light chain CDR3 (LCDR3). In some embodiments, the anti- ENTPD2 antibodies or antigen binding fragments (e.g., anti-human ENTPD2 antibodies or antigen binding fragments) provided herein include a heavy chain variable region (VH) comprising CDR1, CDR2, and CDR3 and a light chain variable region (VL) comprising CDR1, CDR2, and CDR3. In some embodiments, the anti- ENTPD2 antibodies or antigen-binding fragments (e.g., anti-human ENTPD2 antibodies or antigen binding fragments) provided herein include a full length heavy chain sequence (HC) and a full length light chain sequence (LC).

[0107] Table 1 lists the sequences of exemplary the ENTPD2 antibodies or antigen-binding fragments that specifically bind to human ENTPD2 protein.

Table 1. Sequences of Exemplary Monoclonal Antibodies (MABs) and Antibody Fragments (FABs) That Bind Human ENTPD2

ANTI-HUMAN ENTPD2 MAB1		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI

SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 10	VH	EVQLVQSGAEVKKPGESLKISCKASGYTFTDYNMD WVRQMPGKGLEWMGDINPKYDISTYNQQFKGQVTI SADKSIRTAYLQWSSLKASDTAMYYCARRGFFLYYG INYYYFDVWGQGTLVTVSS
SEQ ID NO: 11	VH DNA	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGA AGAAGCCTGGCGAGTCCCTGAAGATCTCCTGCAAG GCCTCCGGCTACACCTTCACCGACTACAACATGGA CTGGGTGCGACAGATGCCCGGCAAGGGCCTGGAA TGGATGGGCGACATCAACCCTAAGTACGACATCTC CACCTACAACCAGCAGTTCAAGGGCCAAGTGACC ATCTCCGCCGACAAGTCCATCCGGACCGCCTACCT GCAGTGGTCCTCCCTGAAGGCCTCTGACACCGCCA TGTACTACTGCGCCAGACGGGGCTTCTTCCTGTAC TACGGCATCAACTACTACTACTTCGACGTGTGGGG CCAGGGCACCCTCGTGACAGTGTCATCT
SEQ ID NO: 12	HC	EVQLVQSGAEVKKPGESLKISCKASGYTFTDYNMD WVRQMPGKGLEWMGDINPKYDISTYNQQFKGQVTI SADKSIRTAYLQWSSLKASDTAMYYCARRGFFLYYG INYYYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 13	HC DNA	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGA AGAAGCCTGGCGAGTCCCTGAAGATCTCCTGCAAG GCCTCCGGCTACACCTTCACCGACTACAACATGGA CTGGGTGCGACAGATGCCCGGCAAGGGCCTGGAA TGGATGGGCGACATCAACCCTAAGTACGACATCTC CACCTACAACCAGCAGTTCAAGGGCCAAGTGACC ATCTCCGCCGACAAGTCCATCCGGACCGCCTACCT GCAGTGGTCCTCCCTGAAGGCCTCTGACACCGCCA TGTACTACTGCGCCAGACGGGGCTTCTTCCTGTAC TACGGCATCAACTACTACTACTTCGACGTGTGGGG CCAGGGCACCCTCGTGACAGTGTCATCTGCTAGCA CCAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGC AGCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGG TTGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGA CAGTGTCCTGGAACTCTGGGGCTCTGACTTCCGGC GTGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGG CCTGTACAGCCTGAGCAGCGTGGTGACAGTGCCCT

		CCAGCTCTCTGGGAACCCAGACCTATATCTGCAAC GTGAACCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTGGAGCCCAAGAGCTGCGACAAGACCCA CACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGG GAGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCC AAGGACACCCTGATGATCAGCAGGACCCCCGAGG TGACCTGCGTGGTGGTGGACGTGTCCCACGAGGAC CCAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACTACAAGACCACCCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 21	VL	DIQLTQSPSSLSASVGDRVTITCSASSSVSYIHWFQQK PGKAPKLLIYSTSNLASGVPSRFSGSGSGTFFTLTISSL QPEDFATYFCHQWSSYPWTFGQGTKVEIK
SEQ ID NO: 22	VL DNA	GATATCCAGCTGACCCAGTCCCCTTCCAGCCTGTC TGCCTCTGTGGGCGACAGAGTGACAATTACCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTTCC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGAT CTACTCCACCTCCAACCTGGCCTCCGGCGTGCCCT CTAGATTCTCCGGCTCTGGCTCTGGCACCTTTTTTA CCCTGACCATCTCCAGCCTGCAGCCCGAGGACTTC GCCACCTACTTTTGCCACCAGTGGTCCAGCTACCC CTGGACCTTTGGCCAGGGCACCAAGGTGGAAATCA AG

SEQ ID NO: 23	LC	DIQLTQSPSSLSASVGDRVTITCSASSSVSYIHWFQQK PGKAPKLLIYSTSNLASGVPSRFSGSGSGTFFTLTISSL QPEDFATYFCHQWSSYPWTFGQGTKVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 24	LC DNA	GATATCCAGCTGACCCAGTCCCCTTCCAGCCTGTC TGCCTCTGTGGGCGACAGAGTGACAATTACCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTTCC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGAT CTACTCCACCTCCAACCTGGCCTCCGGCGTGCCCT CTAGATTCTCCGGCTCTGGCTCTGGCACCTTTTTTA CCCTGACCATCTCCAGCCTGCAGCCCGAGGACTTC GCCACCTACTTTTGCCACCAGTGGTCCAGCTACCC CTGGACCTTTGGCCAGGGCACCAAGGTGGAAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTCATCTTC CCCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB2		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 25	VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGTLVTVSS
SEQ ID NO: 26	VH DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCCTCC

SEQ ID NO: 27	HC	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 28	HC DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCCTCCGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCCTGGAACTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGG AGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCA AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACTACAAGACCACCCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS

SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 29	VL	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAVYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 30	VL DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCCTGTCCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAAATCA AG
SEQ ID NO: 31	LC	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAVYYCHQWSSYPWTFGGGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 32	LC DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCCTGTCCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTCATCTTC CCCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB3		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV

SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 33	VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDTSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGTLVTVSS
SEQ ID NO: 34	VH DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACACCTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCCTCC
SEQ ID NO: 35	HC	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDTSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 36	HC DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACACCTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCCTCCGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCCTGGAACTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGG AGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCA

		AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACTACAAGACCACCCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 29	VL	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAVYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 30	VL DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCCTGTCCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAAATCA AG
SEQ ID NO: 31	LC	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAVYYCHQWSSYPWTFGGGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 32	LC DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCCTGTCCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC

		CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTCATCTTC CCCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB4		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 38	HCDR2 (KABAT)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (KABAT)	GYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 41	HCDR2 (CHOTHIA)	SYDAD
SEQ ID NO: 39	HCDR3 (CHOTHIA)	GYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 38	HCDR2 (COMBINED)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (COMBINED)	GYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 44	HCDR2 (IMGT)	ISYDADN
SEQ ID NO: 45	HCDR3 (IMGT)	AGGYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 46	VH	QIQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYYRYGLGSYR GSYYYVMDYWGQGTTVTVSS
SEQ ID NO: 47	VH DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCT
SEQ ID NO: 48	HC	QIQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYYRYGLGSYR GSYYYVMDYWGQGTTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP

		PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 49	HC DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCTGCTAGCACCAAGGGCCCAAGTGTGTTTCCCC TGGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACT GCTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCC CGAGCCCGTGACAGTGTCCTGGAACTCTGGGGCTC TGACTTCCGGCGTGCACACCTTCCCCGCCGTGCTG CAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGG TGACAGTGCCCTCCAGCTCTCTGGGAACCCAGACC TATATCTGCAACGTGAACCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGC GACAAGACCCACACCTGCCCCCCCTGCCCAGCTCC AGAACTGCTGGGAGGGCCTTCCGTGTTCCTGTTCC CCCCCAAGCCCAAGGACACCCTGATGATCAGCAG GACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGT CCCACGAGGACCCAGAGGTGAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACAGCACCTACA GGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGAC TGGCTGAACGGCAAAGAATACAAGTGCAAAGTCT CCAACAAGGCCCTGCCAGCCCCAATCGAAAAGAC AATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCC CAGGTGTACACCCTGCCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCCGAGAACAACTACAAGA CCACCCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 50	LCDR1 (KABAT)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEDPPT
SEQ ID NO: 53	LCDR1 (CHOTHIA)	SQSVDYEGHSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 50	LCDR1 (COMBINED)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEDPPT
SEQ ID NO: 56	LCDR1 (IMGT)	QSVDYEGHSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS

SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 57	VL	ETVLTQSPATLSVSPGERATISCKASQSVDYEGHSYM NWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSGTD FTLTISSVEPEDAATYYCQQSNEDPPTFGGGTKLEIK
SEQ ID NO: 58	VL DNA	GAGACAGTGCTGACCCAGTCCCCTGCCACCCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAG
SEQ ID NO: 59	LC	ETVLTQSPATLSVSPGERATISCKASQSVDYEGHSYM NWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSGTD FTLTISSVEPEDAATYYCQQSNEDPPTFGGGTKLEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 60	LC DNA	GAGACAGTGCTGACCCAGTCCCCTGCCACCCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAGCGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGCT GAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB5		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 38	HCDR2 (KABAT)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (KABAT)	GYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 41	HCDR2 (CHOTHIA)	SYDAD
SEQ ID NO: 39	HCDR3 (CHOTHIA)	GYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 38	HCDR2 (COMBINED)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (COMBINED)	GYYRYGLGSYRGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 44	HCDR2 (IMGT)	ISYDADN
SEQ ID NO: 45	HCDR3 (IMGT)	AGGYYRYGLGSYRGSYYYVMDY

SEQ ID NO: 46	VH	QIQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYYRYGLGSYR GSYYYVMDYWGQGTTVTVSS
SEQ ID NO: 47	VH DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCT
SEQ ID NO: 48	HC	QIQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYYRYGLGSYR GSYYYVMDYWGQGTTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 49	HC DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCTGCTAGCACCAAGGGCCCAAGTGTGTTTCCCC TGGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACT GCTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCC CGAGCCCGTGACAGTGTCCTGGAACTCTGGGGCTC TGACTTCCGGCGTGCACACCTTCCCCGCCGTGCTG CAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGG TGACAGTGCCCTCCAGCTCTCTGGGAACCCAGACC TATATCTGCAACGTGAACCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGC GACAAGACCCACACCTGCCCCCCCTGCCCAGCTCC AGAACTGCTGGGAGGGCCTTCCGTGTTCCTGTTCC CCCCCAAGCCCAAGGACACCCTGATGATCAGCAG GACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGT CCCACGAGGACCCAGAGGTGAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACAGCACCTACA GGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGAC TGGCTGAACGGCAAAGAATACAAGTGCAAAGTCT CCAACAAGGCCCTGCCAGCCCCAATCGAAAAGAC AATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCC

		CAGGTGTACACCCTGCCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCCGAGAACAACTACAAGA CCACCCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 61	LCDR1 (KABAT)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEDPPT
SEQ ID NO: 62	LCDR1 (CHOTHIA)	SQSVDYDGNSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 61	LCDR1 (COMBINED)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEDPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDYDGNSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 64	VL	ETVLTQSPATLSVSPGERATISCKASQSVDYDGNSYM NWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSGTD FTLTISSVEPEDAATYYCQQSNEDPPTFGGGTKLEIK
SEQ ID NO: 65	VL DNA	GAGACAGTGCTGACCCAGTCCCCTGCCACCCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCCAGTCCGTGGACTACGACGGCAACTCC TACATGAACTGGTATCAGCAGAAGCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAG
SEQ ID NO: 66	LC	ETVLTQSPATLSVSPGERATISCKASQSVDYDGNSYM NWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSGTD FTLTISSVEPEDAATYYCQQSNEDPPTFGGGTKLEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 67	LC DNA	GAGACAGTGCTGACCCAGTCCCCTGCCACCCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCCAGTCCGTGGACTACGACGGCAACTCC TACATGAACTGGTATCAGCAGAAGCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAGCGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGCT GAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG

		CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB6		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 38	HCDR2 (KABAT)	YISYDADNNYNPSLKN
SEQ ID NO: 68	HCDR3 (KABAT)	GYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 41	HCDR2 (CHOTHIA)	SYDAD
SEQ ID NO: 68	HCDR3 (CHOTHIA)	GYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 38	HCDR2 (COMBINED)	YISYDADNNYNPSLKN
SEQ ID NO: 68	HCDR3 (COMBINED)	GYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 44	HCDR2 (IMGT)	ISYDADN
SEQ ID NO: 69	HCDR3 (IMGT)	AGGYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 70	VH	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWN WIRQHPGKGLEWMGYISYDADNNYNPSLKNRITISR DTSKNQFSLKLSSVTAADTAVYYCAGGYYRYGLGS YSGSYYYVMDYWGQGTTVTVSS
SEQ ID NO: 71	VH DNA	CAGGTGCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATGGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCCAGCCTGAAGAACAGAATCACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACTCCGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCT
SEQ ID NO: 72	HC	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWN WIRQHPGKGLEWMGYISYDADNNYNPSLKNRITISR DTSKNQFSLKLSSVTAADTAVYYCAGGYYRYGLGS YSGSYYYVMDYWGQGTTVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 73	HC DNA	CAGGTGCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATGGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCCAGCCTGAAGAACAGAATCACCA

		TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACTCCGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCTGCTAGCACCAAGGGCCCAAGTGTGTTTCCCC TGGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACT GCTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCC CGAGCCCGTGACAGTGTCCTGGAACTCTGGGGCTC TGACTTCCGGCGTGCACACCTTCCCCGCCGTGCTG CAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGG TGACAGTGCCCTCCAGCTCTCTGGGAACCCAGACC TATATCTGCAACGTGAACCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGC GACAAGACCCACACCTGCCCCCCCTGCCCAGCTCC AGAACTGCTGGGAGGGCCTTCCGTGTTCCTGTTCC CCCCCAAGCCCAAGGACACCCTGATGATCAGCAG GACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGT CCCACGAGGACCCAGAGGTGAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACAGCACCTACA GGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGAC TGGCTGAACGGCAAAGAATACAAGTGCAAAGTCT CCAACAAGGCCCTGCCAGCCCCAATCGAAAAGAC AATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCC CAGGTGTACACCCTGCCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCCGAGAACAACTACAAGA CCACCCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 50	LCDR1 (KABAT)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEDPPT
SEQ ID NO: 53	LCDR1 (CHOTHIA)	SQSVDYEGHSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 50	LCDR1 (COMBINED)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEDPPT
SEQ ID NO: 56	LCDR1 (IMGT)	QSVDYEGHSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 74	VL	DTQMTQSPSSLSVSVGDRATITCKASQSVDYEGHSY MNWYQQKPGKAPKLLIYAASNLESGVPSRFSGSGSG TDFTLTISSVQPEDFATYYCQQSNEDPPTFGGGTKLEI K
SEQ ID NO: 75	VL DNA	GACACCCAGATGACCCAGTCCCCCTCCTCCCTGTC CGTGTCCGTGGGCGACAGAGCCACCATCACATGCA AGGCCTCCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCAAGG

		CCCCCAAGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCGTGCCCTCCAGATTCTCCGGCTCCGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAG
SEQ ID NO: 76	LC	DTQMTQSPSSLSVSVGDRATITCKASQSVDYEGHSY MNWYQQKPGKAPKLLIYAASNLESGVPSRFSGSGSG TDFTLTISSVQPEDFATYYCQQSNEDPPTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 77	LC DNA	GACACCCAGATGACCCAGTCCCCCTCCTCCCTGTC CGTGTCCGTGGGCGACAGAGCCACCATCACATGCA AGGCCTCCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCAAGG CCCCCAAGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCGTGCCCTCCAGATTCTCCGGCTCCGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAGCGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGCT GAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB7		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 25	VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGTLVTVSS
SEQ ID NO: 26	VH DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC

		ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCCTCC
SEQ ID NO: 27	HC	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 28	HC DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCCTCCGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCCTGGAACTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGG AGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCA AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACTACAAGACCACCCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH

SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 78	VL	EIVLTQSPATLSASPGEEITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAVYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 79	VL DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGGAGATCACCCTGTCCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAAATCA AG
SEQ ID NO: 80	LC	EIVLTQSPATLSASPGEEITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAVYYCHQWSSYPWTFGGGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 81	LC DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGGAGATCACCCTGTCCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTCATCTTC CCCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB8		
SEQ ID NO: 82	HCDR1 (KABAT)	SSSAAWN
SEQ ID NO: 83	HCDR2 (KABAT)	RIYYRSKWYNDYAVSVKS
SEQ ID NO: 84	HCDR3 (KABAT)	GSYVTSSYEGFDY

SEQ ID NO: 85	HCDR1 (CHOTHIA)	GDSVSSSSA
SEQ ID NO: 86	HCDR2 (CHOTHIA)	YYRSKWY
SEQ ID NO: 84	HCDR3 (CHOTHIA)	GSYVTSSYEGFDY
SEQ ID NO: 87	HCDR1 (COMBINED)	GDSVSSSSAAWN
SEQ ID NO: 83	HCDR2 (COMBINED)	RIYYRSKWYNDYAVSVKS
SEQ ID NO: 84	HCDR3 (COMBINED)	GSYVTSSYEGFDY
SEQ ID NO: 88	HCDR1 (IMGT)	GDSVSSSSAA
SEQ ID NO: 89	HCDR2 (IMGT)	IYYRSKWYN
SEQ ID NO: 90	HCDR3 (IMGT)	ARGSYVTSSYEGFDY
SEQ ID NO: 91	VH	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSSSAAWN WIRQSPSRGLEWLGRIYYRSKWYNDYAVSVKSRITIN PDTSKNQFSLQLNSVTPEDTAVYYCARGSYVTSSYE GFDYWGQGTLVTVSS
SEQ ID NO: 92	VH DNA	CAGGTGCAATTGCAGCAGAGCGGTCCGGGCCTGGT GAAACCGAGCCAGACCCTGAGCCTGACCTGCGCG ATTTCCGGAGATAGCGTGAGCTCTAGCTCTGCTGC TTGGAACTGGATTCGTCAGAGCCCGAGCCGTGGCC TCGAGTGGCTGGGCCGTATCTACTACCGTAGCAAA TGGTACAACGACTATGCCGTGAGCGTGAAAAGCC GCATTACCATTAACCCGGATACTTCGAAAAACCAG TTTAGCCTGCAACTGAACAGCGTGACCCCGGAAGA TACGGCCGTGTATTATTGCGCGCGTGGTTCTTACGT TACTTCTTCTTACGAAGGTTTCGATTACTGGGGCCA AGGCACCCTGGTGACTGTTAGCTCA
SEQ ID NO: 93	HC	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSSSAAWN WIRQSPSRGLEWLGRIYYRSKWYNDYAVSVKSRITIN PDTSKNQFSLQLNSVTPEDTAVYYCARGSYVTSSYE GFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK
SEQ ID NO: 94	HC DNA	CAGGTGCAATTGCAGCAGAGCGGTCCGGGCCTGGT GAAACCGAGCCAGACCCTGAGCCTGACCTGCGCG ATTTCCGGAGATAGCGTGAGCTCTAGCTCTGCTGC TTGGAACTGGATTCGTCAGAGCCCGAGCCGTGGCC TCGAGTGGCTGGGCCGTATCTACTACCGTAGCAAA TGGTACAACGACTATGCCGTGAGCGTGAAAAGCC GCATTACCATTAACCCGGATACTTCGAAAAACCAG TTTAGCCTGCAACTGAACAGCGTGACCCCGGAAGA TACGGCCGTGTATTATTGCGCGCGTGGTTCTTACGT TACTTCTTCTTACGAAGGTTTCGATTACTGGGGCCA AGGCACCCTGGTGACTGTTAGCTCAGCCTCCACCA AGGGTCCATCGGTCTTCCCCCTGGCACCCTCCTCC AAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCT GCCTGGTCAAGGACTACTTCCCCGAACCGGTGACG GTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGT GCACACCTTCCCGGCTGTCCTACAGTCCTCAGGAC TCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC AGCAGCTTGGGCACCCAGACCTACATCTGCAACGT

		GAATCACAAGCCCAGCAACACCAAGGTGGACAAG AGAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGG GACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAG GACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCT GAGGTCAAGTTCAACTGGTACGTGGACGGCGTGG AGGTGCATAATGCCAAGACAAAGCCGCGGGAGGA GCAGTACAACAGCACGTACCGGGTGGTCAGCGTCC TCACCGTCCTGCACCAGGACTGGCTGAATGGCAAG GAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCC AGCCCCCATCGAGAAAACCATCTCCAAAGCCAAA GGGCAGCCCCGAGAACCACAGGTGTACACCCTGC CCCCATCCCGGGAGGAGATGACCAAGAACCAGGT CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCA GCGACATCGCCGTGGAGTGGGAGAGCAATGGGCA GCCGGAGAACAACTACAAGACCACGCCTCCCGTG CTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAA GCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGG AACGTCTTCTCATGCTCCGTGATGCATGAGGCTCT GCACAACCACTACACGCAGAAGAGCCTCTCCCTGT CTCCGGGTAAA
SEQ ID NO: 95	LCDR1 (KABAT)	SGDNLPEKYAY
SEQ ID NO: 96	LCDR2 (KABAT)	DDNKRPS
SEQ ID NO: 97	LCDR3 (KABAT)	QSYGKWGWTWV
SEQ ID NO: 98	LCDR1 (CHOTHIA)	DNLPEKY
SEQ ID NO: 99	LCDR2 (CHOTHIA)	DDN
SEQ ID NO: 100	LCDR3 (CHOTHIA)	YGKWGWTW
SEQ ID NO: 95	LCDR1 (COMBINED)	SGDNLPEKYAY
SEQ ID NO: 96	LCDR2 (COMBINED)	DDNKRPS
SEQ ID NO: 97	LCDR3 (COMBINED)	QSYGKWGWTWV
SEQ ID NO: 101	LCDR1 (IMGT)	NLPEKY
SEQ ID NO: 99	LCDR2 (IMGT)	DDN
SEQ ID NO: 97	LCDR3 (IMGT)	QSYGKWGWTWV
SEQ ID NO: 102	VL	SYELTQPLSVSVALGQTARITCSGDNLPEKYAYWYQ QKPGQAPVLVIYDDNKRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCQSYGKWGWTWVFGGGTKLTVL
SEQ ID NO: 103	VL DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATAACCTGCCGGAAAAATACGCTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAAACGTCCGAGCGGCATCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCCAGTCTTACGGTAAATG GGGTTGGACTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 104	LC	SYELTQPLSVSVALGQTARITCSGDNLPEKYAYWYQ QKPGQAPVLVIYDDNKRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCQSYGKWGWTWVFGGGTKLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

SEQ ID NO: 105	LC DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATAACCTGCCGGAAAAATACGCTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAAACGTCCGAGCGGCATCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCCAGTCTTACGGTAAATG GGGTTGGACTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTAGGTCAGCCCAAGGCTGCCCCCTCG GTCACTCTGTTCCCGCCCTCCTCTGAGGAGCTTCAA GCCAACAAGGCCACACTGGTGTGTCTCATAAGTGA CTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGG CAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGAC CACCACACCCTCCAAACAAAGCAACAACAAGTAC GCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCA GTGGAAGTCCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGTGG CCCCTACAGAATGTTCA
ANTI-HUMAN ENTPD2 MAB9		
SEQ ID NO: 106	HCDR1 (KABAT)	SYAVS
SEQ ID NO: 107	HCDR2 (KABAT)	RIVPWLGHTQYAQKFQG
SEQ ID NO: 108	HCDR3 (KABAT)	ESPGYRYSFDV
SEQ ID NO: 109	HCDR1 (CHOTHIA)	GGTFDSY
SEQ ID NO: 110	HCDR2 (CHOTHIA)	VPWLGH
SEQ ID NO: 108	HCDR3 (CHOTHIA)	ESPGYRYSFDV
SEQ ID NO: 111	HCDR1 (COMBINED)	GGTFDSYAVS
SEQ ID NO: 107	HCDR2 (COMBINED)	RIVPWLGHTQYAQKFQG
SEQ ID NO: 108	HCDR3 (COMBINED)	ESPGYRYSFDV
SEQ ID NO: 112	HCDR1 (IMGT)	GGTFDSYA
SEQ ID NO: 113	HCDR2 (IMGT)	IVPWLGHT
SEQ ID NO: 114	HCDR3 (IMGT)	ARESPGYRYSFDV
SEQ ID NO: 115	VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGHTQYAQKFQGRVTI TADESTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLVTVSS
SEQ ID NO: 116	VH DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCCGGGCCAGGGCCTCGAG TGGATGGGCCGTATCGTTCCGTGGCTGGGCCATAC TCAGTACGCCCAGAAATTTCAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCA
SEQ ID NO: 117	HC	QVQLVQSGAEVKKPGSSVKVSCKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGHTQYAQKFQGRVTI TADESTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK

		RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
SEQ ID NO: 118	HC DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCCGGGCCAGGGCCTCGAG TGGATGGGCCGTATCGTTCCGTGGCTGGGCCATAC TCAGTACGCCCAGAAATTTCAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGT CTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCA CCCAGACCTACATCTGCAACGTGAATCACAAGCCC AGCAACACCAAGGTGGACAAGAGAGTTGAGCCCA AATCTTGTGACAAAACTCACACATGCCCACCGTGC CCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCCAAAACCCAAGGACACCCTCATGA TCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCA ACTGGTACGTGGACGGCGTGGAGGTGCATAATGCC AAGACAAAGCCGCGGGAGGAGCAGTACAACAGCA CGTACCGGGTGGTCAGCGTCCTCACCGTCCTGCAC CAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAG AACCACAGGTGTACACCCTGCCCCCATCCCGGGAG GAGATGACCAAGAACCAGGTCAGCCTGACCTGCCT GGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGG AGTGGGAGAGCAATGGGCAGCCGGAGAACAACTA CAAGACCACGCCTCCCGTGCTGGACTCCGACGGCT CCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGC AGAAGAGCCTCTCCCTGTCTCCGGGTAAA
SEQ ID NO: 119	LCDR1 (KABAT)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (KABAT)	DDNNRPS
SEQ ID NO: 121	LCDR3 (KABAT)	ASYDLQQARWV
SEQ ID NO: 122	LCDR1 (CHOTHIA)	DAIGEKY
SEQ ID NO: 99	LCDR2 (CHOTHIA)	DDN
SEQ ID NO: 123	LCDR3 (CHOTHIA)	YDLQQARW
SEQ ID NO: 119	LCDR1 (COMBINED)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (COMBINED)	DDNNRPS
SEQ ID NO: 121	LCDR3 (COMBINED)	ASYDLQQARWV

SEQ ID NO: 124	LCDR1 (IMGT)	AIGEKY
SEQ ID NO: 99	LCDR2 (IMGT)	DDN
SEQ ID NO: 121	LCDR3 (IMGT)	ASYDLQQARWV
SEQ ID NO: 125	VL	SYELTQPLSVSVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL
SEQ ID NO: 126	VL DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 127	LC	SYELTQPLSVSVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 128	LC DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTAGGTCAGCCCAAGGCTGCCCCCTCG GTCACTCTGTTCCCGCCCTCCTCTGAGGAGCTTCAA GCCAACAAGGCCACACTGGTGTGTCTCATAAGTGA CTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGG CAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGAC CACCACACCCTCCAAACAAAGCAACAACAAGTAC GCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCA GTGGAAGTCCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGTGG CCCCTACAGAATGTTCA
ANTI-HUMAN ENTPD2 MAB10		
SEQ ID NO: 106	HCDR1 (KABAT)	SYAVS
SEQ ID NO: 129	HCDR2 (KABAT)	RIVPWLGFTRYAQKFQG
SEQ ID NO: 108	HCDR3 (KABAT)	ESPGYRYSFDV
SEQ ID NO: 109	HCDR1 (CHOTHIA)	GGTFDSY
SEQ ID NO: 130	HCDR2 (CHOTHIA)	VPWLGF
SEQ ID NO: 108	HCDR3 (CHOTHIA)	ESPGYRYSFDV
SEQ ID NO: 111	HCDR1 (COMBINED)	GGTFDSYAVS
SEQ ID NO: 129	HCDR2 (COMBINED)	RIVPWLGFTRYAQKFQG
SEQ ID NO: 108	HCDR3 (COMBINED)	ESPGYRYSFDV
SEQ ID NO: 112	HCDR1 (IMGT)	GGTFDSYA
SEQ ID NO: 131	HCDR2 (IMGT)	IVPWLGFT

SEQ ID NO: 114	HCDR3 (IMGT)	ARESPGYRYSFDV
SEQ ID NO: 132	VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGFTRYAQKFQGRVTI TADESTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLVTVSS
SEQ ID NO: 133	VH DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCCGGGCCAGGGCCTCGAG TGGATGGGCCGTATCGTTCCGTGGCTGGGCTTCAC TCGTTACGCCCAGAAATTTCAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCA
SEQ ID NO: 134	HC	QVQLVQSGAEVKKPGSSVKVSCKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGFTRYAQKFQGRVTI TADESTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
SEQ ID NO: 135	HC DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCCGGGCCAGGGCCTCGAG TGGATGGGCCGTATCGTTCCGTGGCTGGGCTTCAC TCGTTACGCCCAGAAATTTCAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGT CTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCGTGGAACT CAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCA CCCAGACCTACATCTGCAACGTGAATCACAAGCCC AGCAACACCAAGGTGGACAAGAGAGTTGAGCCCA AATCTTGTGACAAAACTCACACATGCCCACCGTGC CCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCCAAAACCCAAGGACACCCTCATGA TCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCA ACTGGTACGTGGACGGCGTGGAGGTGCATAATGCC AAGACAAAGCCGCGGGAGGAGCAGTACAACAGCA CGTACCGGGTGGTCAGCGTCCTCACCGTCCTGCAC CAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAG AACCACAGGTGTACACCCTGCCCCCATCCCGGGAG

		GAGATGACCAAGAACCAGGTCAGCCTGACCTGCCT GGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGG AGTGGGAGAGCAATGGGCAGCCGGAGAACAACTA CAAGACCACGCCTCCCGTGCTGGACTCCGACGGCT CCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGC AGAAGAGCCTCTCCCTGTCTCCGGGTAAA
SEQ ID NO: 119	LCDR1 (KABAT)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (KABAT)	DDNNRPS
SEQ ID NO: 121	LCDR3 (KABAT)	ASYDLQQARWV
SEQ ID NO: 122	LCDR1 (CHOTHIA)	DAIGEKY
SEQ ID NO: 99	LCDR2 (CHOTHIA)	DDN
SEQ ID NO: 123	LCDR3 (CHOTHIA)	YDLQQARW
SEQ ID NO: 119	LCDR1 (COMBINED)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (COMBINED)	DDNNRPS
SEQ ID NO: 121	LCDR3 (COMBINED)	ASYDLQQARWV
SEQ ID NO: 124	LCDR1 (IMGT)	AIGEKY
SEQ ID NO: 99	LCDR2 (IMGT)	DDN
SEQ ID NO: 121	LCDR3 (IMGT)	ASYDLQQARWV
SEQ ID NO: 125	VL	SYELTQPLSVSVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL
SEQ ID NO: 126	VL DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 127	LC	SYELTQPLSVSVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 128	LC DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTAGGTCAGCCCAAGGCTGCCCCCTCG GTCACTCTGTTCCCGCCCTCCTCTGAGGAGCTTCAA GCCAACAAGGCCACACTGGTGTGTCTCATAAGTGA CTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGG CAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGAC CACCACACCCTCCAAACAAAGCAACAACAAGTAC

		GCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCA GTGGAAGTCCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGTGG CCCCTACAGAATGTTCA
ANTI-HUMAN ENTPD2 MAB11		
SEQ ID NO: 136	HCDR1 (KABAT)	SYAMS
SEQ ID NO: 137	HCDR2 (KABAT)	VISGSGGSTYYADSVKG
SEQ ID NO: 138	HCDR3 (KABAT)	GDDYGDDYYYYGMDV
SEQ ID NO: 139	HCDR1 (CHOTHIA)	GFTFSSY
SEQ ID NO: 140	HCDR2 (CHOTHIA)	SGSGGS
SEQ ID NO: 138	HCDR3 (CHOTHIA)	GDDYGDDYYYYGMDV
SEQ ID NO: 141	HCDR1 (COMBINED)	GFTFSSYAMS
SEQ ID NO: 137	HCDR2 (COMBINED)	VISGSGGSTYYADSVKG
SEQ ID NO: 138	HCDR3 (COMBINED)	GDDYGDDYYYYGMDV
SEQ ID NO: 142	HCDR1 (IMGT)	GFTFSSYA
SEQ ID NO: 143	HCDR2 (IMGT)	ISGSGGST
SEQ ID NO: 144	HCDR3 (IMGT)	ARGDDYGDDYYYYGMDV
SEQ ID NO: 145	VH	EVQLLESGGGLVQSGGSLRLSCAASGFTFSSYAMSW VRQAPGKGLEWVSVISGSGGSTYYADSVKGRFTISR DNSKNTLYLQMNSLRAEDTAVYYCARGDDYGDDY YYYGMDVWGQGTTVTVSS
SEQ ID NO: 146	VH DNA	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGT ACAGTCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGATTCACCTTTAGCAGCTATGCCATGAGC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTCTCAGTTATTAGTGGTAGTGGTGGTAGCACA TACTACGCAGACTCCGTGAAGGGCCGGTTCACCAT CTCCAGAGACAATTCCAAGAACACGCTGTATCTGC AAATGAACAGCCTGAGAGCCGAGGACACGGCCGT ATATTACTGTGCGAGAGGGGATGACTACGGTGACG ACTACTACTACTACGGTATGGACGTCTGGGGCCAA GGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 147	HC	EVQLLESGGGLVQSGGSLRLSCAASGFTFSSYAMSW VRQAPGKGLEWVSVISGSGGSTYYADSVKGRFTISR DNSKNTLYLQMNSLRAEDTAVYYCARGDDYGDDY YYYGMDVWGQGTTVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 148	HC DNA	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGT ACAGTCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGATTCACCTTTAGCAGCTATGCCATGAGC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTCTCAGTTATTAGTGGTAGTGGTGGTAGCACA TACTACGCAGACTCCGTGAAGGGCCGGTTCACCAT CTCCAGAGACAATTCCAAGAACACGCTGTATCTGC

		AAATGAACAGCCTGAGAGCCGAGGACACGGCCGT ATATTACTGTGCGAGAGGGGATGACTACGGTGACG ACTACTACTACTACGGTATGGACGTCTGGGGCCAA GGGACCACGGTCACCGTCTCCTCAGCTAGCACCAA GGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAGCA AGTCTACTTCCGGCGGAACTGCTGCCCTGGGTTGC CTGGTGAAGGACTACTTCCCCGAGCCCGTGACAGT GTCCTGGAACTCTGGGGCTCTGACTTCCGGCGTGC ACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCTG TACAGCCTGAGCAGCGTGGTGACAGTGCCCTCCAG CTCTCTGGGAACCCAGACCTATATCTGCAACGTGA ACCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTGGAGCCCAAGAGCTGCGACAAGACCCACACC TGCCCCCCCTGCCCAGCTCCAGAACTGCTGGGAGG GCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCAAGG ACACCCTGATGATCAGCAGGACCCCCGAGGTGACC TGCGTGGTGGTGGACGTGTCCCACGAGGACCCAGA GGTGAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCCAGAGAGGAGC AGTACAACAGCACCTACAGGGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGACTGGCTGAACGGCAAAG AATACAAGTGCAAAGTCTCCAACAAGGCCCTGCCA GCCCCAATCGAAAAGACAATCAGCAAGGCCAAGG GCCAGCCACGGGAGCCCCAGGTGTACACCCTGCCC CCCAGCCGGGAGGAGATGACCAAGAACCAGGTGT CCCTGACCTGTCTGGTGAAGGGCTTCTACCCCAGC GATATCGCCGTGGAGTGGGAGAGCAACGGCCAGC CCGAGAACAACTACAAGACCACCCCCCCAGTGCTG GACAGCGACGGCAGCTTCTTCCTGTACAGCAAGCT GACCGTGGACAAGTCCAGGTGGCAGCAGGGCAAC GTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGTCCCTGAGCCTGAGCC CCGGCAAG
SEQ ID NO: 149	LCDR1 (KABAT)	RSSQSLLHGNRYNYLD
SEQ ID NO: 150	LCDR2 (KABAT)	LGSNRAS
SEQ ID NO: 151	LCDR3 (KABAT)	MQALQTPPT
SEQ ID NO: 152	LCDR1 (CHOTHIA)	SQSLLHGNRYNY
SEQ ID NO: 153	LCDR2 (CHOTHIA)	LGS
SEQ ID NO: 154	LCDR3 (CHOTHIA)	ALQTPP
SEQ ID NO: 149	LCDR1 (COMBINED)	RSSQSLLHGNRYNYLD
SEQ ID NO: 150	LCDR2 (COMBINED)	LGSNRAS
SEQ ID NO: 151	LCDR3 (COMBINED)	MQALQTPPT
SEQ ID NO: 155	LCDR1 (IMGT)	QSLLHGNRYNY
SEQ ID NO: 153	LCDR2 (IMGT)	LGS
SEQ ID NO: 151	LCDR3 (IMGT)	MQALQTPPT
SEQ ID NO: 156	VL	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHGNRYNYL DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPPTFGQGTKVE IK
SEQ ID NO: 157	VL DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATGGTAATCGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG

		GCCTCCGGGGTCCCTGACAGGTTCAGTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAAACTCCTCCGACGTTCGGCCAAGG GACCAAGGTGGAAATCAAA
SEQ ID NO: 158	LC	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHGNRYNYL DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPPTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 159	LC DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATGGTAATCGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG GCCTCCGGGGTCCCTGACAGGTTCAGTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAAACTCCTCCGACGTTCGGCCAAGG GACCAAGGTGGAAATCAAACGAACTGTGGCTGCA CCAAGCGTGTTCATCTTCCCCCCCAGCGACGAGCA GCTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGC TGAACAACTTCTACCCCCGGGAGGCCAAGGTGCAG TGGAAGGTGGACAACGCCCTGCAGAGCGGCAACA GCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGA CTCCACCTACAGCCTGAGCAGCACCCTGACCCTGA GCAAGGCCGACTACGAGAAGCATAAGGTGTACGC CTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCG TGACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB12		
SEQ ID NO: 160	HCDR1 (KABAT)	SCSMN
SEQ ID NO: 161	HCDR2 (KABAT)	YISSSSSTIYYADSVKG
SEQ ID NO: 162	HCDR3 (KABAT)	DQGNWNYDDYYNGLDV
SEQ ID NO: 163	HCDR1 (CHOTHIA)	GFTFNSC
SEQ ID NO: 164	HCDR2 (CHOTHIA)	SSSSST
SEQ ID NO: 162	HCDR3 (CHOTHIA)	DQGNWNYDDYYNGLDV
SEQ ID NO: 165	HCDR1 (COMBINED)	GFTFNSCSMN
SEQ ID NO: 161	HCDR2 (COMBINED)	YISSSSSTIYYADSVKG
SEQ ID NO: 162	HCDR3 (COMBINED)	DQGNWNYDDYYNGLDV
SEQ ID NO: 166	HCDR1 (IMGT)	GFTFNSCS
SEQ ID NO: 167	HCDR2 (IMGT)	ISSSSSTI
SEQ ID NO: 168	HCDR3 (IMGT)	ARDQGNWNYDDYYNGLDV
SEQ ID NO: 169	VH	EVLLVESGGGLVQPGGSLRLSCAASGFTFNSCSMNW VRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRD NAKNSLYLQMNSLKDEDTAVYYCARDQGNWNYDD YYNGLDVWGQGTTVTVSS
SEQ ID NO: 170	VH DNA	GAGGTGCTGCTGGTGGAGTCTGGGGGAGGCTTGGT ACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGGTTCACCTTCAATAGCTGTAGCATGAAC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTTTCATACATTAGTAGTAGTAGTAGTACCATT TACTACGCAGACTCTGTGAAGGGCCGATTCACCAT

		CTCCAGAGACAATGCCAAGAACTCACTGTATCTGC AAATGAACAGCCTGAAAGACGAGGACACGGCTGT GTATTACTGTGCGAGAGATCAGGGTAACTGGAACT ACGACGACTACTACAACGGTTTGGACGTCTGGGGC CAAGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 171	HC	EVLLVESGGGLVQPGGSLRLSCAASGFTFNSCSMNW VRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRD NAKNSLYLQMNSLKDEDTAVYYCARDQGNWNYDD YYNGLDVWGQGTTVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 172	HC DNA	GAGGTGCTGCTGGTGGAGTCTGGGGGAGGCTTGGT ACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGGTTCACCTTCAATAGCTGTAGCATGAAC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTTTCATACATTAGTAGTAGTAGTAGTACCATT TACTACGCAGACTCTGTGAAGGGCCGATTCACCAT CTCCAGAGACAATGCCAAGAACTCACTGTATCTGC AAATGAACAGCCTGAAAGACGAGGACACGGCTGT GTATTACTGTGCGAGAGATCAGGGTAACTGGAACT ACGACGACTACTACAACGGTTTGGACGTCTGGGGC CAAGGGACCACGGTCACCGTCTCCTCAGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCCTGGAACTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGG AGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCA AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACTACAAGACCACCCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 173	LCDR1 (KABAT)	RSSQSLLHSNGYNYLD

SEQ ID NO: 150	LCDR2 (KABAT)	LGSNRAS
SEQ ID NO: 174	LCDR3 (KABAT)	MQALQTPLT
SEQ ID NO: 175	LCDR1 (CHOTHIA)	SQSLLHSNGYNY
SEQ ID NO: 153	LCDR2 (CHOTHIA)	LGS
SEQ ID NO: 176	LCDR3 (CHOTHIA)	ALQTPL
SEQ ID NO: 173	LCDR1 (COMBINED)	RSSQSLLHSNGYNYLD
SEQ ID NO: 150	LCDR2 (COMBINED)	LGSNRAS
SEQ ID NO: 174	LCDR3 (COMBINED)	MQALQTPLT
SEQ ID NO: 177	LCDR1 (IMGT)	QSLLHSNGYNY
SEQ ID NO: 153	LCDR2 (IMGT)	LGS
SEQ ID NO: 174	LCDR3 (IMGT)	MQALQTPLT
SEQ ID NO: 178	VL	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYL DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVE IK
SEQ ID NO: 179	VL DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACTCCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATAGTAATGGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG GCCTCCGGGGTCCCTGACAGGTTCAGTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAAACTCCTCTCACTTTCGGCGGAGG GACCAAGGTGGAGATCAAA
SEQ ID NO: 180	LC	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYL DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 181	LC DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACTCCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATAGTAATGGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG GCCTCCGGGGTCCCTGACAGGTTCAGTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAAACTCCTCTCACTTTCGGCGGAGG GACCAAGGTGGAGATCAAACGTACGGTGGCCGCT CCCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCA GCTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGC TGAACAACTTCTACCCCCGGGAGGCCAAGGTGCAG TGGAAGGTGGACAACGCCCTGCAGAGCGGCAACA GCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGA CTCCACCTACAGCCTGAGCAGCACCCTGACCCTGA GCAAGGCCGACTACGAGAAGCATAAGGTGTACGC CTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCG TGACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB16		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 220	HCDR2 (KABAT)	YISYDGDNNYNPSLKN

SEQ ID NO: 221	HCDR3 (KABAT)	GYYRYGLSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 222	HCDR2 (CHOTHIA)	SYDGD
SEQ ID NO: 221	HCDR3 (CHOTHIA)	GYYRYGLSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 220	HCDR2 (COMBINED)	YISYDGDNNYNPSLKN
SEQ ID NO: 221	HCDR3 (COMBINED)	GYYRYGLSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 223	HCDR2 (IMGT)	ISYDGDN
SEQ ID NO: 224	HCDR3 (IMGT)	AGGYYRYGLSYYYVMDY
SEQ ID NO: 225	VH	DIQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTTEDTATYYCAGGYYRYGLSYYYV MDYWGQGTSVTVSS
SEQ ID NO: 226	VH DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTTCCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GTCGTATTACTATGTTATGGACTACTGGGGTCAAG GAACCTCAGTCACCGTCTCCTCA
SEQ ID NO: 227	HC	DIQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTTEDTATYYCAGGYYRYGLSYYYV MDYWGQGTSVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK
SEQ ID NO: 228	HC DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTTCCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GTCGTATTACTATGTTATGGACTACTGGGGTCAAG GAACCTCAGTCACCGTCTCCTCAGCTAGCACCAAG GGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAGCAA GTCTACTTCCGGCGGAACTGCTGCCCTGGGTTGCC TGGTGAAGGACTACTTCCCCGAGCCCGTGACAGTG TCCTGGAACTCTGGGGCTCTGACTTCCGGCGTGCA CACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCTGT ACAGCCTGAGCAGCGTGGTGACAGTGCCCTCCAGC

		TCTCTGGGAACCCAGACCTATATCTGCAACGTGAA CCACAAGCCCAGCAACACCAAGGTGGACAAGAGA GTGGAGCCCAAGAGCTGCGACAAGACCCACACCT GCCCCCCCTGCCCAGCTCCAGAACTGCTGGGAGGG CCTTCCGTGTTCCTGTTCCCCCCCAAGCCCAAGGA CACCCTGATGATCAGCAGGACCCCCGAGGTGACCT GCGTGGTGGTGGACGTGTCCCACGAGGACCCAGA GGTGAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCCAGAGAGGAGC AGTACAACAGCACCTACAGGGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGACTGGCTGAACGGCAAAG AATACAAGTGCAAAGTCTCCAACAAGGCCCTGCCA GCCCCAATCGAAAAGACAATCAGCAAGGCCAAGG GCCAGCCACGGGAGCCCCAGGTGTACACCCTGCCC CCCAGCCGGGAGGAGATGACCAAGAACCAGGTGT CCCTGACCTGTCTGGTGAAGGGCTTCTACCCCAGC GATATCGCCGTGGAGTGGGAGAGCAACGGCCAGC CCGAGAACAACTACAAGACCACCCCCCCAGTGCTG GACAGCGACGGCAGCTTCTTCCTGTACAGCAAGCT GACCGTGGACAAGTCCAGGTGGCAGCAGGGCAAC GTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGTCCCTGAGCCTGAGCC CCGGCAAG
SEQ ID NO: 61	LCDR1 (KABAT)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEDPPT
SEQ ID NO: 62	LCDR1 (CHOTHIA)	SQSVDYDGNSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 61	LCDR1 (COMBINED)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEDPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDYDGNSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 229	VL	DTVLTQSPASLAVSLGQRATISCKASQSVDYDGNSY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGT DFTLNIHPVEEEDAATYYCQQSNEDPPTFGGGTKLEI K
SEQ ID NO: 230	VL DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAAATCAAA
SEQ ID NO: 231	LC	DTVLTQSPASLAVSLGQRATISCKASQSVDYDGNSY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGT DFTLNIHPVEEEDAATYYCQQSNEDPPTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE

		AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 232	LC DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAAATCAAACGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGCT GAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB17		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 233	VH	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSS
SEQ ID NO: 234	VH DNA	GAGGTCCAACTGCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 235	HC	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS

		GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 236	HC DNA	GAGGTCCAACTGCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCAGCTAGCACCA AGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAGC AAGTCTACTTCCGGCGGAACTGCTGCCCTGGGTTG CCTGGTGAAGGACTACTTCCCCGAGCCCGTGACAG TGTCCTGGAACTCTGGGGCTCTGACTTCCGGCGTG CACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCT GTACAGCCTGAGCAGCGTGGTGACAGTGCCCTCCA GCTCTCTGGGAACCCAGACCTATATCTGCAACGTG AACCACAAGCCCAGCAACACCAAGGTGGACAAGA GAGTGGAGCCCAAGAGCTGCGACAAGACCCACAC CTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGGAG GGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCAAG GACACCCTGATGATCAGCAGGACCCCCGAGGTGA CCTGCGTGGTGGTGGACGTGTCCCACGAGGACCCA GAGGTGAAGTTCAACTGGTACGTGGACGGCGTGG AGGTGCACAACGCCAAGACCAAGCCCAGAGAGGA GCAGTACAACAGCACCTACAGGGTGGTGTCCGTGC TGACCGTGCTGCACCAGGACTGGCTGAACGGCAA AGAATACAAGTGCAAAGTCTCCAACAAGGCCCTG CCAGCCCCAATCGAAAAGACAATCAGCAAGGCCA AGGGCCAGCCACGGGAGCCCCAGGTGTACACCCT GCCCCCCAGCCGGGAGGAGATGACCAAGAACCAG GTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACCC CAGCGATATCGCCGTGGAGTGGGAGAGCAACGGC CAGCCCGAGAACAACTACAAGACCACCCCCCCAG TGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGC AAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGTCCCTGAGCCT GAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH

SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 237	VL	QIVLTQSPAIMSASLGEEITLTCSASSSVSYIHWYQQK SGTSPTLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 238	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACACTGGTACC AGCAGAAGTCAGGCACTTCTCCCACACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 239	LC	QIVLTQSPAIMSASLGEEITLTCSASSSVSYIHWYQQK SGTSPTLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 240	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACACTGGTACC AGCAGAAGTCAGGCACTTCTCCCACACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB18		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 220	HCDR2 (KABAT)	YISYDGDNNYNPSLKN
SEQ ID NO: 68	HCDR3 (KABAT)	GYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 222	HCDR2 (CHOTHIA)	SYDGD
SEQ ID NO: 68	HCDR3 (CHOTHIA)	GYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 220	HCDR2 (COMBINED)	YISYDGDNNYNPSLKN

SEQ ID NO: 68	HCDR3 (COMBINED)	GYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 223	HCDR2 (IMGT)	ISYDGDN
SEQ ID NO: 69	HCDR3 (IMGT)	AGGYYRYGLGSYSGSYYYVMDY
SEQ ID NO: 241	VH	DIQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTTEDTATYYCAGGYYRYGLGSYSG SYYYVMDYWGQGTSVTVSS
SEQ ID NO: 242	VH DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTTCCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GGGCTCCTACTCCGGCTCGTATTACTATGTTATGG ACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCC TCA
SEQ ID NO: 243	HC	DIQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTTEDTATYYCAGGYYRYGLGSYSG SYYYVMDYWGQGTSVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 244	HC DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTTCCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GGGCTCCTACTCCGGCTCGTATTACTATGTTATGG ACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCC TCAGCTAGCACCAAGGGCCCAAGTGTGTTTCCCCT GGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACTG CTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCCC GAGCCCGTGACAGTGTCCTGGAACTCTGGGGCTCT GACTTCCGGCGTGCACACCTTCCCCGCCGTGCTGC AGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGT GACAGTGCCCTCCAGCTCTCTGGGAACCCAGACCT ATATCTGCAACGTGAACCACAAGCCCAGCAACACC AAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGCG ACAAGACCCACACCTGCCCCCCCTGCCCAGCTCCA GAACTGCTGGGAGGGCCTTCCGTGTTCCTGTTCCC CCCCAAGCCCAAGGACACCCTGATGATCAGCAGG ACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTC CCACGAGGACCCAGAGGTGAAGTTCAACTGGTAC

		GTGGACGGCGTGGAGGTGCACAACGCCAAGACCA AGCCCAGAGAGGAGCAGTACAACAGCACCTACAG GGTGGTGTCCGTGCTGACCGTGCTGCACCAGGACT GGCTGAACGGCAAAGAATACAAGTGCAAAGTCTC CAACAAGGCCCTGCCAGCCCCAATCGAAAAGACA ATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCCC AGGTGTACACCCTGCCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCCGAGAACAACTACAAGA CCACCCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 61	LCDR1 (KABAT)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEDPPT
SEQ ID NO: 62	LCDR1 (CHOTHIA)	SQSVDYDGNSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 61	LCDR1 (COMBINED)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEDPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDYDGNSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 229	VL	DTVLTQSPASLAVSLGQRATISCKASQSVDYDGNSY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGT DFTLNIHPVEEEDAATYYCQQSNEDPPTFGGGTKLEI K
SEQ ID NO: 230	VL DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAAATCAAA
SEQ ID NO: 231	LC	DTVLTQSPASLAVSLGQRATISCKASQSVDYDGNSY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGT DFTLNIHPVEEEDAATYYCQQSNEDPPTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 232	LC DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG

		TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAAATCAAACGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGCT GAACAACTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB19		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 245	HCDR2 (KABAT)	DINPNYDITTYNQRFKG
SEQ ID NO: 246	HCDR3 (KABAT)	RGFFPYYGNSYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 247	HCDR2 (CHOTHIA)	NPNYDI
SEQ ID NO: 246	HCDR3 (CHOTHIA)	RGFFPYYGNSYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 245	HCDR2 (COMBINED)	DINPNYDITTYNQRFKG
SEQ ID NO: 246	HCDR3 (COMBINED)	RGFFPYYGNSYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 248	HCDR2 (IMGT)	INPNYDIT
SEQ ID NO: 249	HCDR3 (IMGT)	ARRGFFPYYGNSYYYFDV
SEQ ID NO: 250	VH	EVQLQQFGAELVKPGTSVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITTYNQRFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFPYYGN SYYYFDVWGAGTTVTVSS
SEQ ID NO: 251	VH DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGACTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT ACCTACAACCAGAGGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGATTTTTTCCTTATTA CGGTAATAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 252	HC	EVQLQQFGAELVKPGTSVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITTYNQRFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFPYYGN SYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 253	HC DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGACTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT ACCTACAACCAGAGGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGATTTTTTCCTTATTA CGGTAATAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCAGCTAGCACC AAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAG CAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGTT GCCTGGTGAAGGACTACTTCCCCGAGCCCGTGACA GTGTCCTGGAACTCTGGGGCTCTGACTTCCGGCGT GCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCC TGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTCC AGCTCTCTGGGAACCCAGACCTATATCTGCAACGT GAACCACAAGCCCAGCAACACCAAGGTGGACAAG AGAGTGGAGCCCAAGAGCTGCGACAAGACCCACA CCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGGA GGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCAA GGACACCCTGATGATCAGCAGGACCCCCGAGGTG ACCTGCGTGGTGGTGGACGTGTCCCACGAGGACCC AGAGGTGAAGTTCAACTGGTACGTGGACGGCGTG GAGGTGCACAACGCCAAGACCAAGCCCAGAGAGG AGCAGTACAACAGCACCTACAGGGTGGTGTCCGTG CTGACCGTGCTGCACCAGGACTGGCTGAACGGCAA AGAATACAAGTGCAAAGTCTCCAACAAGGCCCTG CCAGCCCCAATCGAAAAGACAATCAGCAAGGCCA AGGGCCAGCCACGGGAGCCCCAGGTGTACACCCT GCCCCCCAGCCGGGAGGAGATGACCAAGAACCAG GTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACCC CAGCGATATCGCCGTGGAGTGGGAGAGCAACGGC CAGCCCGAGAACAACTACAAGACCACCCCCCCAG TGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGC AAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGTCCCTGAGCCT GAGCCCCGGCAAG
SEQ ID NO: 254	LCDR1 (KABAT)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 255	LCDR3 (KABAT)	HQWSNYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 256	LCDR3 (CHOTHIA)	WSNYPW
SEQ ID NO: 254	LCDR1 (COMBINED)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 255	LCDR3 (COMBINED)	HQWSNYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 255	LCDR3 (IMGT)	HQWSNYPWT

SEQ ID NO: 257	VL	QIVLTQSPTIMSASLGEEITLTCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSNYPWTFGGGTKLEIK
SEQ ID NO: 258	VL DNA	CAAATTGTTCTCACCCAGTCTCCAACAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTTACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCCAAACTCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAATTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 259	LC	QIVLTQSPTIMSASLGEEITLTCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSNYPWTFGGGTKLEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADY EKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 260	LC DNA	CAAATTGTTCTCACCCAGTCTCCAACAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTTACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCCAAACTCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAATTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB20		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 261	HCDR2 (KABAT)	DINPNYDITSYNQKFKG
SEQ ID NO: 262	HCDR3 (KABAT)	RGFFLYYGSSYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 247	HCDR2 (CHOTHIA)	NPNYDI
SEQ ID NO: 262	HCDR3 (CHOTHIA)	RGFFLYYGSSYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 261	HCDR2 (COMBINED)	DINPNYDITSYNQKFKG
SEQ ID NO: 262	HCDR3 (COMBINED)	RGFFLYYGSSYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 248	HCDR2 (IMGT)	INPNYDIT
SEQ ID NO: 263	HCDR3 (IMGT)	ARRGFFLYYGSSYYYFDV
SEQ ID NO: 264	VH	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITSYNQKFKGKATLT

		VDKSSSTAYMELRSLTSEDTAVYYCARRGFFLYYGS SYYYFDVWGAGTTVTVSS
SEQ ID NO: 265	VH DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT AGCTACAACCAGAAGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGGTTTTTTCTTTACTA CGGTAGTAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 266	HC	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITSYNQKFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFLYYGS SYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 267	HC DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT AGCTACAACCAGAAGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGGTTTTTTCTTTACTA CGGTAGTAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCAGCTAGCACC AAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAG CAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGTT GCCTGGTGAAGGACTACTTCCCCGAGCCCGTGACA GTGTCCTGGAACTCTGGGGCTCTGACTTCCGGCGT GCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCC TGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTCC AGCTCTCTGGGAACCCAGACCTATATCTGCAACGT GAACCACAAGCCCAGCAACACCAAGGTGGACAAG AGAGTGGAGCCCAAGAGCTGCGACAAGACCCACA CCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGGGA GGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCAA GGACACCCTGATGATCAGCAGGACCCCCGAGGTG ACCTGCGTGGTGGTGGACGTGTCCCACGAGGACCC AGAGGTGAAGTTCAACTGGTACGTGGACGGCGTG GAGGTGCACAACGCCAAGACCAAGCCCAGAGAGG AGCAGTACAACAGCACCTACAGGGTGGTGTCCGTG CTGACCGTGCTGCACCAGGACTGGCTGAACGGCAA AGAATACAAGTGCAAAGTCTCCAACAAGGCCCTG CCAGCCCCAATCGAAAAGACAATCAGCAAGGCCA AGGGCCAGCCACGGGAGCCCCAGGTGTACACCCT GCCCCCCAGCCGGGAGGAGATGACCAAGAACCAG GTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACCC CAGCGATATCGCCGTGGAGTGGGAGAGCAACGGC

		CAGCCCGAGAACAACTACAAGACCACCCCCCCAG TGCTGGACAGCGACGGCAGCTTCTTCCTGTACAGC AAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGTCCCTGAGCCT GAGCCCCGGCAAG
SEQ ID NO: 254	LCDR1 (KABAT)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 254	LCDR1 (COMBINED)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 268	VL	QIVLTQSPAIMSASLGEEITLTCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 269	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCCAAACTCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 270	LC	QIVLTQSPAIMSASLGEEITLTCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGTKLEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADY EKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 271	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCCAAACTCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC

		CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB21		
SEQ ID NO: 272	HCDR1 (KABAT)	EYTMH
SEQ ID NO: 273	HCDR2 (KABAT)	GINPNNGITTYNQKFKG
SEQ ID NO: 274	HCDR3 (KABAT)	RGFPIYYYGTSLYYFDY
SEQ ID NO: 275	HCDR1 (CHOTHIA)	GYTFTEY
SEQ ID NO: 276	HCDR2 (CHOTHIA)	NPNNGI
SEQ ID NO: 274	HCDR3 (CHOTHIA)	RGFPIYYYGTSLYYFDY
SEQ ID NO: 277	HCDR1 (COMBINED)	GYTFTEYTMH
SEQ ID NO: 273	HCDR2 (COMBINED)	GINPNNGITTYNQKFKG
SEQ ID NO: 274	HCDR3 (COMBINED)	RGFPIYYYGTSLYYFDY
SEQ ID NO: 278	HCDR1 (IMGT)	GYTFTEYT
SEQ ID NO: 279	HCDR2 (IMGT)	INPNNGIT
SEQ ID NO: 280	HCDR3 (IMGT)	ARRGFPIYYYGTSLYYFDY
SEQ ID NO: 281	VH	EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHW VKQSHGKSLEWIGGINPNNGITTYNQKFKGKATLTV DKSSSTAYMDLRSLTSEGSAVYYCARRGFPIYYYGTS LYYFDYWGQGTTLTVSS
SEQ ID NO: 282	VH DNA	GAGGTCCAGCTGCAACAGTCTGGACCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGA CTTCTGGATACACATTCACTGAATACACCATGCAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGGTATTAATCCTAACAATGGTATTACT ACTTACAACCAGAAGTTCAAGGGCAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG ACCTCCGCAGCCTGACATCTGAGGGTTCTGCAGTC TATTACTGTGCAAGAAGGGGATTCCCTATTTATTA CTACGGTACTAGCCTCTACTACTTTGACTACTGGG GCCAAGGCACCACTCTCACAGTCTCCTCA
SEQ ID NO: 283	HC	EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHW VKQSHGKSLEWIGGINPNNGITTYNQKFKGKATLTV DKSSSTAYMDLRSLTSEGSAVYYCARRGFPIYYYGTS LYYFDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 284	HC DNA	GAGGTCCAGCTGCAACAGTCTGGACCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGA CTTCTGGATACACATTCACTGAATACACCATGCAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGGTATTAATCCTAACAATGGTATTACT ACTTACAACCAGAAGTTCAAGGGCAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG ACCTCCGCAGCCTGACATCTGAGGGTTCTGCAGTC TATTACTGTGCAAGAAGGGGATTCCCTATTTATTA CTACGGTACTAGCCTCTACTACTTTGACTACTGGG

		GCCAAGGCACCACTCTCACAGTCTCCTCAGCTAGC ACCAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAG CAGCAAGTCTACTTCCGGCGGAACTGCTGCCCTGG GTTGCCTGGTGAAGGACTACTTCCCCGAGCCCGTG ACAGTGTCCTGGAACTCTGGGGCTCTGACTTCCGG CGTGCACACCTTCCCCGCCGTGCTGCAGAGCAGCG GCCTGTACAGCCTGAGCAGCGTGGTGACAGTGCCC TCCAGCTCTCTGGGAACCCAGACCTATATCTGCAA CGTGAACCACAAGCCCAGCAACACCAAGGTGGAC AAGAGAGTGGAGCCCAAGAGCTGCGACAAGACCC ACACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTG GGAGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCC CAAGGACACCCTGATGATCAGCAGGACCCCCGAG GTGACCTGCGTGGTGGTGGACGTGTCCCACGAGGA CCCAGAGGTGAAGTTCAACTGGTACGTGGACGGC GTGGAGGTGCACAACGCCAAGACCAAGCCCAGAG AGGAGCAGTACAACAGCACCTACAGGGTGGTGTC CGTGCTGACCGTGCTGCACCAGGACTGGCTGAACG GCAAAGAATACAAGTGCAAAGTCTCCAACAAGGC CCTGCCAGCCCCAATCGAAAAGACAATCAGCAAG GCCAAGGGCCAGCCACGGGAGCCCCAGGTGTACA CCCTGCCCCCCAGCCGGGAGGAGATGACCAAGAA CCAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTCT ACCCCAGCGATATCGCCGTGGAGTGGGAGAGCAA CGGCCAGCCCGAGAACAACTACAAGACCACCCCC CCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGTA CAGCAAGCTGACCGTGGACAAGTCCAGGTGGCAG CAGGGCAACGTGTTCAGCTGCAGCGTGATGCACGA GGCCCTGCACAACCACTACACCCAGAAGTCCCTGA GCCTGAGCCCCGGCAAG
SEQ ID NO: 254	LCDR1 (KABAT)	SASSSVSYMH
SEQ ID NO: 285	LCDR2 (KABAT)	TTSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 286	LCDR2 (CHOTHIA)	TTS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 254	LCDR1 (COMBINED)	SASSSVSYMH
SEQ ID NO: 285	LCDR2 (COMBINED)	TTSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 286	LCDR2 (IMGT)	TTS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 287	VL	QIVLTQSPAIMSASLGEEITLTCSASSSVSYMHWYQQ RSGTSPKLLIYTTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 288	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAGGTCAGGCACTTCTCCCAAACTCTTGATT TATACCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCGT

		GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 289	LC	QIVLTQSPAIMSASLGEEITLTCSASSSVSYMHWYQQ RSGTSPKLLIYTTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGTKLEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADY EKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 290	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAGGTCAGGCACTTCTCCCAAACTCTTGATT TATACCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCGT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 FAB22		
SEQ ID NO: 37	HCDR1 (Kabat)	SGYYWN
SEQ ID NO: 220	HCDR2 (Kabat)	YISYDGDNNYNPSLKN
SEQ ID NO: 221	HCDR3 (Kabat)	GYYRYGLSYYYVMDY
SEQ ID NO: 40	HCDR1 (Chothia)	GYSITSGY
SEQ ID NO: 222	HCDR2 (Chothia)	SYDGD
SEQ ID NO: 221	HCDR3 (Chothia)	GYYRYGLSYYYVMDY
SEQ ID NO: 42	HCDR1 (Combined)	GYSITSGYYWN
SEQ ID NO: 220	HCDR2 (Combined)	YISYDGDNNYNPSLKN
SEQ ID NO: 221	HCDR3 (Combined)	GYYRYGLSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 223	HCDR2 (IMGT)	ISYDGDN
SEQ ID NO: 224	HCDR3 (IMGT)	AGGYYRYGLSYYYVMDY
SEQ ID NO: 328	VH	EVKLEQSGPGLVKPSQSLSLTCSVTGYSITSGYYWN WIRQFPGNKLEWMSYISYDGDNNYNPSLKNRISITRD TSKNQFFLKLSSVTTEDTATYYCAGGYYRYGLSYYY VMDYWGQGTSVTVSA
SEQ ID NO: 329	VH DNA	GAAGTGAAGCTGGAGCAGTCAGGACCTGGCCTCG TGAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTG TCACTGGCTACTCCATCACCAGTGGTTATTACTGG AACTGGATCCGGCAGTTTCCAGGAAACAAACTGG AATGGATGAGCTACATAAGCTACGACGGTGACAA TAACTACAACCCATCTCTCAAAAATCGAATCTCCA TCACTCGTGACACATCTAAGAACCAGTTTTTCCTG AAGTTGAGTTCTGTGACTACTGAGGACACAGCTAC ATATTACTGTGCAGGAGGCTACTATAGGTACGGCC TGTCGTATTACTATGTTATGGACTACTGGGGTCAA GGAACCTCAGTCACAGTCTCCGCA

SEQ ID NO: 330	HC	EVKLEQSGPGLVKPSQSLSLTCSVTGYSITSGYYWN WIRQFPGNKLEWMSYISYDGDNNYNPSLKNRISITRD TSKNQFFLKLSSVTTEDTATYYCAGGYYRYGLSYYY VMDYWGQGTSVTVSAASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSC
SEQ ID NO: 331	HC DNA	GAAGTGAAGCTGGAGCAGTCAGGACCTGGCCTCG TGAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTG TCACTGGCTACTCCATCACCAGTGGTTATTACTGG AACTGGATCCGGCAGTTTCCAGGAAACAAACTGG AATGGATGAGCTACATAAGCTACGACGGTGACAA TAACTACAACCCATCTCTCAAAAATCGAATCTCCA TCACTCGTGACACATCTAAGAACCAGTTTTTCCTG AAGTTGAGTTCTGTGACTACTGAGGACACAGCTAC ATATTACTGTGCAGGAGGCTACTATAGGTACGGCC TGTCGTATTACTATGTTATGGACTACTGGGGTCAA GGAACCTCAGTCACAGTCTCCGCAgctagcaccaagggccc aagtgtgtttcccctggcccccagcagcaagtctacttccggcggaactgctgccct gggttgcctggtgaaggactacttccccgagcccgtgacagtgtcctggaactctg gggctctgacttccggcgtgcacaccttccccgccgtgctgcagagcagcggcct gtacagcctgagcagcgtggtgacagtgccctccagctctctgggaacccagacct atatctgcaacgtgaaccacaagcccagcaacaccaaggtggacaagagagtgg agcccaagagctgc
SEQ ID NO: 61	LCDR1 (Kabat)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (Kabat)	AASNLES
SEQ ID NO: 52	LCDR3 (Kabat)	QQSNEDPPT
SEQ ID NO: 62	LCDR1 (Chothia)	SQSVDYDGNSY
SEQ ID NO: 54	LCDR2 (Chothia)	AAS
SEQ ID NO: 55	LCDR3 (Chothia)	SNEDPP
SEQ ID NO: 61	LCDR1 (Combined)	KASQSVDYDGNSYMN
SEQ ID NO: 51	LCDR2 (Combined)	AASNLES
SEQ ID NO: 52	LCDR3 (Combined)	QQSNEDPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDYDGNSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 332	VL	DIKMTQSPASLAVSLGQRATISCKASQSVDYDGNSY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGT DFTLNIHPVEEEDAATYYCQQSNEDPPTFGGGTKLEL K
SEQ ID NO: 333	VL DNA	GATATTAAGATGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAACTCAAA
SEQ ID NO: 334	LC	DIKMTQSPASLAVSLGQRATISCKASQSVDYDGNSY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGT DFTLNIHPVEEEDAATYYCQQSNEDPPTFGGGTKLEL KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 335	LC DNA	GATATTAAGATGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAACTCAAAcgtacggtggccgctcccagcgtgt tcatcttccccccagcgacgagcagctgaagagtggcaccgccagcgtggtgtg cctgctgaacaacttctaccccccgggaggccaaggtgcagtggaaggtggacaac gccctgcagagcggcaacagccaggagagcgtcaccgagcaggacagcaagg actccacctacagcctgagcagcaccctgaccctgagcaaggccgactacgagaa gcataaggtgtacgcctgcgaggtgacccaccagggcctgtccagccccgtgacc aagagcttcaacaggggcgagtgc
ANTI-HUMAN ENTPD2 FAB23		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 233	VH	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSS
SEQ ID NO: 234	VH DNA	GAGGTCCAACTGCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 336	HC	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDTAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSC
SEQ ID NO: 337	HC DNA	GAGGTCCAACTGCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG

		CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCAgctagcaccaagggc ccaagtgtgtttcccctggcccccagcagcaagtctacttccggcggaactgctgcc ctgggttgcctggtgaaggactacttccccgagcccgtgacagtgtcctggaactct ggggctctgacttccggcgtgcacaccttcccegccgtgctgcagagcagcggcc tgtacagcctgagcagcgtggtgacagtgccctccagctctctgggaacccagacc tatatctgcaacgtgaaccacaagcccagcaacaccaaggtggacaagagagtgg agcccaagagctgc
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 237	VL	QIVLTQSPAIMSASLGEEITLTCSASSSVSYIHWYQQK SGTSPTLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 238	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACACTGGTACC AGCAGAAGTCAGGCACTTCTCCCACACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 239	LC	QIVLTQSPAIMSASLGEEITLTCSASSSVSYIHWYQQK SGTSPTLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 240	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACACTGGTACC AGCAGAAGTCAGGCACTTCTCCCACACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT

		GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC

[0108] In some embodiments, the anti-human ENTPD2 antibody or antibody fragment (e.g., an antigen binding fragment) comprises a VH domain having an amino acid sequence of any VH domain described in Table 1. Other suitable anti-human ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VH domain with the VH regions depicted in the sequences described in Table 1. The present disclosure in certain embodiments also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human ENTPD2, wherein the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VH CDR having an amino acid sequence of any one of the VH CDRs listed in Table 1. In particular embodiments, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human ENTPD2, comprising (or alternatively, consist of) one, two, three, four, five or more VH CDRs having an amino acid sequence of any one of the VH CDRs listed in Table 1.

[0109] In some embodiments, the anti-human ENTPD2 antibody or antibody fragment (e.g., antigen binding fragment) comprises a VL domain having an amino acid sequence of any VL domain described in Table 1. Other suitable anti-human ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VL domain with the VL regions depicted in the sequences described in Table 1. The present disclosure also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human ENTPD2, the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VL CDR having an amino acid sequence of any one of the VL CDRs listed in Table 1. In particular, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human

ENTPD2, which comprise (or alternatively, consist of) one, two, three or more VL CDRs having an amino acid sequence of any one of the VL CDRs listed in Table 1.

[0110] Other anti-human ENTPD2 antibodies or antibody fragments (*e.g.*, antigen binding fragment) disclosed herein include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the CDR regions with the CDR regions depicted in the sequences described in Table 1. In some embodiments, it includes mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the CDR regions when compared with the CDR regions depicted in the sequence described in Table 1.

[0111] Also provided herein are nucleic acid sequences that encode VH, VL, full length heavy chain, and full length light chain of antibodies and antigen binding fragments thereof that specifically bind to human ENTPD2, e.g., the nucleic acid sequences in Table 1. Such nucleic acid sequences can be optimized for expression in mammalian cells.

[0112] Other anti-human ENTPD2 antibodies disclosed herein include those where the amino acids or nucleic acids encoding the amino acids have been mutated, yet have at least 80, 85, 90 95, 96, 97, 98, or 99 percent identity to the sequences described in Table 1. In some embodiments, antibodies or antigen binding fragments thereof include mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the variable regions when compared with the variable regions depicted in the sequence described in Table 1, while retaining substantially the same therapeutic activity.

[0113] Since each provided antibody binds to human ENTPD2, the VH, VL, full length light chain, and full length heavy chain sequences (amino acid sequences and the nucleotide sequences encoding the amino acid sequences) can be "mixed and matched" to create other ENTPD2-binding antibodies disclosed herein. Such "mixed and matched" ENTPD2-binding antibodies can be tested using binding assays known in the art (*e.g.*, ELISAs, assays described in the Exemplification). When chains are mixed and matched, a VH sequence from a particular VH/VL pairing should be replaced with a structurally similar VH sequence. A full length heavy chain sequence from a particular full length heavy chain / full length light chain pairing should be replaced with a structurally similar full length heavy chain sequence. A VL sequence from a particular VH/VL pairing should be replaced with a structurally similar VL sequence. A full length light chain sequence from a particular full length heavy chain / full length light chain pairing should be replaced with a structurally similar full length light chain sequence.

[0114] Accordingly, in one embodiment, the invention provides an isolated monoclonal antibody or antigen binding fragment thereof having: a heavy chain variable region (VH) comprising an amino acid sequence selected from any one of SEQ ID NOs: 10, 25, 33, 46, 70, 91, 115, 132, 145, 169, 225, 233, 241, 250, 264, 281, 328; and a light chain variable region (VL) comprising an amino acid sequence selected from any one of SEQ ID NOs: 21, 29, 57, 64, 74, 78, 102, 125, 156, 178, 229, 237, 257, 268, 287, 332; wherein the antibody specifically binds to human ENTPD2.

[0115] In another embodiment, the invention provides (i) an isolated monoclonal antibody having: a full length heavy chain (HC) comprising an amino acid sequence selected from any one of SEQ ID NOs: 12, 27, 35, 48, 72, 93, 117, 134, 147, 171, 227, 235, 243, 252, 266, 283, 330; and a full length light chain (LC) comprising an amino acid sequence selected from any one of SEQ ID NOs: 23, 31, 59, 66, 76, 80, 104, 127, 158, 180, 231, 239, 259, 270, 289, 334; or (ii) a functional protein comprising an antigen binding portion thereof.

[0116] In another embodiment, the present disclosure provides human ENTPD2-binding antibodies or antibody fragments thereof that comprise the heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 as described in Table 1, or combinations thereof. The amino acid sequences of the VH CDR1s of the antibodies are shown in SEQ ID NOs: 1, 4, 6, 7, 37, 40, 42, 43, 82, 85, 87, 88, 106, 109, 111, 112, 136, 139, 141, 142, 160, 163, 165, 166, 185, 187, 188, 206, 207, 208, 213, 214, 215, 272, 275, 277. The amino acid sequences of the VH CDR2s of the antibodies and are shown in SEQ ID NOs: 2, 5, 8, 38, 41, 44, 83, 86, 89, 107, 110, 113, 129, 130, 131, 137, 140, 143, 161, 164, 167, 186, 189, 220, 222, 223, 245, 247, 248, 261, 273, 276, 279. The amino acid sequences of the VH CDR3s of the antibodies are shown in SEQ ID NO: 3, 39, 68, 84, 108, 138, 162, 221, 246, 262, 277, 274, 9, 45, 69, 90, 114, 144, 168, 190, 224, 249, 263, 274, 280. The amino acid sequences of the VL CDR1s of the antibodies are shown in SEQ ID NOs: 14, 17, 20, 50, 53, 56, 61, 62, 63, 95, 98, 101, 119, 122, 124, 149, 152, 155, 173, 175, 177, 198, 201, 254. The amino acid sequences of the VL CDR2s of the antibodies are shown in SEQ ID NOs: 15, 18, 51, 54, 96, 99, 120, 150, 153, 199, 285, 286. The amino acid sequences of the VL CDR3s of the antibodies are shown in SEQ ID NOs: 16, 19, 52, 55, 97, 100, 121, 123, 151, 154, 174, 176, 200, 255, 256.

[0117] Given that each of the antibodies binds human ENTPD2 and that antigen-binding specificity is provided primarily by the CDR1, CDR2 and CDR3 regions, the VH CDR1, CDR2 and CDR3 sequences and VL CDR1, CDR2 and CDR3 sequences can be "mixed and matched" (i.e., CDRs from different antibodies can be mixed and matched),

although each antibody must contain a VH CDR1, CDR2 and CDR3 and a VL CDR1, CDR2 and CDR3 to create other human ENTPD2-binding antibodies disclosed herein. Such "mixed and matched" ENTPD2-binding antibodies can be tested using the binding assays known in the art and those described in the Examples (*e.g.*, ELISAs). When VH CDR sequences are mixed and matched, the CDR1, CDR2 and/or CDR3 sequence from a particular VH sequence should be replaced with a structurally similar CDR sequence(s). Likewise, when VL CDR sequences are mixed and matched, the CDR1, CDR2 and/or CDR3 sequence from a particular VL sequence should be replaced with a structurally similar CDR sequence(s). It will be readily apparent to the ordinarily skilled artisan that novel VH and VL sequences can be created by substituting one or more VH and/or VL CDR region sequences with structurally similar sequences from CDR sequences shown herein for monoclonal antibodies of the present disclosure.

[0118] Accordingly, the present disclosure provides an isolated monoclonal antibody or antigen binding region thereof comprising a heavy chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 4, 6, 7, 37, 40, 42, 43, 82, 85, 87, 88, 106, 109, 111, 112, 136, 139, 141, 142, 160, 163, 165, 166, 182, 187, 188, 206, 207, 208, 213, 214, 215, 272, 275, 277; a heavy chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 5, 8, 38, 41, 44, 83, 86, 89, 107, 110, 113, 129, 130, 131, 137, 140, 143, 161, 164, 167, 183, 189, 220, 222, 223, 245, 247, 248, 261, 273, 276; a heavy chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 3, 39, 68, 84, 108, 138, 162, 221, 246, 262, 277, 274, 9, 45, 69, 90, 114, 144, 168, 190, 224, 249, 263, 274, 280; a light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 17, 20, 50, 53, 56, 61, 62, 63, 95, 98, 101, 119, 122, 124, 149, 152, 155, 173, 175, 177, 195, 201, 254; a light chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 15, 18, 51, 54, 96, 99, 120, 150, 153, 196, 285, 286; and a light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 16, 19, 52, 55, 97, 100, 121, 123, 151, 154, 174, 176, 197, 255, 256; wherein the antibody specifically binds human ENTPD2.

[0119] In certain embodiments, an antibody that specifically binds to human ENTPD2 is an antibody or antibody fragment (*e.g.*, antigen binding fragment) that is described in Table 1.

[0120] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain complementarity determining

region 1 (HCDR1) comprising the amino acid sequence of SEQ ID NO: 1, 4, 6 or 7; a heavy chain complementarity determining region 2 (HCDR2) comprising the amino acid sequence of SEQ ID NO: 2, 5 or 8; a heavy chain complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 3 or 9; a light chain complementarity determining region 1 (LCDR1) comprising the amino acid sequence of SEQ ID NO: 14, 17, or 20; a light chain complementarity determining region 2 (LCDR2) comprising the amino acid sequence of SEQ ID NO:15 or 18; and a light chain complementarity determining region 3 (LCDR3) comprising the amino acid sequence of SEQ ID NO: 16 or 19.

[0121] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 2; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 14; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0122] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 5; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 19.

[0123] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 2; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 14; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0124] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 8; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 9; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0125] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid

sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 38, 41, or 44; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 39 or 45; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 50, 53 or 56; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0126] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0127] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 41; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 53; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0128] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0129] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 44; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 45; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 56; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0130] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 38, 41, or 44; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 39 or 45; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 61, 62, or 63; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0131] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0132] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 41; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 62; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0133] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0134] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 44; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 45; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63; an LCDR2 comprising the amino

acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0135] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 38, 41, or 44; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 68 or 69; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 50, 53 or 56; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0136] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0137] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 41; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 53; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0138] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0139] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 44; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 69; an LCDR1

comprising the amino acid sequence of SEQ ID NO: 56; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0140] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 82, 85, 87, or 88; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 83, 86, or 89; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 84 or 90; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 95, 98, or 101; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 96 or 99; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 97 or 100.

[0141] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 82; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 83; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 84; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 95; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 96; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 97.

[0142] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 85; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 86; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 84; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 98; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 100.

[0143] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 87; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 83; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 84; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 95; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 96; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 97.

[0144] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 88; an HCDR2 comprising the amino acid sequence of SEQ ID

NO: 89; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 90; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 101; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 97.

[0145] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 106, 109, 111, or 112; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 107, 110, or 113; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 108 or 114; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 119, 122, or 124; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 99 or 120; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 121 or 123.

[0146] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 106; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 107; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 120; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0147] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 109; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 110; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 122; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 123.

[0148] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 111; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 107; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 120; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 121; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 108.

[0149] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid

sequence of SEQ ID NO: 112; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 113; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 114; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 124; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0150] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 106, 109, 111, or 112; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 129, 130, or 131; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 108 or 114; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 119, 122, or 124; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 99 or 120; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 121 or 123.

[0151] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 106; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 129; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 120; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0152] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 109; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 130; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 122; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 123.

[0153] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 111; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 129; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 120; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0154] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 112; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 131; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 114; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 124; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0155] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 136, 139, 141, or 142; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 137, 140, or 143; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 138 or 144; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 149, 152, or 155; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 150 or 153; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 151 or 154.

[0156] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 136; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 137; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 138; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 149; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 151.

[0157] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 139; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 140; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 138; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 152; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 154.

[0158] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 141; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 137; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 138; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 149; an LCDR2 comprising the amino

acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 151.

[0159] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 142; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 143; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 144; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 155; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 151.

[0160] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 160, 163, 165, or 166; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 161, 164, or 167; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 162 or 168; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 173, 175, or 177; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 150 or 153; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 174 or 176.

[0161] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 160; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 161; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 162; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 173; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 174.

[0162] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 163; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 164; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 162; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 175; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 176.

[0163] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 165; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 161; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 162; an LCDR1

comprising the amino acid sequence of SEQ ID NO: 173; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 174.

[0164] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 166; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 167; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 168; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 177; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 174.

[0165] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42, or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 220, 222, or 223; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 221 or 224; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 61, 62, or 63; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0166] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 221; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0167] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 222; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 221; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 62; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0168] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID

NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 221; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0169] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 223; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 224; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0170] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 220, 222, or 223; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 68 or 69; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 61, 62, or 63; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0171] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0172] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 222; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 62; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0173] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid

sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0174] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 223; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 69; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0175] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 1, 4, 6, or 7; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 245, 247, or 248; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 246 or 249; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 17, 20, or 254; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 15 or 18; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 255 or 256.

[0176] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 245; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 246; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 255.

[0177] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 247; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 246; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 256.

[0178] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 254; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 246; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 255.

[0179] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 248; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 249; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 255.

[0180] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 1, 4, 6, or 7; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 247, 248, or 261; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 262 or 263; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 17, 20, or 254; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 15 or 18; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 16 or 19.

[0181] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 261; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 262; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0182] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 247; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 262; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino

acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 19.

[0183] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 261; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 262; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0184] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 248; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 263; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0185] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 272, 275, or 278; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 273, 276, or 279; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 274, 277, or 280; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 17, 20, or 254; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 285 or 286; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 16 or 19.

[0186] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 272; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 273; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 274; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0187] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 275; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 276; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 274; an LCDR1

comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 286; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 19.

[0188] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 277; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 273; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 274; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0189] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 278; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 279; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 286; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0190] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 10 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 21(or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0191] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 25 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 29 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0192] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 33 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 29 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0193] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 46 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 57 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0194] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 46 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 64(or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0195] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 70 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 74 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0196] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH)

comprising the amino acid sequence of SEQ ID NO: 25 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 78 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0197] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 91 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 102 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0198] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 115 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 125 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0199] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 132 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 125 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0200] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 145 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions,

insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 156 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0201] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 169 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 178 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0202] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 225 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 229 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0203] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 233 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 237 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0204] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 241 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 229 (or a sequence at least about 90%, 95%, 99% or

more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0205] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 250 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 257 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0206] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 264 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 268 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0207] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 281 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 287 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0208] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 12 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 23 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0209] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 31 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0210] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 35 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 31 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0211] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 48 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 59 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0212] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 48 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 66 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0213] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 72 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 76 (or a sequence at least about 90%,

95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0214] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 80 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0215] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 93 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 104 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0216] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 117 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 127 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0217] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 134 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 127 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0218] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 147 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain

comprising the amino acid sequence of SEQ ID NO: 158 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0219] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 171 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising SEQ ID NO: 180 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0220] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 227 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 231 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0221] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 235 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 239 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0222] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 243 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 231 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0223] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 252 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two,

three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 259 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0224] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 266 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 270 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0225] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 283 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 289 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0226] In some embodiments, the present invention provides an antibody or antigen-binding fragment thereof, which bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 10nM, e.g., a K_D of less than 9nM, less than 8nM, less than 7nM, less than 6nM, less than 5nM, less than 4nM, less than 3nM, less than 2nM, less than 1nM, e.g., as measured by Biacore. In some embodiments, the antibodies or antigen-binding fragments provided herein bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 5nM, e.g., as measured by Biacore. In some embodiments, the antibodies or antigen-binding fragments provided herein bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 3nM, e.g., as measured by Biacore. In some embodiments, the antibodies or antigen-binding fragments provided herein bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 1nM, e.g., as measured by Biacore. In some embodiments, the dissociation constant of the antibodies or antigen binding fragments thereof described herein to human ENTPD2 is measured by Biacore at 25 °C.

[0227] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one

(e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: His50, Asp76, Pro78, Gly79, Gly80, Tyr85, Asp87, Asn88, Gly91, Gln94, Ser95, Gly98, Glu101, Gln102, Gln105, Asp106, Arg245, Thr272, Gln273, Leu275, Asp278, Arg298, Ala347, Ala350, Thr351, Arg392, Ala393, Arg394, or Tyr398. In some embodiments, such antibodies or antigen binding fragments include, but are not limited to, MAb1, MAb2, MAb3, MAb7, MAb17, MAb19, MAb20, MAb21, and Fab23 as disclosed in Table 1.

[0228] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: Gly79, Gln250, Leu253, Trp266, Arg268, Gly269, Phe270, Ser271, Thr272, Gln273, Val274, Leu275, Asp278, Arg298, Ser300, Ser302, Gly303, Thr380, Trp381, Ala382, Gly390, Gln391, Arg392, Ala393, Arg394, or Asp397. In some embodiments, such antibodies or antigen binding fragments include, but are not limited to, MAb4, MAb5, MAb6, MAb16, MAb18, and Fab22 as disclosed in Table 1.

[0229] Once a desired epitope on an antigen is determined, it is possible to generate antibodies to that epitope, e.g., using the techniques described in the present invention. Alternatively, during the discovery process, the generation and characterization of antibodies may elucidate information about desirable epitopes. From this information, it is then possible to competitively screen antibodies for binding to the same epitope. An approach to achieve this is to conduct cross-competition studies to find antibodies that competitively bind with one another, e.g., the antibodies compete for binding to the antigen. A high throughput process for "binning" antibodies based upon their cross-competition is described in International Patent Application No. WO 2003/48731. As will be appreciated by one of skill in the art, practically anything to which an antibody can specifically bind could be an epitope. An epitope can comprises those residues to which the antibody binds.

[0230] Generally, antibodies specific for a particular target antigen will preferentially recognize an epitope on the target antigen in a complex mixture of proteins and/or macromolecules.

[0231] Regions of a given polypeptide that include an epitope can be identified using any number of epitope mapping techniques, well known in the art. See, e.g., Epitope Mapping Protocols in Methods in Molecular Biology, Vol. 66 (Glenn E. Morris, Ed., 1996, Humana Press, Totowa, N.J). For example, linear epitopes may be determined by e.g., concurrently synthesizing large numbers of peptides on solid supports, the peptides corresponding to portions of the protein molecule, and reacting the peptides with antibodies while the peptides are still attached to the supports. Such techniques are known in the art and described in, e.g., U.S. Pat. No. 4,708,871; Geysen et al., (1984) Proc. Natl. Acad. Sci. USA 8:3998-4002; Geysen et al., (1985) Proc. Natl. Acad. Sci. USA 82:78-182; Geysen et al., (1986) Mol. Immunol. 23:709-715. Similarly, conformational epitopes are readily identified by determining spatial conformation of amino acids such as by, e.g., x-ray crystallography and two-dimensional nuclear magnetic resonance. See, e.g., Epitope Mapping Protocols, supra. Antigenic regions of proteins can also be identified using standard antigenicity and hydropathy plots, such as those calculated using, e.g., the Omiga version 1.0 software program available from the Oxford Molecular Group. This computer program employs the Hopp/Woods method, Hopp et al., (1981) Proc. Natl. Acad. Sci USA 78:3824-3828; for determining antigenicity profiles, and the Kyte-Doolittle technique, Kyte et al., (1982) J. Mol. Biol. 157:105-132; for hydropathy plots.

[0232] The antibody molecule can be a polyclonal or a monoclonal antibody. A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (e.g., recombinant methods). In some embodiments, the antibody can be recombinantly produced, e.g., produced by phage display or by combinatorial methods.

[0233] Phage display and combinatorial methods for generating antibodies are known in the art (as described in, e.g., Ladner et al. U.S. Patent 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 Antibod Hybridomas 3:81-85; Huse et al. (1989) Science 246:1275-1281; Griffths 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).

[0234] 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.

[0235] An antibody 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. Antibodies 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.

[0236] Chimeric and/or humanized antibodies, can be engineered to minimize the immune response by a human patient to antibodies produced in non-human subjects or derived from the expression of non-human antibody genes. Chimeric antibodies comprise a non-human animal antibody variable region and a human antibody constant region. Such antibodies retain the epitope binding specificity of the original monoclonal antibody, but may be less immunogenic when administered to humans, and therefore more likely to be tolerated by the patient. For example, one or all (e.g., one, two, or three) of the variable regions of the light chain(s) and/or one or all (e.g., one, two, or three) of the variable regions the heavy chain(s) of a mouse antibody (e.g., a mouse monoclonal antibody) can each be joined to a human constant region, such as, without limitation an IgG1 human constant region. Chimeric monoclonal antibodies can be produced by recombinant DNA techniques known in the art. For example, a gene encoding the constant region of a non-human antibody molecule can be substituted with a gene encoding a human constant region (see Robinson et al., PCT Patent Publication PCT/US86/02269; Akira, et al., European Patent Application 184,187; or Taniguchi, M., European Patent Application 171,496). In addition, other suitable techniques that can be used to generate chimeric antibodies are described, for example, in U.S. Patent Nos. 4,816,567; 4,978,775; 4,975,369; and 4,816,397.

[0237] A chimeric antibody can be further "humanized" by replacing portions of the variable region not involved in antigen binding with equivalent portions from human variable regions. Humanized antibodies comprise one or more human framework regions in the variable region together with non-human (e.g., mouse, rat, or hamster) complementarity-determining regions (CDRs) of the heavy and/or light chain. In some embodiments, a

humanized antibody comprises sequences that are entirely human except for the CDR regions. Humanized antibodies are typically less immunogenic to humans, relative to non-humanized antibodies, and thus offer therapeutic benefits in certain situations. Humanized ENTPD2 antibodies can be generated using methods known in the art. See for example, Hwang et al., Methods 36:35, 2005; Queen et al., Proc. Natl. Acad. Sci. U.S.A. 86:10029-10033, 1989; Jones et al., Nature 321:522-25, 1986; Riechmann et al., Nature 332:323-27, 1988; Verhoeyen et al., Science 239:1534-36, 1988; Orlandi et al., Proc. Natl. Acad. Sci. U.S.A. 86:3833-3837, 1989; U.S. Patent Nos. 5,225,539; 5,530,101; 5,585,089; 5,693,761; 5,693,762; and 6,180,370; and WO 90/07861.

[0238] Human ENTPD2 antibodies can be generated using methods that are known in the art. For example, the humaneering technology used to converting non-human antibodies into engineered human antibodies. U.S. Patent Publication No. 20050008625 describes an *in vivo* method for replacing a nonhuman antibody variable region with a human variable region in an antibody while maintaining the same or providing better binding characteristics relative to that of the nonhuman antibody. The method relies on epitope guided replacement of variable regions of a non-human reference antibody with a fully human antibody. The resulting human antibody is generally structurally unrelated to the reference nonhuman antibody, but binds to the same epitope on the same antigen as the reference antibody. Briefly, the serial epitope-guided complementarity replacement approach is enabled by setting up a competition in cells between a "competitor" and a library of diverse hybrids of the reference antibody ("test antibodies") for binding to limiting amounts of antigen in the presence of a reporter system which responds to the binding of test antibody to antigen. The competitor can be the reference antibody or derivative thereof such as a single-chain Fv fragment. The competitor can also be a natural or artificial ligand of the antigen which binds to the same epitope as the reference antibody. The only requirements of the competitor are that it binds to the same epitope as the reference antibody, and that it competes with the reference antibody for antigen binding. The test antibodies have one antigen-binding V-region in common from the nonhuman reference antibody, and the other V-region selected at random from a diverse source such as a repertoire library of human antibodies. The common V-region from the reference antibody serves as a guide, positioning the test antibodies on the same epitope on the antigen, and in the same orientation, so that selection is biased toward the highest antigen-binding fidelity to the reference antibody.

[0239] Many types of reporter system can be used to detect desired interactions between test antibodies and antigen. For example, complementing reporter fragments may be linked to antigen and test antibody, respectively, so that reporter activation by fragment complementation only occurs when the test antibody binds to the antigen. When the test antibody- and antigen-reporter fragment fusions are co-expressed with a competitor, reporter activation becomes dependent on the ability of the test antibody to compete with the competitor, which is proportional to the affinity of the test antibody for the antigen. Other reporter systems that can be used include the reactivator of an auto-inhibited reporter reactivation system (RAIR) as disclosed in U.S. patent application Ser. No. 10/208,730 (Publication No. 20030198971), or competitive activation system disclosed in U.S. patent application Ser. No. 10/076,845 (Publication No. 20030157579).

[0240] With the serial epitope-guided complementarity replacement system, selection is made to identify cells expresses a single test antibody along with the competitor, antigen, and reporter components. In these cells, each test antibody competes one-on-one with the competitor for binding to a limiting amount of antigen. Activity of the reporter is proportional to the amount of antigen bound to the test antibody, which in turn is proportional to the affinity of the test antibody for the antigen and the stability of the test antibody. Test antibodies are initially selected on the basis of their activity relative to that of the reference antibody when expressed as the test antibody. The result of the first round of selection is a set of "hybrid" antibodies, each of which is comprised of the same non-human V-region from the reference antibody and a human V-region from the library, and each of which binds to the same epitope on the antigen as the reference antibody. One of more of the hybrid antibodies selected in the first round will have an affinity for the antigen comparable to or higher than that of the reference antibody.

[0241] In the second V-region replacement step, the human V-regions selected in the first step are used as guide for the selection of human replacements for the remaining non-human reference antibody V-region with a diverse library of cognate human V-regions. The hybrid antibodies selected in the first round may also be used as competitors for the second round of selection. The result of the second round of selection is a set of fully human antibodies which differ structurally from the reference antibody, but which compete with the reference antibody for binding to the same antigen. Some of the selected human antibodies bind to the same epitope on the same antigen as the reference antibody. Among these selected

human antibodies, one or more binds to the same epitope with an affinity which is comparable to or higher than that of the reference antibody.

[0242] Using a mouse or chimeric ENTPD2 antibody, human antibodies that bind to human ENTPD2 with the same binding specificity and the same or better binding affinity can be generated. In addition, such human ENTPD2 antibodies can also be commercially obtained from companies which customarily produce human antibodies, e.g., KaloBios, Inc. (Mountain View, Calif.).

[0243] In some embodiments, the present invention provides an antibody or antigen-binding fragment thereof that bind to human ENTPD2 protein and modulates one or more ENTPD2 activities/functions, e.g., inhibiting the enzymatic actitivies of human ENTPD2, e.g., by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In some embodiments, the enzymatic activity of human ENTPD2 is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0244] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein inhibit ENTPD2's ability of hydrolysis of adenosine triphosphate (ATP). In some embodiments, ENTPD2's ability of hydrolysis of ATP is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0245] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein interfere with ATP binding to ENTPD2 or trap ATP within the catalytic domain of ENTPD2. In some embodiments, interference with ATP binding to ENTPD2 or trapping ATP within the catalytic domain of ENTPD2 is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

Antibodies and Antigen-Binding Fragments Thereof That Specifically Bind To Mouse ENTPD2

[0246] Also provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to mouse ENTPD2 protein. Table 26 lists the sequences of exemplary the ENTPD2 antibodies or antigen-binding fragments that specifically bind to mouse ENTPD2 protein.

Table 26. Sequences of Exemplary Monoclonal Antibodies (MABs) and Antibody Fragments (FABs) That Bind Mouse ENTPD2

ANTI-mouse ENTPD2 MAB13		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFFDS
SEQ ID NO: 185	HCDR1 (CHOTHIA)	GYTFTHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFFDS
SEQ ID NO: 187	HCDR1 (COMBINED)	GYTFTHYGMN
SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFFDS
SEQ ID NO: 188	HCDR1 (IMGT)	GYTFTHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFFDS
SEQ ID NO: 191	VH	QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSS
SEQ ID NO: 192	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 193	HC	QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSSAKTTAPSVYPLAPVCGDTT GSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAV

		LQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKD VLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHT AQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFKC KVNNKDLPAPIERTISKPKGSVRAPQVYVLPPPEEEM TKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKN TEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVV HEGLHNHHTTKSFSRTPGK
SEQ ID NO: 194	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAGCCAAGACCACCGC CCCCAGCGTGTACCCCCTGGCCCCCGTGTGCGGCG ATACCACCGGCAGCAGCGTGACCCTGGGCTGCCTG GTGAAGGGCTACTTCCCCGAGCCCGTGACCCTGAC CTGGAACAGCGGCTCCCTGAGCAGCGGCGTGCAC ACCTTCCCCGCCGTGCTGCAGAGCGACCTGTACAC CCTGTCCAGCTCCGTGACCGTGACAAGCAGCACCT GGCCCAGCCAGAGCATCACCTGCAACGTGGCCCAC CCCGCCAGCAGCACCAAGGTGGACAAGAAGATCG AGCCCAGGGGCCCCACCATCAAGCCCTGCCCCCCC TGCAAGTGCCCAGCCCCCAACCTGCTGGGCGGACC CAGCGTGTTCATCTTCCCCCCCAAGATCAAGGACG TGCTGATGATCAGCCTGAGCCCCATCGTGACCTGC GTGGTGGTGGACGTGAGCGAGGACGACCCCGACG TGCAGATCAGCTGGTTCGTGAACAACGTGGAGGTG CACACCGCCCAGACCCAGACCCACCGGGAGGACT ACAACAGCACCCTGCGCGTCGTGTCCGCCCTGCCC ATCCAGCACCAGGACTGGATGAGCGGCAAAGAAT TCAAGTGCAAGGTGAACAACAAGGACCTGCCTGC CCCCATCGAGCGGACCATCAGCAAGCCCAAGGGC AGCGTGAGAGCCCCCCAGGTGTACGTGCTGCCCCC TCCCGAGGAAGAGATGACCAAGAAACAGGTGACA CTGACCTGCATGGTGACCGACTTCATGCCCGAGGA CATCTACGTGGAGTGGACCAACAACGGCAAGACC GAGCTGAACTACAAGAACACCGAGCCTGTGCTGG ACAGCGACGGCAGCTACTTCATGTACAGCAAGCTG CGGGTGGAGAAGAAAAACTGGGTGGAGCGGAACA GCTACAGCTGCAGCGTGGTGCACGAGGGCCTGCAC AACCACCACACCACCAAGAGCTTCAGCCGGACCCC CGGCAAG
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN

SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 204	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP KDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMS STLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE C
SEQ ID NO: 205	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC

		AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAACGCGCTGATGC CGCCCCTACCGTGAGCATCTTCCCCCCCAGCAGCG AGCAGCTGACCAGCGGCGGAGCCAGCGTGGTGTG CTTCCTGAACAACTTCTACCCCAAGGACATCAACG TGAAGTGGAAGATCGACGGCAGCGAGCGGCAGAA CGGCGTGCTGAACAGCTGGACCGACCAGGACAGC AAGGACTCCACCTACAGCATGAGCAGCACCCTGAC CCTGACCAAGGACGAGTACGAGCGGCACAACAGC TACACCTGCGAGGCCACCCACAAGACCAGCACCA GCCCCATCGTGAAGAGCTTCAACCGGAACGAGTGC
ANTI-mouse ENTPD2 MAB14		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFFDS
SEQ ID NO: 206	HCDR1 (CHOTHIA)	GYTFWHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFFDS
SEQ ID NO: 207	HCDR1 (COMBINED)	GYTFWHYGMN
SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFFDS
SEQ ID NO: 208	HCDR1 (IMGT)	GYTFWHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFFDS
SEQ ID NO: 209	VH	QVQLVQSGAELKQPGQSVKISCKASGYTFWHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSS
SEQ ID NO: 210	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCTGGCACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT

		TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 211	HC	QVQLVQSGAELKQPGQSVKISCKASGYTFWHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSSAKTTAPSVYPLAPVCGDTT GSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAV LQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKD VLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHT AQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFKC KVNNKDLPAPIERTISKPKGSVRAPQVYVLPPPEEEM TKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKN TEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVV HEGLHNHHTTKSFSRTPGK
SEQ ID NO: 212	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCTGGCACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAGCCAAGACCACCGC CCCCAGCGTGTACCCCCTGGCCCCCGTGTGCGGCG ATACCACCGGCAGCAGCGTGACCCTGGGCTGCCTG GTGAAGGGCTACTTCCCCGAGCCCGTGACCCTGAC CTGGAACAGCGGCTCCCTGAGCAGCGGCGTGCAC ACCTTCCCCGCCGTGCTGCAGAGCGACCTGTACAC CCTGTCCAGCTCCGTGACCGTGACAAGCAGCACCT GGCCCAGCCAGAGCATCACCTGCAACGTGGCCCAC CCCGCCAGCAGCACCAAGGTGGACAAGAAGATCG AGCCCAGGGGCCCCACCATCAAGCCCTGCCCCCCC TGCAAGTGCCCAGCCCCCAACCTGCTGGGCGGACC CAGCGTGTTCATCTTCCCCCCCAAGATCAAGGACG TGCTGATGATCAGCCTGAGCCCCATCGTGACCTGC GTGGTGGTGGACGTGAGCGAGGACGACCCCGACG TGCAGATCAGCTGGTTCGTGAACAACGTGGAGGTG CACACCGCCCAGACCCAGACCCACCGGGAGGACT ACAACAGCACCCTGCGCGTCGTGTCCGCCCTGCCC ATCCAGCACCAGGACTGGATGAGCGGCAAAGAAT TCAAGTGCAAGGTGAACAACAAGGACCTGCCTGC CCCCATCGAGCGGACCATCAGCAAGCCCAAGGGC AGCGTGAGAGCCCCCCAGGTGTACGTGCTGCCCCC TCCCGAGGAAGAGATGACCAAGAAACAGGTGACA CTGACCTGCATGGTGACCGACTTCATGCCCGAGGA

		CATCTACGTGGAGTGGACCAACAACGGCAAGACC GAGCTGAACTACAAGAACACCGAGCCTGTGCTGG ACAGCGACGGCAGCTACTTCATGTACAGCAAGCTG CGGGTGGAGAAGAAAAACTGGGTGGAGCGGAACA GCTACAGCTGCAGCGTGGTGCACGAGGGCCTGCAC AACCACCACACCACCAAGAGCTTCAGCCGGACCCC CGGCAAG
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 204	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP

		KDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMS STLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE C
SEQ ID NO: 205	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAACGCGCTGATGC CGCCCCTACCGTGAGCATCTTCCCCCCCAGCAGCG AGCAGCTGACCAGCGGCGGAGCCAGCGTGGTGTG CTTCCTGAACAACTTCTACCCCAAGGACATCAACG TGAAGTGGAAGATCGACGGCAGCGAGCGGCAGAA CGGCGTGCTGAACAGCTGGACCGACCAGGACAGC AAGGACTCCACCTACAGCATGAGCAGCACCCTGAC CCTGACCAAGGACGAGTACGAGCGGCACAACAGC TACACCTGCGAGGCCACCCACAAGACCAGCACCA GCCCCATCGTGAAGAGCTTCAACCGGAACGAGTGC
ANTI-mouse ENTPD2 MAB15		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFFDS
SEQ ID NO: 213	HCDR1 (CHOTHIA)	GYTFHHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFFDS
SEQ ID NO: 214	HCDR1 (COMBINED)	GYTFHHYGMN
SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFFDS
SEQ ID NO: 215	HCDR1 (IMGT)	GYTFHHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFFDS

SEQ ID NO: 216	VH	QVQLVQSGAELKQPGQSVKISCKASGYTFHHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSS
SEQ ID NO: 217	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCCACCACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 218	HC	QVQLVQSGAELKQPGQSVKISCKASGYTFHHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSSAKTTAPSVYPLAPVCGDTT GSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAV LQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKD VLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHT AQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFKC KVNNKDLPAPIERTISKPKGSVRAPQVYVLPPPEEEM TKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKN TEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVV HEGLHNHHTTKSFSRTPGK
SEQ ID NO: 219	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCCACCACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAGCCAAGACCACCGC CCCCAGCGTGTACCCCCTGGCCCCCGTGTGCGGCG ATACCACCGGCAGCAGCGTGACCCTGGGCTGCCTG GTGAAGGGCTACTTCCCCGAGCCCGTGACCCTGAC CTGGAACAGCGGCTCCCTGAGCAGCGGCGTGCAC ACCTTCCCCGCCGTGCTGCAGAGCGACCTGTACAC CCTGTCCAGCTCCGTGACCGTGACAAGCAGCACCT GGCCCAGCCAGAGCATCACCTGCAACGTGGCCCAC CCCGCCAGCAGCACCAAGGTGGACAAGAAGATCG AGCCCAGGGGCCCCACCATCAAGCCCTGCCCCCCC TGCAAGTGCCCAGCCCCCAACCTGCTGGGCGGACC CAGCGTGTTCATCTTCCCCCCCAAGATCAAGGACG

		TGCTGATGATCAGCCTGAGCCCCATCGTGACCTGC GTGGTGGTGGACGTGAGCGAGGACGACCCCGACG TGCAGATCAGCTGGTTCGTGAACAACGTGGAGGTG CACACCGCCCAGACCCAGACCCACCGGGAGGACT ACAACAGCACCCTGCGCGTCGTGTCCGCCCTGCCC ATCCAGCACCAGGACTGGATGAGCGGCAAAGAAT TCAAGTGCAAGGTGAACAACAAGGACCTGCCTGC CCCCATCGAGCGGACCATCAGCAAGCCCAAGGGC AGCGTGAGAGCCCCCCAGGTGTACGTGCTGCCCCC TCCCGAGGAAGAGATGACCAAGAAACAGGTGACA CTGACCTGCATGGTGACCGACTTCATGCCCGAGGA CATCTACGTGGAGTGGACCAACAACGGCAAGACC GAGCTGAACTACAAGAACACCGAGCCTGTGCTGG ACAGCGACGGCAGCTACTTCATGTACAGCAAGCTG CGGGTGGAGAAGAAAAACTGGGTGGAGCGGAACA GCTACAGCTGCAGCGTGGTGCACGAGGGCCTGCAC AACCACCACACCACCAAGAGCTTCAGCCGGACCCC CGGCAAG
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG

		GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 204	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP KDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMS STLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE C
SEQ ID NO: 205	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAACGCGCTGATGC CGCCCCTACCGTGAGCATCTTCCCCCCCAGCAGCG AGCAGCTGACCAGCGGCGGAGCCAGCGTGGTGTG CTTCCTGAACAACTTCTACCCCAAGGACATCAACG TGAAGTGGAAGATCGACGGCAGCGAGCGGCAGAA CGGCGTGCTGAACAGCTGGACCGACCAGGACAGC AAGGACTCCACCTACAGCATGAGCAGCACCCTGAC CCTGACCAAGGACGAGTACGAGCGGCACAACAGC TACACCTGCGAGGCCACCCACAAGACCAGCACCA GCCCCATCGTGAAGAGCTTCAACCGGAACGAGTGC
ANTI-mouse ENTPD2 FAB24		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFFDS
SEQ ID NO: 185	HCDR1 (CHOTHIA)	GYTFTHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFFDS
SEQ ID NO: 187	HCDR1 (COMBINED)	GYTFTHYGMN

SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFFDS
SEQ ID NO: 188	HCDR1 (IMGT)	GYTFTHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFFDS
SEQ ID NO: 191	VH	QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSS
SEQ ID NO: 192	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 338	HC	QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFFDSWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSC
SEQ ID NO: 339	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAgctagcaccaagggcccaagtg tgtttcccctggcccccagcagcaagtctacttccggcggaactgctgccctgggtt gcctggtgaaggactacttccccgagcccgtgacagtgtcctggaactctggggct ctgacttccggcgtgcacaccttccccgccgtgctgcagagcagcggcctgtacag cctgagcagcgtggtgacagtgccctccagctctctgggaacccagacctatatct

		gcaacgtgaaccacaagcccagcaacaccaaggtggacaagagagtggagccc aagagctgc
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 340	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSS TLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C
SEQ ID NO: 341	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA

		AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCGGA CCTGGCACCAAGCTGGAAATCAAAcgtacggtggccgctcc cagcgtgttcatcttccccccagcgacgagcagctgaagagtggcaccgccagc gtggtgtgcctgctgaacaacttctacccccgggaggccaaggtgcagtggaagg tggacaacgccctgcagagcggcaacagccaggagagcgtcaccgagcaggac agcaaggactccacctacagcctgagcagcaccctgaccctgagcaaggccgac tacgagaagcataaggtgtacgcctgcgaggtgacccaccagggcctgtccagcc ccgtgaccaagagcttcaacaggggcgagtgc

[0247] In some embodiments, the anti-mouse ENTPD2 antibody or antibody fragment (e.g., an antigen binding fragment) comprises a VH domain having an amino acid sequence of any VH domain described in Table 26. Other suitable anti-mouse ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VH domain with the VH regions depicted in the sequences described in Table 26. The present disclosure in certain embodiments also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, wherein the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VH CDR having an amino acid sequence of any one of the VH CDRs listed in Table 26. In particular embodiments, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, comprising (or alternatively, consist of) one, two, three, four, five or more VH CDRs having an amino acid sequence of any one of the VH CDRs listed in Table 26.

[0248] In some embodiments, the anti-mouse ENTPD2 antibody or antibody fragment (e.g., antigen binding fragment) comprises a VL domain having an amino acid sequence of any VL domain described in Table 26. Other suitable anti-mouse ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VL domain with the VL regions depicted in the sequences described in Table 26. The present disclosure also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VL CDR having an amino acid sequence of any

one of the VL CDRs listed in Table 26. In particular, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, which comprise (or alternatively, consist of) one, two, three or more VL CDRs having an amino acid sequence of any one of the VL CDRs listed in Table 26.

[0249] Other anti-mouse ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragment) disclosed herein include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the CDR regions with the CDR regions depicted in the sequences described in Table 26. In some embodiments, it includes mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the CDR regions when compared with the CDR regions depicted in the sequence described in Table 26.

[0250] Also provided herein are nucleic acid sequences that encode VH, VL, full length heavy chain, and full length light chain of antibodies and antigen binding fragments thereof that specifically bind to mouse ENTPD2, e.g., the nucleic acid sequences in Table 26. Such nucleic acid sequences can be optimized for expression in mammalian cells.

[0251] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in mouse ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: Ser74, Cys75, Asp76, Tyr349, Tyr350, Asp353, Phe354, Thr357, Val358, Gly360, Gln385, Ala386, Arg387, Val388, Pro389, Gly390, Gln391, Thr393, Arg394, or Tyr398.

Framework and Engineered or Modified Antibodies

[0252] An antibody of the invention further can be prepared using an antibody having one or more of the VH and/or VL sequences as starting material to engineer a modified antibody, which modified antibody may have altered properties from the starting antibody. An antibody can be engineered by modifying one or more residues within one or both variable regions (i.e., VH and/or VL), for example within one or more CDR regions and/or within one or more framework regions. Additionally or alternatively, an antibody can be engineered by modifying residues within the constant region(s), for example to alter the effector function(s) of the antibody.

[0253] One type of variable region engineering that can be performed is CDR grafting. Antibodies interact with target antigens predominantly through amino acid residues

that are located in the six heavy and light chain complementarity determining regions (CDRs). For this reason, the amino acid sequences within CDRs are more diverse between individual antibodies than sequences outside of CDRs. Because CDR sequences are responsible for most antibody-antigen interactions, it is possible to express recombinant antibodies that mimic the properties of specific naturally occurring antibodies by constructing expression vectors that include CDR sequences from the specific naturally occurring antibody grafted onto framework sequences from a different antibody with different properties (see, e.g., Riechmann, L. et al., 1998 Nature 332:323-327; Jones, P. et al., 1986 Nature 321:522-525; Queen, C. et al., 1989 Proc. Natl. Acad., U.S.A. 86:10029-10033; U.S. Pat. No. 5,225,539 to Winter, and U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al.)

[0254] Such framework sequences can be obtained from public DNA databases or published references that include germline antibody gene sequences or rearranged antibody sequences. For example, germline DNA sequences for human heavy and light chain variable region genes can be found in the "VBase" human germline sequence database (available on the Internet at www.mrc-cpe.cam.ac.uk/vbase), as well as 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; Tomlinson, I. M., et al., 1992 J. fol. Biol. 227:776-798; and Cox, J. P. L. et al., 1994 Eur. J Immunol. 24:827-836). ; For example, germline DNA sequences for human heavy and light chain variable region genes and rearranged antibody sequences can be found in "IMGT" database (available on the Internet at www.imgt.org; see Lefranc, M.P. et al., 1999 Nucleic Acids Res. 27:209-212).

[0255] An example of framework sequences for use in the antibodies and antigen binding fragments thereof of the invention are those that are structurally similar to the framework sequences used by selected antibodies and antigen binding fragments thereof of the invention, e.g., consensus sequences and/or framework sequences used by monoclonal antibodies of the invention. The VH CDR1, 2 and 3 sequences, and the VL CDR1, 2 and 3 sequences, can be grafted onto framework regions that have the identical sequence as that found in the germline immunoglobulin gene from which the framework sequence derive, or the CDR sequences can be grafted onto framework regions that contain one or more mutations as compared to the germline sequences. For example, it has been found that in certain instances it is beneficial to mutate residues within the framework regions to maintain or enhance the antigen binding ability of the antibody (see e.g., U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al).

[0256] Another type of variable region modification is to mutate amino acid residues within the VH and/or VL CDR1, CDR2 and/or CDR3 regions to thereby improve one or more binding properties (e.g., affinity) of the antibody of interest, known as "affinity maturation". Site-directed mutagenesis or PCR-mediated mutagenesis can be performed to introduce the mutation(s) and the effect on antibody binding, or other functional property of interest, can be evaluated in in vitro or *in vivo* assays as described herein and provided in the Examples. Conservative modifications (as discussed above) can be introduced. The mutations may be amino acid substitutions, additions or deletions. Moreover, typically no more than one, two, three, four or five residues within a CDR region are altered.

[0257] A wide variety of antibody/immunoglobulin frameworks or scaffolds can be employed so long as the resulting polypeptide includes at least one binding region which specifically binds to ENTPD2 (e.g., human ENTPD2 protein). Such frameworks or scaffolds include the 5 main idiotypes of human immunoglobulins, antigen-binding fragments thereof, and include immunoglobulins of other animal species, preferably having humanized aspects. Single heavy-chain antibodies such as those identified in camelids are of particular interest in this regard. Novel frameworks, scaffolds and fragments continue to be discovered and developed by those skilled in the art.

[0258] In one aspect, the invention pertains to a method of generating non-immunoglobulin based antibodies using non-immunoglobulin scaffolds onto which CDRs of the invention can be grafted. Known or future non-immunoglobulin frameworks and scaffolds may be employed, as long as they comprise a binding region specific for the target ENTPD2 protein. Known non-immunoglobulin frameworks or scaffolds include, but are not limited to, fibronectin (Compound Therapeutics, Inc., Waltham, Mass.), ankyrin (Molecular Partners AG, Zurich, Switzerland), domain antibodies (Domantis, Ltd., Cambridge, Mass., and Ablynx nv, Zwijnaarde, Belgium), lipocalin (Pieris Proteolab AG, Freising, Germany), small modular immuno-pharmaceuticals (Trubion Pharmaceuticals Inc., Seattle, Wash.), maxybodies (Avidia, Inc., Mountain View, Calif.), Protein A (Affibody AG, Sweden), and affilin (gamma-crystallin or ubiquitin) (SciI Proteins GmbH, Halle, Germany).

[0259] The fibronectin scaffolds are based on fibronectin type III domain (e.g., the tenth module of the fibronectin type III (10 Fn3 domain)). The fibronectin type III domain has 7 or 8 beta strands which are distributed between two beta sheets, which themselves pack against each other to form the core of the protein, and further containing loops (analogous to CDRs) which connect the beta strands to each other and are solvent exposed. There are at least three such loops at each edge of the beta sheet sandwich, where the edge is the boundary

of the protein perpendicular to the direction of the beta strands (see U.S. Pat. No. 6,818,418). These fibronectin-based scaffolds are not an immunoglobulin, although the overall fold is closely related to that of the smallest functional antibody fragment, the variable region of the heavy chain, which comprises the entire antigen recognition unit in camel and llama IgG. Because of this structure, the non-immunoglobulin antibody mimics antigen binding properties that are similar in nature and affinity for those of antibodies. These scaffolds can be used in a loop randomization and shuffling strategy in vitro that is similar to the process of affinity maturation of antibodies *in vivo*. These fibronectin-based molecules can be used as scaffolds where the loop regions of the molecule can be replaced with CDRs of the invention using standard cloning techniques.

[0260] The ankyrin technology is based on using proteins with ankyrin derived repeat modules as scaffolds for bearing variable regions which can be used for binding to different targets. The ankyrin repeat module is a 33 amino acid polypeptide consisting of two anti-parallel alpha-helices and a beta-turn. Binding of the variable regions is mostly optimized by using ribosome display.

[0261] Avimers are derived from natural A-domain containing protein such as LRP-1. These domains are used by nature for protein-protein interactions and in human over 250 proteins are structurally based on A-domains. Avimers consist of a number of different "A-domain" monomers (2-10) linked via amino acid linkers. Avimers can be created that can bind to the target antigen using the methodology described in, for example, U.S. Patent Application Publication Nos. 20040175756; 20050053973; 20050048512; and 20060008844.

[0262] Affibody affinity ligands are small, simple proteins composed of a three-helix bundle based on the scaffold of one of the IgG-binding domains of Protein A. Protein A is a surface protein from the bacterium Staphylococcus aureus. This scaffold domain consists of 58 amino acids, 13 of which are randomized to generate affibody libraries with a large number of ligand variants (See e.g., U.S. Pat. No. 5,831,012). Affibody molecules mimic antibodies, they have a molecular weight of 6 kDa, compared to the molecular weight of antibodies, which is 150 kDa. In spite of its small size, the binding site of affibody molecules is similar to that of an antibody.

[0263] Anticalins are products developed by the company Pieris ProteoLab AG. They are derived from lipocalins, a widespread group of small and robust proteins that are usually involved in the physiological transport or storage of chemically sensitive or insoluble compounds. Several natural lipocalins occur in human tissues or body liquids. The protein architecture is reminiscent of immunoglobulins, with hypervariable loops on top of a rigid

framework. However, in contrast with antibodies or their recombinant fragments, lipocalins are composed of a single polypeptide chain with 160 to 180 amino acid residues, being just marginally bigger than a single immunoglobulin domain. The set of four loops, which makes up the binding pocket, shows pronounced structural plasticity and tolerates a variety of side chains. The binding site can thus be reshaped in a proprietary process in order to recognize prescribed target molecules of different shape with high affinity and specificity. One protein of lipocalin family, the bilin-binding protein (BBP) of Pieris Brassicae has been used to develop anticalins by mutagenizing the set of four loops. One example of a patent application describing anticalins is in PCT Publication No. WO 199916873.

[0264] Affilin molecules are small non-immunoglobulin proteins which are designed for specific affinities towards proteins and small molecules. New affilin molecules can be very quickly selected from two libraries, each of which is based on a different human derived scaffold protein. Affilin molecules do not show any structural homology to immunoglobulin proteins. Currently, two affilin scaffolds are employed, one of which is gamma crystalline, a human structural eye lens protein and the other is "ubiquitin" superfamily proteins. Both human scaffolds are very small, show high temperature stability and are almost resistant to pH changes and denaturing agents. This high stability is mainly due to the expanded beta sheet structure of the proteins. Examples of gamma crystalline derived proteins are described in WO200104144 and examples of "ubiquitin-like" proteins are described in WO2004106368.

[0265] Protein epitope mimetics (PEM) are medium-sized, cyclic, peptide-like molecules (MW 1-2 kDa) mimicking beta-hairpin secondary structures of proteins, the major secondary structure involved in protein-protein interactions.

[0266] Engineered antibodies and antigen-binding fragments thereof of the invention include those in which modifications have been made to framework residues within VH and/or VL, e.g. to improve the properties of the antibody. Typically such framework modifications are made to decrease the immunogenicity of the antibody. For example, one approach is to “backmutate” one or more framework residues to the corresponding germline sequence. More specifically, an antibody that has undergone somatic mutation may contain framework residues that differ from the germline sequence from which the antibody is derived. Such residues can be identified by comparing the antibody framework sequences to the germline sequences from which the antibody is derived. To return the framework region sequences to their germline configuration, the somatic mutations can be “backmutated” to the germline sequence by, for example, site-directed mutagenesis. Such “backmutated”

antibodies are also intended to be encompassed by the invention.

[0267] Another type of framework modification involves mutating one or more residues within the framework region, or even within one or more CDR regions, to remove T cell-epitopes to thereby reduce the potential immunogenicity of the antibody. This approach is also referred to as "deimmunization" and is described in further detail in U.S. Patent Publication No. 20030153043 by Carr et al.

[0268] In addition or alternative to modifications made within the framework or CDR regions, antibodies of the invention may be engineered to include modifications within the Fc region, typically to alter one or more functional properties of the antibody, such as serum half-life, complement fixation, Fc receptor binding, and/or antigen-dependent cellular cytotoxicity. Furthermore, an antibody of the invention may be chemically modified (e.g., one or more chemical moieties can be attached to the antibody) or be modified to alter its glycosylation, again to alter one or more functional properties of the antibody. Each of these embodiments is described in further detail below. The numbering of residues in the Fc region is that of the EU index of Kabat.

[0269] In one embodiment, the hinge region of CH1 is modified such that the number of cysteine residues in the hinge region is altered, e.g., increased or decreased. This approach is described further in U.S. Pat. No. 5,677,425 by Bodmer et al. The number of cysteine residues in the hinge region of CH1 is altered to, for example, facilitate assembly of the light and heavy chains or to increase or decrease the stability of the antibody.

[0270] In another embodiment, the Fc hinge region of an antibody is mutated to decrease the biological half-life of the antibody. More specifically, one or more amino acid mutations are introduced into the CH2-CH3 domain interface region of the Fc-hinge fragment such that the antibody has impaired Staphylococcyl protein A (SpA) binding relative to native Fc-hinge domain SpA binding. This approach is described in further detail in U.S. Pat. No. 6,165,745 by Ward et al.

[0271] In another embodiment, the antibody is modified to increase its biological half-life. Various approaches are possible. For example, one or more of the following mutations can be introduced: T252L, T254S, T256F, as described in U.S. Pat. No. 6,277,375 to Ward. Alternatively, to increase the biological half life, the antibody can be altered within the CH1 or CL region to contain a salvage receptor binding epitope taken from two loops of a CH2 domain of an Fc region of an IgG, as described in U.S. Pat. Nos. 5,869,046 and 6,121,022 by Presta et al.

[0272] In one embodiment, the Fc region is altered by replacing at least one amino

acid residue with a different amino acid residue to alter the effector functions of the antibody. For example, one or more amino acids can be replaced with a different amino acid residue such that the antibody has an altered affinity for an effector ligand but retains the antigen-binding ability of the parent antibody. The effector ligand to which affinity is altered can be, for example, an Fc receptor or the C1 component of complement. This approach is described in further detail in U.S. Pat. Nos. 5,624,821 and 5,648,260, both by Winter et al.

[0273] In another embodiment, one or more amino acids selected from amino acid residues can be replaced with a different amino acid residue such that the antibody has altered C1q binding and/or reduced or abolished complement dependent cytotoxicity (CDC). This approach is described in further detail in U.S. Pat. No. 6,194,551 by Idusogie et al.

[0274] In another embodiment, one or more amino acid residues are altered to thereby alter the ability of the antibody to fix complement. This approach is described further in PCT Publication WO 94/29351 by Bodmer et al.

[0275] In some embodiments, the ENTPD2-binding antibodies or antigen binding fragments thereof contain a human IgG1 constant region. In some embodiments, the human IgG1 constant region includes an Fc region.

[0276] In some embodiments, the Fc region of the ENTPD2-binding antibodies or antigen binding fragments thereof includes one or more mutations mediating reduced or no antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC). In some embodiments, amino acid residues L234 and L235 of the IgG1 constant region are substituted to A234 and A235. In some embodiments, amino acid residue N267 of the IgG1 constant region is substituted to A267. In some embodiments, amino acid residues D265 and P329 of the IgG1 constant region are substituted to A265 and A329. In certain embodiments, the Fc region optionally comprises a mutation or combination of mutations conferring reduced effector function selected from any one of D265A, P329A, P329G, N297A, D265A/P329A, D265A/N297A, L234/L235A, P329A/L234A/L235A, and P329G/L234A/L235A. In some embodiments, the Fc region comprises a mutation or combination of mutations conferring reduced effector function selected from any one of D265A, P329A, P329G, N297A, D265A/P329A, D265A/N297A, L234/L235A, P329A/L234A/L235A, and P329G/L234A/L235A (all positions by EU numbering).

[0277] In yet another embodiment, the Fc region is modified to increase the ability of the antibody to mediate antibody dependent cellular cytotoxicity (ADCC) and/or to increase the affinity of the antibody for an Fc-gamma receptor by modifying one or more amino acids. This approach is described further in PCT Publication WO 00/42072 by Presta. Moreover,

the binding sites on human IgG1 for Fc-gamma RI, Fc-gamma RII, Fc-gamma RIII and FcRn have been mapped and variants with improved binding have been described (see Shields, R. L. et al., 2001 J. Biol. Chen. 276:6591-6604). For example, the Fc region can comprise a mutation or combination of mutations conferring increased effector function selected from any one of S239D, I332E, A330L, S298A, E333A, E333S, K334A, K236A, K236W, F243L, P247I, D280H, K290S, R292P, S298D, S298V, Y300L, V305I, A339D, A339Q, A339T, P396L (all positions by EU numbering).

[0278] In still another embodiment, the glycosylation of an antibody is modified. For example, an aglycoslated antibody can be made (i.e., the antibody lacks glycosylation). Glycosylation can be altered to, for example, increase the affinity of the antibody for antigen. Such carbohydrate modifications can be accomplished by, for example, altering one or more sites of glycosylation within the antibody sequence. For example, one or more amino acid substitutions can be made that result in elimination of one or more variable region framework glycosylation sites to thereby eliminate glycosylation at that site. Such aglycosylation may increase the affinity of the antibody for antigen. Such an approach is described in further detail in U.S. Pat. Nos. 5,714,350 and 6,350,861 by Co et al.

[0279] Additionally or alternatively, an antibody can be made that has an altered type of glycosylation, such as a hypofucosylated antibody having reduced amounts of fucosyl residues or an antibody having increased bisecting GlcNac structures. Such altered glycosylation patterns have been demonstrated to increase the ADCC ability of antibodies. Such carbohydrate modifications can be accomplished by, for example, expressing the antibody in a host cell with altered glycosylation machinery. Cells with altered glycosylation machinery have been described in the art and can be used as host cells in which to express recombinant antibodies of the invention to thereby produce an antibody with altered glycosylation. For example, EP 1,176,195 by Hang et al. describes a cell line with a functionally disrupted FUT8 gene, which encodes a fucosyl transferase, such that antibodies expressed in such a cell line exhibit hypofucosylation. PCT Publication WO 03/035835 by Presta describes a variant CHO cell line, LecI3 cells, with reduced ability to attach fucose to Asn (297)-linked carbohydrates, also resulting in hypofucosylation of antibodies expressed in that host cell (see also Shields, R. L. et al., 2002 J. Biol. Chem. 277:26733-26740). PCT Publication WO 99/54342 by Umana et al. describes cell lines engineered to express glycoprotein-modifying glycosyl transferases (e.g., beta (1,4)--N acetylglucosaminyltransferase III (GnTIII)) such that antibodies expressed in the engineered cell lines exhibit increased bisecting GlcNac structures which results in increased ADCC

activity of the antibodies (see also Umana et al., 1999 Nat. Biotech. 17:176-180).

[0280] In some embodiments, the ENTPD2 antibody has an IgG1 isotype with one or more mutations *(e.g.,* relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more mutations are selected from N297A, N297Q (BoltS et al. (1993) *Eur J Immunol* 23:403-411), D265A, L234A, L235A (McEarchern et al., (2007) *Blood,* 109:1185-1192), C226S, C229S (McEarchern et al., (2007) *Blood,* 109:1185-1192), P238S (Davis et al., (2007) *J Rheumatol,* 34:2204-2210), E233P, L234V (McEarchern et al., (2007) *Blood,* 109:1185-1192), P238A, A327Q, A327G, P329A (Shields RL. et al., (2001) *J Bioi Chern.* 276(9):6591-604), K322A, L234F, L235E (Hezareh,et al., (2001) **J** Viral *75,* 12161-12168; Oganesyan et al., (2008). *Acta Crystallographica 64,* 700-704), P331S (Oganesyan et al., (2008) *Acta Crystallographica 64,* 700-704), T394D (Wilkinson et al. (2013) *MAbs* 5(3): 406-417), A330L, M252Y, S254T, and/or T256E, where the amino acid position is according to the EU or Kabat numbering convention. In certain embodiments, the Fc region further includes an amino acid deletion at a position corresponding to glycine 236 according to the EU or Kabat numbering convention.

[0281] In some embodiments, the antibody has an IgG1 isotype with a heavy chain constant region that contains a C220S mutation according to the EU or Kabat numbering convention.

[0282] In some embodiments, the Fc region contains one or more mutations selected from L234F, L235E, P331S, D265A, and/or N297Q, according to EU or Kabat numbering convention. In some embodiments, the Fc region contains one or more mutations selected from L234A, L235A, D265A, P329A, N297A, N297Q according to EU or Kabat numbering convention.

[0283] In certain embodiments, the antibody has an IgG2 isotype. In some embodiments, the antibody contains a human IgG2 constant region. In some embodiments, the human IgG2 constant region includes an Fc region. In some embodiments, the Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more mutations *(e.g.,* relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more mutations are selected from V234A, G237A, P238S, H268A, H268E, H268Q, V309L, N297A, N297Q, V309L, A330S, P331S, C232S, C233S, M252Y, S254T, and/or T256E, where the amino acid position is according to the EU or Kabat numbering convention.

[0284] In certain embodiments, the antibody has an IgG4 isotype. In some embodiments, the antibody contains a human IgG4 constant region. In some embodiments,

the human IgG4 constant region includes an Fc region. In some embodiments, the Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more mutations *(e.g.,* relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more mutations are selected from E233P, F234V, L234A, L235A, G237A, E318A (Hutchins et al. (1995) Proc Natl A cad Sci USA, 92:11980-11984), S228P, L236E, S241P, L248E (Reddy et al., (2000) J Immunol,164:1925-1933; Angal et al., (1993) Mol Immunol. 30(1):105-8; US 8614299 B2), T394D, M252Y, S254T, T256E, N297A, and/or N297Q, where the amino acid position is according to the EU or Kabat numbering convention.

[0285] In some embodiments, the Fc region further contains one or more additional mutations selected from a M252Y, S254T, and/or T256E, where the amino acid position is according to the EU or Kabat numbering convention.

[0286] In some embodiments, one or more of the IgG1 variants described herein may be combined with an A330L mutation (Lazaret al., (2006) Proc Natl Acad Sci USA, 103:4005-4010), or one or more of L234F, L235E, and/or P331S mutations (Sazinsky et al., (2008) Proc Natl Acad Sci USA, 105:20167-20172), where the amino acid position is according to the EU or Kabat numbering convention, to eliminate complement activation. In some embodiments, the IgG variants described herein may be combined with one or more mutations to enhance the antibody half-life in human serum (e.g. M252Y, S254T,T256E mutations according to the EU or Kabat numbering convention) (Dall' Acqua et al., (2006) J Biol Chern, 281:23514-23524; and Strohl et al., (2009) Current Opinion in Biotechnology, 20:685-691).

[0287] In some embodiments, an IgG4 variant of the present disclosure may be combined with an S228P mutation according to the EU or Kabat numbering convention (Angal et al., (1993) Mol Immunol, 30:105-108) and/or with one or more mutations described in Peters et al., (2012) J Biol Chern. 13;287(29):24525-33) to enhance antibody stabilization.

[0288] In some embodiments, the antibody has an Fc region selected from an IgG2 Fc region, an IgG4 Fc region, or an IgG2/IgG4 hybrid Fc region.

Camelid Antibodies

[0289] Antibody proteins obtained from members of the camel and dromedary (Camelus bactrianus and Calelus dromaderius) family including new world members such as llama species (Lama paccos, Lama glama and Lama vicugna) have been characterized with respect to size, structural complexity and antigenicity for human subjects. Certain IgG

antibodies from this family of mammals as found in nature lack light chains, and are thus structurally distinct from the typical four chain quaternary structure having two heavy and two light chains, for antibodies from other animals. See PCT/EP93/02214 (WO 94/04678 published 3 Mar. 1994).

[0290] A region of the camelid antibody which is the small single variable domain identified as VHH can be obtained by genetic engineering to yield a small protein having high affinity for a target, resulting in a low molecular weight antibody-derived protein known as a "camelid nanobody." See U.S. Pat. No. 5,759,808 issued Jun. 2, 1998; see also Stijlemans, B. et al., 2004 J Biol Chem 279: 1256-1261; Dumoulin, M. et al., 2003 Nature 424: 783-788; Pleschberger, M. et al. 2003 Bioconjugate Chem 14: 440-448; Cortez-Retamozo, V. et al. 2002 Int J Cancer 89: 456-62; and Lauwereys, M. et al. 1998 EMBO J 17: 3512-3520. Engineered libraries of camelid antibodies and antibody fragments are commercially available, for example, from Ablynx, Ghent, Belgium. As with other antibodies and antigen-binding fragments thereof of non-human origin, an amino acid sequence of a camelid antibody can be altered recombinantly to obtain a sequence that more closely resembles a human sequence, i.e., the nanobody can be "humanized." Thus the natural low antigenicity of camelid antibodies to humans can be further reduced.

[0291] The camelid nanobody has a molecular weight approximately one-tenth that of a human IgG molecule, and the protein has a physical diameter of only a few nanometers. One consequence of the small size is the ability of camelid nanobodies to bind to antigenic sites that are functionally invisible to larger antibody proteins, i.e., camelid nanobodies are useful as reagents detect antigens that are otherwise cryptic using classical immunological techniques, and as possible therapeutic agents. Thus yet another consequence of small size is that a camelid nanobody can inhibit as a result of binding to a specific site in a groove or narrow cleft of a target protein, and hence can serve in a capacity that more closely resembles the function of a classical low molecular weight drug than that of a classical antibody.

[0292] The low molecular weight and compact size further result in camelid nanobodies being extremely thermostable, stable to extreme pH and to proteolytic digestion, and poorly antigenic. Another consequence is that camelid nanobodies readily move from the circulatory system into tissues, and even cross the blood-brain barrier and can treat disorders that affect nervous tissue. Nanobodies can further facilitated drug transport across the blood brain barrier. See U.S. patent application 20040161738 published Aug. 19, 2004. These features combined with the low antigenicity to humans indicate great therapeutic potential. Further, these molecules can be fully expressed in prokaryotic cells such as *E. coli* and are

expressed as fusion proteins with bacteriophage and are functional.

[0293] Accordingly, a feature of the present invention is a camelid antibody or nanobody having high affinity for ENTPD2. In one embodiment herein, the camelid antibody or nanobody is naturally produced in the camelid animal, i.e., is produced by the camelid following immunization with ENTPD2 or a peptide fragment thereof, using techniques described herein for other antibodies. Alternatively, the ENTPD2-binding camelid nanobody is engineered, i.e., produced by selection for example from a library of phage displaying appropriately mutagenized camelid nanobody proteins using panning procedures with ENTPD2 as a target as described in the examples herein. Engineered nanobodies can further be customized by genetic engineering to have a half life in a recipient subject of from 45 minutes to two weeks. In a specific embodiment, the camelid antibody or nanobody is obtained by grafting the CDRs sequences of the heavy or light chain of the human antibodies of the invention into nanobody or single domain antibody framework sequences, as described for example in PCT/EP93/02214.

Bispecific Molecules and Multivalent Antibodies

[0294] In another aspect, the present invention features bispecific or multispecific molecules comprising a ENTPD2-binding antibody, or a fragment thereof, of the invention. An antibody of the invention, or antigen-binding regions thereof, can be derivatized or linked to another functional molecule, e.g., another peptide or protein (e.g., another antibody or ligand for a receptor) to generate a bispecific molecule that binds to at least two different binding sites or target molecules. The antibody of the invention may in fact be derivatized or linked to more than one other functional molecule to generate multi-specific molecules that bind to more than two different binding sites and/or target molecules; such multi-specific molecules are also intended to be encompassed by the term "bispecific molecule" as used herein. To create a bispecific molecule of the invention, an antibody of the invention can be functionally linked (e.g., by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other binding molecules, such as another antibody, antibody fragment, peptide or binding mimetic, such that a bispecific molecule results.

[0295] Accordingly, the present invention includes bispecific molecules comprising at least one first binding specificity for ENTPD2 and a second binding specificity for a second target epitope. For example, the second target epitope is another epitope of ENTPD2 different from the first target epitope.

[0296] Additionally, for the invention in which the bispecific molecule is multi-

specific, the molecule can further include a third binding specificity, in addition to the first and second target epitope.

[0297] In one embodiment, the bispecific molecules of the invention comprise as a binding specificity at least one antibody, or an antibody fragment thereof, including, e.g., a Fab, Fab', F (ab')2, Fv, or a single chain Fv. The antibody may also be a light chain or heavy chain dimer, or any minimal fragment thereof such as a Fv or a single chain construct as described in Ladner et al. U.S. Pat. No. 4,946,778.

[0298] Diabodies are bivalent, bispecific molecules in which VH and VL domains are expressed on a single polypeptide chain, connected by a linker that is too short to allow for pairing between the two domains on the same chain. The VH and VL domains pair with complementary domains of another chain, thereby creating two antigen binding sites (see e.g., Holliger et al., 1993 Proc. Natl. Acad. Sci. USA 90:6444-6448; Poijak et al., 1994 Structure 2:1121-1123). Diabodies can be produced by expressing two polypeptide chains with either the structure VHA-VLB and VHB-VLA (VH-VL configuration), or VLA-VHB and VLB-VHA (VL-VH configuration) within the same cell. Most of them can be expressed in soluble form in bacteria. Single chain diabodies (scDb) are produced by connecting the two diabody-forming polypeptide chains with linker of approximately 15 amino acid residues (see Holliger and Winter, 1997 Cancer Immunol. Immunother., 45 (3-4):128-30; Wu et al., 1996 Immunotechnology, 2 (1):21-36). scDb can be expressed in bacteria in soluble, active monomeric form (see Holliger and Winter, 1997 Cancer Immunol. Immunother., 45 (34): 128-30; Wu et al., 1996 Immunotechnology, 2 (1):21-36; Pluckthun and Pack, 1997 Immunotechnology, 3 (2): 83-105; Ridgway et al., 1996 Protein Eng., 9 (7):617-21). A diabody can be fused to Fc to generate a "di-diabody" (see Lu et al., 2004 J. Biol. Chem., 279 (4):2856-65).

[0299] Other antibodies which can be employed in the bispecific molecules of the invention are murine, chimeric and humanized monoclonal antibodies.

[0300] The bispecific molecules of the present invention can be prepared by conjugating the constituent binding specificities, using methods known in the art. For example, each binding specificity of the bispecific molecule can be generated separately and then conjugated to one another. When the binding specificities are proteins or peptides, a variety of coupling or cross-linking agents can be used for covalent conjugation. Examples of cross-linking agents include protein A, carbodiimide, N-succinimidyl-5-acetyl-thioacetate (SATA), 5,5'-dithiobis (2-nitrobenzoic acid) (DTNB), o-phenylenedimaleimide (oPDM), N-succinimidyl-3- (2-pyridyldithio)propionate (SPDP), and sulfosuccinimidyl 4- (N-

maleimidomethyl)cyclohaxane-1-carboxylate (sulfo-SMCC) (see e.g., Karpovsky et al., 1984 J. Exp. Med. 160:1686; Liu, M A et al., 1985 Proc. Natl. Acad. Sci. USA 82:8648). Other methods include those described in Paulus, 1985 Behring Ins. Mitt. No. 78, 118-132; Brennan et al., 1985 Science 229:81-83), and Glennie et al., 1987 J. Immunol. 139: 2367-2375). Conjugating agents are SATA and sulfo-SMCC, both available from Pierce Chemical Co. (Rockford, Ill.).

[0301] When the binding specificities are antibodies, they can be conjugated by sulfhydryl bonding of the C-terminus hinge regions of the two heavy chains. In a particularly embodiment, the hinge region is modified to contain an odd number of sulfhydryl residues, for example one, prior to conjugation.

[0302] Alternatively, both binding specificities can be encoded in the same vector and expressed and assembled in the same host cell. This method is particularly useful where the bispecific molecule is a mAb X mAb, mAb X Fab, Fab X F (ab')2 or ligand X Fab fusion protein. A bispecific molecule of the invention can be a single chain molecule comprising one single chain antibody and a binding determinant, or a single chain bispecific molecule comprising two binding determinants. Bispecific molecules may comprise at least two single chain molecules. Methods for preparing bispecific molecules are described for example in U.S. Pat. No. 5,260,203; U.S. Pat. No. 5,455,030; U.S. Pat. No. 4,881,175; U.S. Pat. No. 5,132,405; U.S. Pat. No. 5,091,513; U.S. Pat. No. 5,476,786; U.S. Pat. No. 5,013,653; U.S. Pat. No. 5,258,498; and U.S. Pat. No. 5,482,858.

[0303] Binding of the bispecific molecules to their specific targets can be confirmed by, for example, enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (REA), FACS analysis, bioassay (e.g., growth inhibition), or Western Blot assay. Each of these assays generally detects the presence of protein-antibody complexes of particular interest by employing a labeled reagent (e.g., an antibody) specific for the complex of interest.

[0304] In another aspect, the present invention provides multivalent compounds comprising at least two identical or different antigen-binding portions of the antibodies and antigen-binding fragments thereof of the invention binding to ENTPD2. The antigen-binding portions can be linked together via protein fusion or covalent or noncovalent linkage. Alternatively, methods of linkage has been described for the bispecific molecules. Tetravalent compounds can be obtained for example by cross-linking antibodies and antigen-binding fragments thereof of the invention with an antibody or antigen-binding fragment that binds to the constant regions of the antibodies and antigen-binding fragments thereof of the invention, for example the Fc or hinge region.

[0305] Trimerizing domain are described for example in Borean patent EP 1 012 280B1. Pentamerizing modules are described for example in PCT/EP97/05897.

[0306] In some embodiments, the ENTPD2-binding antibodies or antigen binding fragments thereof are bispecific antibodies that recognize a first antigen and a second antigen. In some embodiments, the first antigen is human ENTPD2 or a naturally occurring variant thereof. In some embodiments, the second antigen may be a protein, lipid, polysaccharide, or glycolipid expressed on one or more tumor cells.

Antibodies with Extended Half Life

[0307] The present invention provides for antibodies that specifically bind to ENTPD2 (e.g., human ENTPD2 protein) and have an extended half-life in vivo.

[0308] Many factors may affect a protein's half life *in vivo*. For examples, kidney filtration, metabolism in the liver, degradation by proteolytic enzymes (proteases), and immunogenic responses (e.g., protein neutralization by antibodies and uptake by macrophages and dendritic cells). A variety of strategies can be used to extend the half life of the antibodies and antigen-binding fragments thereof of the present invention. For example, by chemical linkage to polyethylene glycol (PEG), reCODE PEG, antibody scaffold, polysialic acid (PSA), hydroxyethyl starch (HES), albumin-binding ligands, and carbohydrate shields; by genetic fusion to proteins binding to serum proteins, such as albumin, IgG, FcRn, and transferring; by coupling (genetically or chemically) to other binding moieties that bind to serum proteins, such as nanobodies, Fabs, DARPins, avimers, affibodies, and anticalins; by genetic fusion to rPEG, albumin, domain of albumin, albumin-binding proteins, and Fc; or by incorporation into nancarriers, slow release formulations, or medical devices.

[0309] To prolong the serum circulation of antibodies *in vivo*, inert polymer molecules such as high molecular weight PEG can be attached to the antibodies or a fragment thereof with or without a multifunctional linker either through site-specific conjugation of the PEG to the N- or C-terminus of the antibodies or via epsilon-amino groups present on lysine residues. To pegylate an antibody, the antibody, antigen-binding fragment thereof, typically is reacted with polyethylene glycol (PEG), such as a reactive ester or aldehyde derivative of PEG, under conditions in which one or more PEG groups become attached to the antibody or antibody fragment. The pegylation can be carried out by an acylation reaction or an alkylation reaction with a reactive PEG molecule (or an analogous reactive water-soluble polymer). As used herein, the term "polyethylene glycol" is intended to encompass any one of the forms of PEG that have been used to derivatize other proteins, such as mono (C1-

C10)alkoxy- or aryloxy-polyethylene glycol or polyethylene glycol-maleimide. In one embodiment, the antibody to be pegylated is an aglycosylated antibody. Linear or branched polymer derivatization that results in minimal loss of biological activity will be used. The degree of conjugation can be closely monitored by SDS-PAGE and mass spectrometry to ensure proper conjugation of PEG molecules to the antibodies. Unreacted PEG can be separated from antibody-PEG conjugates by size-exclusion or by ion-exchange chromatography. PEG-derivatized antibodies can be tested for binding activity as well as for *in vivo* efficacy using methods well-known to those of skill in the art, for example, by immunoassays described herein. Methods for pegylating proteins are known in the art and can be applied to the antibodies and antigen-binding fragments thereof of the invention. See for example, EP 0154316 by Nishimura et al. and EP 0401384 by Ishikawa et al.

[0310] Other modified pegylation technologies include reconstituting chemically orthogonal directed engineering technology (ReCODE PEG), which incorporates chemically specified side chains into biosynthetic proteins via a reconstituted system that includes tRNA synthetase and tRNA. This technology enables incorporation of more than 30 new amino acids into biosynthetic proteins in *E. coli*, yeast, and mammalian cells. The tRNA incorporates a normative amino acid any place an amber codon is positioned, converting the amber from a stop codon to one that signals incorporation of the chemically specified amino acid.

[0311] Recombinant pegylation technology (rPEG) can also be used for serum halflife extension. This technology involves genetically fusing a 300-600 amino acid unstructured protein tail to an existing pharmaceutical protein. Because the apparent molecular weight of such an unstructured protein chain is about 15-fold larger than its actual molecular weight, the serum halflife of the protein is greatly increased. In contrast to traditional PEGylation, which requires chemical conjugation and repurification, the manufacturing process is greatly simplified and the product is homogeneous.

[0312] Polysialytion is another technology, which uses the natural polymer polysialic acid (PSA) to prolong the active life and improve the stability of therapeutic peptides and proteins. PSA is a polymer of sialic acid (a sugar). When used for protein and therapeutic peptide drug delivery, polysialic acid provides a protective microenvironment on conjugation. This increases the active life of the therapeutic protein in the circulation and prevents it from being recognized by the immune system. The PSA polymer is naturally found in the human body. It was adopted by certain bacteria which evolved over millions of years to coat their walls with it. These naturally polysialylated bacteria were then able, by virtue of molecular

mimicry, to foil the body's defense system. PSA can be easily produced from such bacteria in large quantities and with predetermined physical characteristics. Bacterial PSA is completely non-immunogenic, even when coupled to proteins, as it is chemically identical to PSA in the human body.

[0313] Another technology include the use of hydroxyethyl starch ("HES") derivatives linked to antibodies. HES is a modified natural polymer derived from waxy maize starch and can be metabolized by the body's enzymes. HES solutions are usually administered to substitute deficient blood volume and to improve the rheological properties of the blood. Hesylation of an antibody enables the prolongation of the circulation half-life by increasing the stability of the molecule, as well as by reducing renal clearance, resulting in an increased biological activity. By varying different parameters, such as the molecular weight of HES, a wide range of HES antibody conjugates can be customized.

[0314] Antibodies having an increased half-life *in vivo* can also be generated introducing one or more amino acid modifications (i.e., substitutions, insertions or deletions) into an IgG constant domain, or FcRn binding fragment thereof (preferably a Fc or hinge Fc domain fragment). See, e.g., International Publication No. WO 98/23289; International Publication No. WO 97/34631; and U.S. Pat. No. 6,277,375.

[0315] Further, antibodies can be conjugated to albumin in order to make the antibody or antibody fragment more stable *in vivo* or have a longer half life *in vivo*. The techniques are well-known in the art, see, e.g., International Publication Nos. WO 93/15199, WO 93/15200, and WO 01/77137; and European Patent No. EP 413,622.

[0316] The strategies for increasing half life is especially useful in nanobodies, fibronectin-based binders, and other antibodies or proteins for which increased in vivo half life is desired.

Antibody Conjugates

[0317] The present invention provides antibodies or antigen-binding fragments thereof that specifically bind to the extracellular domain of ENTPD2 (e.g., human ENTPD2 protein) recombinantly fused or chemically conjugated (including both covalent and non-covalent conjugations) to a heterologous protein or polypeptide (or antigen-binding fragment thereof, preferably to a polypeptide of at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90 or at least 100 amino acids) to generate fusion proteins. In particular, the invention provides fusion proteins comprising an antigen-binding fragment of an antibody described herein (e.g., a Fab fragment, Fd fragment, Fv

fragment, F $(ab)_2$ fragment, a VH domain, a VH CDR, a VL domain or a VL CDR) and a heterologous protein, polypeptide, or peptide. Methods for fusing or conjugating proteins, polypeptides, or peptides to an antibody or an antibody fragment are known in the art. See, e.g., U.S. Pat. Nos. 5,336,603, 5,622,929, 5,359,046, 5,349,053, 5,447,851, and 5,112,946; European Patent Nos. EP 307,434 and EP 367,166; International Publication Nos. WO 96/04388 and WO 91/06570; Ashkenazi et al., 1991, Proc. Natl. Acad. Sci. USA 88: 10535-10539; Zheng et al., 1995, J. Immunol. 154:5590-5600; and Vil et al., 1992, Proc. Natl. Acad. Sci. USA 89:11337-11341.

[0318] Additional fusion proteins may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to alter the activities of antibodies and antigen-binding fragments thereof of the invention (e.g., antibodies and antigen-binding fragments thereof with higher affinities and lower dissociation rates). See, generally, U.S. Pat. Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458; Patten et al., 1997, Curr. Opinion Biotechnol. 8:724-33; Harayama, 1998, Trends Biotechnol. 16 (2):76-82; Hansson, et al., 1999, J. Mol. Biol. 287:265-76; and Lorenzo and Blasco, 1998, Biotechniques 24 (2):308-313). Antibodies and antigen-binding fragments thereof, or the encoded antibodies and antigen-binding fragments thereof, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. A polynucleotide encoding an antibody antigen-binding fragment thereof that specifically binds to ENTPD2 (e.g., human ENTPD2 protein) may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

[0319] Moreover, the antibodies and antigen-binding fragments thereof can be fused to marker sequences, such as a peptide to facilitate purification. In one embodiment, the marker amino acid sequence is a hexa-histidine peptide (SEQ ID NO: 1010), such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, Calif., 91311), among others, many one of which are commercially available. As described in Gentz et al., 1989, Proc. Natl. Acad. Sci. USA 86:821-824, for instance, hexa-histidine (SEQ ID NO: 1010) provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the hemagglutinin ("HA") tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., 1984, Cell 37:767), and the "FLAG" tag.

[0320] In one embodiment, antibodies and antigen-binding fragments thereof of the

present invention antigen-binding fragments thereof conjugated to a diagnostic or detectable agent. Such antibodies can be useful for monitoring or prognosing the onset, development, progression and/or severity of a disease or disorder as part of a clinical testing procedure, such as determining the efficacy of a particular therapy. Such diagnosis and detection can accomplished by coupling the antibody to detectable substances including, but not limited to, various enzymes, such as, but not limited to, horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; prosthetic groups, such as, but not limited to, streptavidin/biotin and avidin/biotin; fluorescent materials, such as, but not limited to, umbelliferone, fluorescein, fluorescein isothiocynate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; luminescent materials, such as, but not limited to, luminol; bioluminescent materials, such as but not limited to, luciferase, luciferin, and aequorin; radioactive materials, such as, but not limited to, iodine (131I, 125I, 123I, and 121I), carbon (14C), sulfur (35S), tritium (3H), indium (115In, 113In, 112In, and 111In), technetium (99Tc), thallium (201Ti), gallium (68Ga, 67Ga), palladium (103Pd), molybdenum (99Mo), xenon (133Xe), fluorine (18F), 153Sm, 177Lu, 159Gd, 149 Pm, 140La, 175Yb, 166Ho, 90Y, 47Sc, 186Re, 188Re, 142Pr, 105Rh, 97Ru, 68Ge, 57Co, 65Zn, 85Sr, 32P, 153Gd, 169Yb, 51Cr, 54Mn, 75Se, 113Sn, and 117Tin; and positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions.

[0321] Further, an antibody antigen-binding fragment thereof may be conjugated to a therapeutic moiety or drug moiety. Therapeutic moieties or drug moieties are not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein, peptide, or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, cholera toxin, or diphtheria toxin; a protein such as tumor necrosis factor, alpha-interferon, beta-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, an anti-angiogenic agent; or, a biological response modifier such as, for example, a lymphokine.

[0322] Moreover, an antibody can be conjugated to therapeutic moieties such as a radioactive metal ion, such as alpha-emitters such as 213Bi or macrocyclic chelators useful for conjugating radiometal ions, including but not limited to, 131In, 131LU, 131Y, 131Ho, 131Sm, to polypeptides. In one embodiment, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N",N"'-tetraacetic acid (DOTA) which can be attached to the antibody via a linker molecule. Such linker molecules are commonly known in the art and described in Denardo et al., 1998, Clin Cancer Res. 4 (10):2483-90; Peterson et al., 1999,

Bioconjug. Chem. 10 (4):553-7; and Zimmerman et al., 1999, Nucl. Med. Biol. 26 (8):943-50, each incorporated by reference in their entireties.

[0323] Techniques for conjugating therapeutic moieties to antibodies are well known, see, e.g., Amon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy," in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies 84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., 1982, Immunol. Rev. 62:119-58.

[0324] Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Nucleic Acids Encoding the Antibodies, Vectors and Host Cells

[0325] Also provided herein are nucleic acids encoding an antibody or antigen binding fragment thereof described herein. Such nucleic acids can encode polypeptides comprising segments or domains of the ENTPD2 antibodies or antigen-binding fragments thereof described above. Such nucleic acids or polynucleotides can encode at least one CDR region and usually all three CDR regions from the heavy or light chain of the ENTPD2 antibodies described herein. Such nucleic acids or polynucleotides can also encode all or substantially all of the variable region sequence of the heavy chain and/or the light chain of the ENTPD2 antibodies described herein. Such nucleic acids or polynucleotides can also encode both a variable region and a constant region of the antibody. Because of the degeneracy of the code, a variety of nucleic acid sequences will encode each of the immunoglobulin amino acid sequences. For example, the invention features a first and second nucleic acid encoding heavy and light chain variable regions, respectively, of an anti-human ENTPD2 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 Table 1, or a sequence substantially identical thereto (*e.g.*, a sequence having at least about 85%, 90%,

95%, or 99% sequence identity thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in Table 1).

[0326] 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 Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity 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 Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity 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 Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions).

[0327] 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 Table 1, a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto). 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 Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto) 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 Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto).

[0328] The polynucleotide sequences can be produced by *de novo* solid-phase DNA synthesis or by PCR mutagenesis of an existing sequence encoding an ENTPD2-binding antibody or its binding fragment. Direct chemical synthesis of nucleic acids can be accomplished by methods known in the art, such as the phosphotriester method of Narang et

al., 1979, Meth. Enzymol. 68:90; the phosphodiester method of Brown et al., Meth. Enzymol. 68:109, 1979; the diethylphosphoramidite method of Beaucage et al., Tetra. Lett., 22:1859, 1981; and the solid support method of U.S. Pat. No. 4,458,066. Introducing mutations to a polynucleotide sequence by PCR can be performed as described in, e.g., PCR Technology: Principles and Applications for DNA Amplification, H. A. Erlich (Ed.), Freeman Press, NY, N.Y., 1992; PCR Protocols: A Guide to Methods and Applications, Innis et al. (Ed.), Academic Press, San Diego, Calif., 1990; Mattila et al., Nucleic Acids Res. 19:967, 1991; and Eckert et al., PCR Methods and Applications 1:17, 1991.

[0329] Also provided herein are vectors (e.g., expression vectors) comprising a nucleic acid encoding a polypeptide comprising a segment or domain of the ENTPD2 antibodies or antigen-binding fragments thereof described herein. Such vectors can be employed to express and/or produce the ENTPD2-binding antibodies or antigen-binding fragments thereof. The term "expression vector" refers to a carrier nucleic acid molecule into which a desired coding sequence can be inserted for introduction into a cell where it can be expressed. The vector can be a DNA vector, a RNA vector, a plasmid, a cosmid, or a viral vector, or artificial chromosomes (see, e.g., Harrington et al., Nat Genet 15:345, 1997). For example, nonviral vectors useful for expression of the ENTPD2-binding antibodies or antigen-binding fragments thereof in mammalian (e.g., human) cells include pThioHis A, B & C, pcDNA3.1/His, pEBVHis A, B & C, (Invitrogen, San Diego, Calif.), MPSV vectors, and numerous other vectors known in the art for expressing proteins. 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.

[0330] Useful viral vectors include vectors based on any one of the following viruses: retroviruses, lentiviruses, adenoviruses, adeno-associated viruses, herpes viruses (e.g., Herpes Simplex Virus (HSV)), vectors based on SV40, papilloma virus, HBP Epstein Barr virus, vaccinia virus, Sinbis virus, influenza virus, reovirus, Newcastle disease virus (NDV), measles virus, vesicular stomatitis virus (VSV), parvovirus, poliovirus, poxvirus, Seneca Valley virus, coxsackievirus, enterovirus, myxoma virus, maraba virus, or Semliki Forest virus (SFV). See, Brent et al., supra; Smith, Annu. Rev. Microbiol. 49:807, 1995; and Rosenfeld et al., Cell 68:143, 1992.

[0331] In some embodiments, the vector is a lentiviral vector. Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. A retroviral vector may also be, e.g., a gammaretroviral vector. A gammaretroviral vector may include, e.g., a promoter, a packaging signal (ψ), a primer binding site (PBS), one or more (e.g., two) long terminal repeats (LTR), and a transgene of interest, e.g., a gene encoding a CAR. A gammaretroviral vector may lack viral structural gens such as gag, pol, and env. Exemplary gammaretroviral vectors include Murine Leukemia Virus (MLV), Spleen-Focus Forming Virus (SFFV), and Myeloproliferative Sarcoma Virus (MPSV), and vectors derived therefrom. Other gammaretroviral vectors are described, e.g., in Tobias Maetzig et al., "Gammaretroviral Vectors: Biology, Technology and Application" Viruses. 2011 Jun; 3(6): 677–713.

[0332] In some embodiments, the vector is an adeno-associated virus (AAV) vector, e.g., a recombinant AAV (rAAV) vector. "AAV" is an abbreviation for adeno-associated virus, and may be used to refer to the virus itself or derivatives thereof. The term covers all subtypes and both naturally occurring and recombinant forms, except where required otherwise. The abbreviation "rAAV" refers to recombinant adeno-associated virus, also referred to as a recombinant AAV vector (or "rAAV vector"). The term "AAV" includes, for example, AAV type 1 (AAV1), AAV type 2 (AAV2), AAV type 3 (AAV3), AAV type 4 (AAV4), AAV type 5 (AAV5), AAV type 6 (AAV6), AAV type 7 (AAV7), AAV type 8 (AAV8), AAV type 9 (AAV9), AAV type 10 (AAV10, including AAVrh10), AAV type 12 (AAV12), avian AAV, bovine AAV, canine AAV, equine AAV, primate AAV, non-primate AAV, and ovine AAV. "Primate AAV" refers to AAV that infect primates, "non-primate AAV" refers to AAV that infect non- primate mammals, "bovine AAV" refers to AAV that infect bovine mammals, and so on.

[0333] The genomic sequences of various serotypes of AAV, as well as the sequences of the native inverted terminal repeats (ITRs), Rep proteins, and capsid subunits are known in the art. Such sequences may be found in the literature or in public databases such as GenBank. See, e.g., GenBank Accession NOs. NC-002077 (AAV1), AF063497 (AAV1), NC-001401 (AAV2), AF043303 (AAV2), NC-001729 (AAV3), NC-001829 (AAV4), U89790 (AAV4), NC-006152 (AAV5), AF513851 (AAV7), AF513852 (AAV8), and NC-

006261 (AAV8); or in publications such as WO2005033321 (AAV1-9), the disclosures of which are incorporated by reference herein. See also, e.g., Srivistava et al. (1983) J. Virology 45:555; Chiorini et al. (1998) J. Virology 71 :6823; Chiorini et al. (1999) J. Virology 73: 1309; Bantel-Schaal et al. (1999) J. Virology 73:939; Xiao et al. (1999) J. Virology 73:3994; Muramatsu et al. (1996) Virology 221 :208; Shade et al.,(1986) J. Virol. 58:921; Gao et al. (2002) Proc. Nat. Acad. Sci. USA 99: 11854; Moris et al. (2004) Virology 33:375-383; international patent publications WO 00/28061, WO 99/61601, WO 98/11244; and U. S. Pat. No. 6,156,303.

[0334] An "rAAV vector" as used herein refers to an AAV vector comprising a polynucleotide sequence not of AAV origin (i.e., a polynucleotide heterologous to AAV), typically a sequence of interest for the genetic transformation of a cell. In some embodiments, the heterologous polynucleotide may be flanked by at least one, and sometimesby two, AAV inverted terminal repeat (ITR) sequences. The term rAAV vector encompasses both rAAV vector particles and rAAV vector plasmids. An rAAV vector may either be single-stranded (ssAAV) or self-complementary (scAAV). An "AAV virus" or "AAV viral particle" or "rAAV vector particle" refers to a viral particle composed of at least one AAV capsid protein (typically by all of the capsid proteins of a wild-type AAV) and an encapsidated polynucleotide rAAV vector. If the particle comprises a heterologous polynucleotide (i.e., a polynucleotide other than a wild-type AAV genome such as a transgene to be delivered to a mammalian cell), it is typically referred to as an "rAAV vector particle" or simply an "rAAV vector." Thus, production of rAAV particle necessarily includes production of rAAV vector, as such a vector is contained within an rAAV particle.

[0335] In some embodiments, the vector can be a recombinant DNA molecule containing a nucleic acid encoding an antibody that binds to human ENTPD2 protein. "Recombinant" as used herein means that the vector, polynucleotide, polypeptide or cell is the product of various combinations of cloning, restriction or ligation steps (e.g. relating to a polynucleotide or polypeptide comprised therein), and/or other procedures that result in a construct that is distinct from a product found in nature. A recombinant virus or vector is a viral particle comprising a recombinant polynucleotide. The terms respectively include replicates of the original polynucleotide construct and progeny of the original virus construct.

[0336] The recombinant vector typically includes one or more regulatory sequences operatively linked to the nucleic acid sequence to be expressed. The term "regulatory sequence" includes promoters, enhancers, and other expression control elements (e.g., polyadenylation signals). Regulatory sequences include those which direct constitutive

expression of a nucleotide sequence, as well as tissue-specific regulatory and/or inducible sequences. Expression vectors can also include elements designed to optimize messenger RNA stability and translatability in host cells, and/or drug selection markers for establishing permanent, stable cell clones expressing an antibody that binds to human ENTPD2 protein. The design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, and the like. General methods for generating such recombinant expression vectors can be found in Sambrook and Russell eds. (2001) Molecular Cloning: A Laboratory Manual, 3rd edition; the series Ausubel et al. eds. (2007 with updated through 2010) Current Protocols in Molecular Biology, among others known in the art.

[0337] A "promoter" is a control sequence that is a region of a nucleic acid sequence at which initiation and rate of transcription are controlled. It may contain genetic elements at which regulatory proteins and molecules may bind such as RNA polymerase and other transcription factors. The phrases "operatively positioned", "operatively linked", "under control", and "under transcriptional control" mean that a promoter is in a correct functional location and/or orientation in relation to a nucleic acid sequence to control transcriptional initiation and/or expression of that sequence. A promoter may or may not be used in conjunction with an "enhancer", which refers to a cis-acting regulatory sequence involved in the transcriptional activation of a nucleic acid sequence.

[0338] A promoter may be one naturally-associated with a gene or sequence, as may be obtained by isolating the 5' non-coding sequences located upstream of the coding segment and/or exon. Such a promoter can be referred to as "endogenous". Similarly, an enhancer may be one naturally associated with a nucleic acid sequence, located either downstream or upstream of that sequence. Alternatively, certain advantages will be gained by positioning the coding nucleic acid segment under the control of a recombinant or heterologous promoter, which refers to a promoter that is not normally associated with a nucleic acid sequence in its natural environment. A recombinant or heterologous enhancer refers also to an enhancer not normally associated with a nucleic acid sequence in its natural environment. Such promoters or enhancers may include promoters or enhancers of other genes, and promoters or enhancers isolated from any other prokaryotic, viral, or eukaryotic cell, and promoters or enhancers not "naturally-occurring", i.e., containing different elements of different transcriptional regulatory regions and/or mutations that alter expression. In addition to producing nucleic acid sequences of promoters and enhancers synthetically, sequences may be produced using recombinant cloning and/or nucleic acid amplification technology, for example PCR, in

connection with the compositions disclosed herein (see US 4683202, US 5928906). Furthermore, it is contemplated the control sequences that direct transcription and/or expression of sequences within non-nuclear organelles such as mitochondria, chloroplasts, and the like, can be employed as well.

[0339] The promoters employed can be constitutive, inducible, synthetic, tissue- or cell-specific, and/or useful under the appropriate conditions to direct high level expression of the introduced DNA segment, such as is advantageous in the large-scale production of recombinant proteins and/or peptides. In addition, other regulatory elements may also be incorporated to improve expression of a nucleic acid encoding an antibody that binds to human ENTPD2 protein, *e.g.,* enhancers, ribosomal binding site, transcription termination sequences, and the like.

[0340] In some embodiments, a constitutive promoter is employed to provide constant expression of an anti-human ENTPD2 antibody. Examples of a constitutive promoter include, but not limited to, the immediate early cytomegalovirus (CMV) promoter, the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV) promoter, human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous sarcoma virus promoter, as well as human gene promoters such as, but not limited to, the actin promoter, the myosin promoter, the elongation factor-1α promoter, the hemoglobin promoter, and the creatine kinase promoter.

[0341] Inducible promoters are also contemplated as part of the present disclosure. The use of an inducible promoter provides a molecular switch capable of turning on expression of the polynucleotide sequence which it is operatively linked when such expression is desired, or turning off the expression when expression is not desired. Examples of inducible promoters include, but are not limited to a metallothionine promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter.

[0342] In some embodiments, a tissue- or cell-specific promoter is employed to provide expression of an anti-human ENTPD2 antibody only in specific tissues or cells. The identity of tissue- or cell-specific promoters or elements, as well as assays to characterize their activities, is well known to those of skill in the art. Examples include the human LIMK2 gene (Nomoto *et al.* 1999, Gene, 236(2):259-271), the somatostatin receptor 2 gene (Kraus *et al.,* 1998, FEES Lett., 428(3): 165-170), murine epididymal retinoic acid-binding gene (Lareyre *et al.,* 1999, J. Biol. Chem., 274(12):8282-8290), human CD4 (Zhao-Emonet *et al.,*

1998, Biochirn. Biophys. Acta, 1442(2-3): 109-119), mouse alpha2 (XI) collagen (Tsumaki, *et al.,* 1998, J. Biol. Chem., 273(36):22861-22864), D1A dopamine receptor gene (Lee, *et al.,* 1997, J. Auton. Nerv. Syst., 74(2-3):86-90), insulin-like growth factor II (Wu *et al.,* 1997, Biochem. Biophys. Res. Commun., 233(1):221-226), human platelet endothelial cell adhesion molecule-1 (Almendro *et al.,* 1996, J. Immunol., 157(12):5411-5421), muscle creatine kinase (MCK) promoter (Wang *et al.*, Gene Ther. 2008 Nov;15(22):1489-99).

[0343] In some embodiments, a synthetic promoter is employed to provide expression of an anti-human ENTPD2 antibody. Synthetic promoters can greatly exceed the transcriptional potencies of natural promoters. For example, the synthetic promoters that do not get shut off or reduced in activity by the endogenous cellular machinery or factors can be selected. Other elements, including trans-acting factor binding sites and enhancers may be inserted into the synthetic promoter to improve transcriptional efficiency. Synthetic promoters can be rationally designed and chemically synthesized to combine the best features of both synthetic and biological promoters. Synthetic oligos are annealed and ligated through several processes to generate the full-length chemically synthesized promoter. Synthetic promters can be inducible or cell-type specific promoters.

[0344] A specific initiation signal also may be required for efficient translation of coding sequences. These signals include the ATG initiation codon or adjacent sequences. Exogenous translational control signals, including the ATG initiation codon, may need to be provided. One of ordinary skill in the art would readily be capable of determining this and providing the necessary signals. It is well known that the initiation codon must be "in-frame" with the reading frame of the desired coding sequence to ensure translation of the entire insert. The exogenous translational control signals and initiation codons can be either natural or synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements.

[0345] Expression can employ any appropriate host cells known in the art, for example, mammalian host cells, bacterial host cells, yeast host cells, insect host cells, etc. Both prokaryotic and eukaryotic expression systems are widely available. In some embodiments, the expression system is a mammalian cell expression, such as a CHO cell expression system. In some embodiments, a nucleic acid may be codon-optimized to facilitate expression in a desired host cell. It will be important to employ a promoter and/or enhancer that effectively directs the expression of the DNA segment in the cell type, organelle, and organism chosen for expression. Those of skill in the art of molecular biology

generally know the use of promoters, enhancers, and cell type combinations for protein expression, for example, see Sambrook *et al.* (2001).

[0346] Most transcribed eukaryotic RNA molecules will undergo RNA splicing to remove introns from the primary transcripts. Vectors containing genomic eukaryotic sequences may require donor and/or acceptor splicing sites to ensure proper processing of the transcript for protein expression (see Chandler *et al.,* 1997, Proc. Natl. Acad. Sci. USA, 94(8):3596-601).

[0347] The vectors or constructs of the present disclosure will generally comprise at least one termination signal. A "termination signal" or "terminator" is comprised of the DNA sequences involved in specific termination of a RNA transcript by a RNA polymerase. Thus, in certain embodiments a termination signal that ends the production of a RNA transcript is contemplated. A terminator may be necessary *in vivo* to achieve desirable message levels. In eukaryotic systems, the terminator region may also comprise specific DNA sequences that permit site-specific cleavage of the new transcript so as to expose a polyadenylation site. This signals a specialized endogenous polymerase to add a stretch of about 200 A residues (poly A) to the 3' end of the transcript. RNA molecules modified with this polyA tail appear to more stable and are translated more efficiently. Thus, in other embodiments involving eukaryotes, it is preferred that the terminator comprises a signal for the cleavage of the RNA, and it is more preferred that the terminator signal promotes polyadenylation of the message. The terminator and/or polyadenylation site elements can serve to enhance message levels and/or to minimize read through from the cassette into other sequences. Terminators contemplated for use in the disclosure include any known terminator of transcription described herein or known to one of ordinary skill in the art, including but not limited to, for example, the termination sequences of genes, such as for example the bovine growth hormone terminator or viral termination sequences, such as for example the SV40 terminator. In certain embodiments, the termination signal may be a lack of transcribable or translatable sequence, such as due to a sequence truncation.

[0348] In expression, particularly eukaryotic expression, one will typically include a polyadenylation signal to effect proper polyadenylation of the transcript. The nature of the polyadenylation signal is not believed to be crucial to the successful practice of the disclosure, and/or any such sequence may be employed. Preferred embodiments include the SV40 polyadenylation signal and/or the bovine growth hormone polyadenylation signal, convenient and/or known to function well in various target cells. Polyadenylation may increase the stability of the transcript or may facilitate cytoplasmic transport.

[0349] To propagate a vector in a host cell, it may contain one or more origins of replication sites (often termed "ori"), which is a specific nucleic acid sequence at which replication is initiated. Alternatively an autonomously replicating sequence (ARS) can be employed if the host cell is yeast.

[0350] In certain embodiments of the disclosure, cells containing a nucleic acid construct of the present disclosure may be identified in vitro or *in vivo* by including a marker in the expression vector. Such markers would confer an identifiable change to the cell permitting easy identification of cells containing the expression vector. Generally, a selectable marker is one that confers a property that allows for selection. A positive selectable marker is one in which the presence of the marker allows for its selection, while a negative selectable marker is one in which its presence prevents its selection. An example of a positive selectable marker is a drug resistance marker.

[0351] Usually the inclusion of a drug selection marker aids in the cloning and identification of transformants, for example, genes that confer resistance to neomycin, puromycin, hygromycin, DHFR, GPT, zeocin and histidinol are useful selectable markers. In addition to markers conferring a phenotype that allows for the discrimination of transformants based on the implementation of conditions, other types of markers including screenable markers such as GFP, whose basis is colorimetric analysis, are also contemplated. Alternatively, screenable enzymes such as herpes simplex virus thymidine kinase (HSV-tk) or chloramphenicol acetyltransferase (CAT) may be utilized. One of skill in the art would also know how to employ immunologic markers, possibly in conjunction with FACS analysis. The marker used is not believed to be important, so long as it is capable of being expressed simultaneously with the nucleic acid encoding a gene product. Further examples of selectable and screenable markers are well known to one of skill in the art.

[0352] The expression vectors may also provide a secretion signal sequence position to form a fusion protein with polypeptides encoded by inserted ENTPD2-binding antibody sequences. More often, the inserted ENTPD2-binding antibody sequences are linked to a signal sequences before inclusion in the vector. Vectors to be used to receive sequences encoding ENTPD2-binding antibody light and heavy chain variable domains sometimes also encode constant regions or parts thereof. Such vectors allow expression of the variable regions as fusion proteins with the constant regions thereby leading to production of intact antibodies and antigen-binding fragments thereof. Typically, such constant regions are human.

[0353] Generation of an expression vector can utilize a vector that includes a multiple cloning site (MCS), which is a nucleic acid region that contains multiple restriction enzyme sites, any one of which can be used in conjunction with standard recombinant technology to digest the vector. See Carbonelli *et al.,* 1999, Levenson et al., 1998, and Cocea, 1997. "Restriction enzyme digestion" refers to catalytic cleavage of a nucleic acid molecule with an enzyme that functions only at specific locations in a nucleic acid molecule. Many one of these restriction enzymes are commercially available. Use of such enzymes is widely understood by those of skill in the art. Frequently, a vector is linearized or fragmented using a restriction enzyme that cuts within the MCS to enable exogenous sequences to be ligated to the vector. "Ligation" refers to the process of forming phosphodiester bonds between two nucleic acid fragments, which may or may not be contiguous with each other. Techniques involving restriction enzymes and ligation reactions are well known to those of skill in the art of recombinant technology.

[0354] Methods for introducing expression vectors containing the polynucleotide sequences of interest vary depending on the type of cellular host. For example, calcium chloride transfection is commonly utilized for prokaryotic cells, whereas calcium phosphate treatment or electroporation may be used for other cellular hosts (see generally Sambrook et al., supra). Other methods include, e.g., electroporation, calcium phosphate treatment, liposome-mediated transformation, injection and microinjection, ballistic methods/gene gun, virosomes, immunoliposomes, polycation:nucleic acid conjugates, naked DNA, artificial virions, fusion to the herpes virus structural protein VP22, agent-enhanced uptake of DNA, *ex vivo* transduction, protoplast fusion, retroviral transduction, viral transfection, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity. For long-term, high-yield production of recombinant proteins, stable expression will often be desired. For example, cell lines which stably express polypeptides can be prepared using expression vectors which contain viral origins of replication or endogenous expression elements and a selectable marker gene. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth of cells which successfully express the introduced sequences in selective media. Resistant, stably transfected cells can be proliferated using tissue culture techniques appropriate to the cell type. 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.

[0355] Also provided herein are cells that include any one of the expression vectors described herein. In some embodiments, the disclosure features a host cell that includes a nucleic acid molecule described herein. Such cells can be a host cell or a therapeutic cell. The terms "host cell" and "recombinant host cell" are used interchangeably herein, which refer to not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

[0356] In one embodiment, the host cells are genetically engineered to comprise nucleic acids encoding the antibody molecule. 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 effectingexpression 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.

[0357] The host cells for harboring and expressing the ENTPD2-binding antibody chains can be can be, but is not limited to, a eukaryotic cell or a prokaryotic cell, such as a bacterial cell, an insect cell, or a human cell. *E. coli* is one prokaryotic host useful for cloning and expressing the polynucleotides of the present invention. Other microbial hosts suitable for use include bacilli, such as *Bacillus subtilis*, and other enterobacteriaceae, such as *Salmonella*, *Serratia*, and various *Pseudomonas* species. In these prokaryotic hosts, one can also make expression vectors, which typically contain expression control sequences compatible with the host cell (e.g., an origin of replication). In addition, any number of a variety of well-known promoters will be present, such as the lactose promoter system, a tryptophan (trp) promoter system, a beta-lactamase promoter system, or a promoter system from phage lambda. The promoters typically control expression, optionally with an operator sequence, and have ribosome binding site sequences and the like, for initiating and completing transcription and translation. Other microbes, such as yeast, can also be employed to express ENTPD2-binding polypeptides of the invention. Insect cells in combination with baculovirus vectors can also be used. Suitable insect cells include, but are not limited to, Sf9 cells.

[0358] In one embodiment, mammalian host cells are used to express and produce the

ENTPD2-binding antibodies of the present invention. For example, they can be either a hybridoma cell line expressing endogenous immunoglobulin genes (e.g., the 1D6.C9 myeloma hybridoma cell) or a mammalian cell line harboring an exogenous expression vector (e.g., the SP2/0 myeloma cell). These include any normal mortal or normal or abnormal immortal animal or human cell. For example, a number of suitable host cell lines capable of secreting intact immunoglobulins have been developed including the CHO cell lines, various Cos cell lines, HeLa cells, myeloma cell lines, transformed B-cells and hybridomas. The use of mammalian tissue cell culture to express polypeptides is discussed generally in, e.g., Winnacker, From Genes to Clones, VCH Publishers, N.Y., N.Y., 1987. Expression vectors for mammalian host cells can include expression control sequences, such as an origin of replication, a promoter, and an enhancer (see, e.g., Queen, et al., Immunol. Rev. 89:49-68, 1986), and necessary processing information sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites, and transcriptional terminator sequences. These expression vectors usually contain promoters derived from mammalian genes or from mammalian viruses. Suitable promoters may be constitutive, cell type-specific, stage-specific, and/or modulatable or regulatable. Useful promoters include, but are not limited to, the metallothionein promoter, the constitutive adenovirus major late promoter, the dexamethasone-inducible MMTV promoter, the SV40 promoter, the MRP pol III promoter, the constitutive MPSV promoter, the tetracycline-inducible CMV promoter (such as the human immediate-early CMV promoter), the constitutive CMV promoter, and promoter-enhancer combinations known in the art.

[0359] A host cell can be used to produce or express an antibody that binds to human ENTPD2 protein. Accordingly, the disclosure also features methods for producing an antibody that binds to human ENTPD2 protein using a host cell. In one embodiment, the method includes culturing the host cell (into which a recombinant expression vector encoding the antibody has been introduced) in a suitable medium, such that the antibody that binds to human ENTPD2 protein is produced. In another embodiment, the method further includes isolating the antibody from the medium or the host 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.

Producing Monoclonal Antibodies

[0360] Monoclonal antibodies (mAbs) can be produced by a variety of techniques, including conventional monoclonal antibody methodology, e.g., the standard somatic cell

hybridization technique of Kohler and Milstein, 1975 Nature 256: 495. Many techniques for producing monoclonal antibody can be employed e.g., viral or oncogenic transformation of B lymphocytes.

[0361] An animal system for preparing hybridomas is the murine system. Hybridoma production in the mouse is a well established procedure. Immunization protocols and techniques for isolation of immunized splenocytes for fusion are known in the art. Fusion partners (e.g., murine myeloma cells) and fusion procedures are also known.

[0362] In some embodiments, the antibodies of the invention are humanized monoclonal antibodies. Chimeric or humanized antibodies and antigen-binding fragments thereof of the present invention can be prepared based on the sequence of a murine monoclonal antibody prepared as described above. DNA encoding the heavy and light chain immunoglobulins can be obtained from the murine hybridoma of interest and engineered to contain non-murine (e.g., human) immunoglobulin sequences using standard molecular biology techniques. For example, to create a chimeric antibody, the murine variable regions can be linked to human constant regions using methods known in the art (see e.g., U.S. Pat. No. 4,816,567 to Cabilly et al.). To create a humanized antibody, the murine CDR regions can be inserted into a human framework using methods known in the art. See e.g., U.S. Pat. No. 5,225,539 to Winter, and U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6180370 to Queen et al.

[0363] In some embodiments, the antibodies of the invention are human monoclonal antibodies. Such human monoclonal antibodies directed against ENTPD2 can be generated using transgenic or transchromosomic mice carrying parts of the human immune system rather than the mouse system. These transgenic and transchromosomic mice include mice referred to herein as HuMAb mice and KM mice, respectively, and are collectively referred to herein as “human Ig mice”.

[0364] The HuMAb Mouse® (Medarex, Inc.) contains human immunoglobulin gene miniloci that encode un-rearranged human heavy (mu and gamma) and kappa light chain immunoglobulin sequences, together with targeted mutations that inactivate the endogenous mu and kappa chain loci (see e.g., Lonberg, et al., 1994 Nature 368 (6474): 856-859). Accordingly, the mice exhibit reduced expression of mouse IgM or K, and in response to immunization, the introduced human heavy and light chain transgenes undergo class switching and somatic mutation to generate high affinity human IgG-kappa monoclonal (Lonberg, N. et al., 1994 supra; reviewed in Lonberg, N., 1994 Handbook of Experimental Pharmacology 113:49-101; Lonberg, N. and Huszar, D., 1995 Intern. Rev. Immunol. 13: 65-

93, and Harding, F. and Lonberg, N., 1995 Ann. N.Y. Acad. Sci. 764:536-546). The preparation and use of HuMAb mice, and the genomic modifications carried by such mice, is further described in Taylor, L. et al., 1992 Nucleic Acids Research 20:6287-6295; Chen, J. et al., 1993 International Immunology 5: 647-656; Tuaillon et al., 1993 Proc. Natl. Acad. Sci. USA 94:3720-3724; Choi et al., 1993 Nature Genetics 4:117-123; Chen, J. et al., 1993 EMBO J. 12: 821-830; Tuaillon et al., 1994 J. Immunol. 152:2912-2920; Taylor, L. et al., 1994 International Immunology 579-591; and Fishwild, D. et al., 1996 Nature Biotechnology 14: 845-851. See further, U.S. Pat. Nos. 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,789,650; 5,877,397; 5,661,016; 5,814,318; 5,874,299; and 5,770,429; all to Lonberg and Kay; U.S. Pat. No. 5,545,807 to Surani et al.; PCT Publication Nos. WO 92103918, WO 93/12227, WO 94/25585, WO 97113852, WO 98/24884 and WO 99/45962, all to Lonberg and Kay; and PCT Publication No. WO 01/14424 to Korman et al.

[0365] In some embodiments, human antibodies can be raised using a mouse that carries human immunoglobulin sequences on transgenes and transchomosomes such as a mouse that carries a human heavy chain transgene and a human light chain transchromosome. Such mice, referred to herein as "KM mice," are described in detail in PCT Publication WO 02/43478 to Ishida et al.

[0366] Still further, alternative transgenic animal systems expressing human immunoglobulin genes are available in the art and can be used to raise ENTPD2-binding antibodies and antigen-binding fragments thereof. For example, an alternative transgenic system referred to as the Xenomouse (Abgenix, Inc.) can be used. Such mice are described in, e.g., U.S. Pat. Nos. 5,939,598; 6,075,181; 6,114,598; 6,150,584 and 6,162,963 to Kucherlapati et al.

[0367] Moreover, alternative transchromosomic animal systems expressing human immunoglobulin genes are available in the art and can be used to raise ENTPD2-binding antibodies of the invention. For example, mice carrying both a human heavy chain transchromosome and a human light chain transchromosome, referred to as "TC mice" can be used; such mice are described in Tomizuka et al., 2000 Proc. Natl. Acad. Sci. USA 97:722-727. Furthermore, cows carrying human heavy and light chain transchromosomes have been described in the art (Kuroiwa et al., 2002 Nature Biotechnology 20:889-894) and can be used to raise ENTPD2 binding antibodies of the invention.

[0368] Human monoclonal antibodies can also be prepared using phage display methods for screening libraries of human immunoglobulin genes. Such phage display methods for isolating human antibodies are established in the art or described in the examples

below. See for example: U.S. Pat. Nos. 5,223,409; 5,403,484; and 5,571,698 to Ladner et al; U.S. Pat. Nos. 5,427,908 and 5,580,717 to Dower et al; U.S. Pat. Nos. 5,969,108 and 6,172,197 to McCafferty et al; and U.S. Pat. Nos. 5,885,793; 6,521,404; 6,544,731; 6,555,313; 6,582,915 and 6,593,081 to Griffiths et al.

[0369] Human monoclonal antibodies of the invention can also be prepared using SCID mice into which human immune cells have been reconstituted such that a human antibody response can be generated upon immunization. Such mice are described in, for example, U.S. Pat. Nos. 5,476,996 and 5,698,767 to Wilson et al.

Methods of Engineering Modified Antibodies

[0370] As discussed above, the ENTPD2-binding antibodies having VH and VL sequences or full length heavy and light chain sequences shown herein can be used to create new ENTPD2-binding antibodies by modifying full length heavy chain and/or light chain sequences, VH and/or VL sequences, or the constant region(s) attached thereto. Thus, in another aspect of the invention, the structural features of ENTPD2-binding antibody of the invention are used to create structurally related ENTPD2-binding antibodies that retain at least one functional property of the antibodies and antigen-binding fragments thereof of the invention, such as binding to and inhibit human ENTPD2.

[0371] For example, one or more CDR regions of the antibodies and antigen-binding fragments thereof of the present invention, or mutations thereof, can be combined recombinantly with known framework regions and/or other CDRs to create additional, recombinantly-engineered, ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention, as discussed above. Other types of modifications include those described in the previous section. The starting material for the engineering method is one or more of the VH and/or VL sequences provided herein, or one or more CDR regions thereof. To create the engineered antibody, it is not necessary to actually prepare (i.e., express as a protein) an antibody having one or more of the VH and/or VL sequences provided herein, or one or more CDR regions thereof. Rather, the information contained in the sequence (s) is used as the starting material to create a "second generation" sequence(s) derived from the original sequence(s) and then the "second generation" sequence(s) is prepared and expressed as a protein.

[0372] The altered antibody sequence can also be prepared by screening antibody libraries having fixed CDR3 sequences or minimal essential binding determinants as described in US20050255552 and diversity on CDR1 and CDR2 sequences. The screening

can be performed according to any screening technology appropriate for screening antibodies from antibody libraries, such as phage display technology.

[0373] Standard molecular biology techniques can be used to prepare and express the altered antibody sequence. The antibody encoded by the altered antibody sequence (s) is one that retains one, some or all of the functional properties of the ENTPD2-binding antibodies described herein, which functional properties include, but are not limited to, specifically binding to and stabilize human ENTPD2 protein.

[0374] The functional properties of the altered antibodies can be assessed using standard assays available in the art and/or described herein, such as those set forth in the Examples (e.g., ELISAs).

[0375] In some embodiments, the methods of engineering antibodies and antigen-binding fragments thereof of the invention, mutations can be introduced randomly or selectively along all or part of an ENTPD2-binding antibody coding sequence and the resulting modified ENTPD2-binding antibodies can be screened for binding activity and/or other functional properties as described herein. Mutational methods have been described in the art. For example, PCT Publication WO 02/092780 describes methods for creating and screening antibody mutations using saturation mutagenesis, synthetic ligation assembly, or a combination thereof. Alternatively, PCT Publication WO 03/074679 describes methods of using computational screening methods to optimize physiochemical properties of antibodies.

Characterization of the Antibodies

[0376] The antibodies and antigen-binding fragments thereof of the invention can be characterized by various functional assays. For example, they can be characterized by their ability to bind to the ENTPD2 protein (e.g., human ENTPD2 protein).

[0377] The ability of an antibody to bind to ENTPD2 (e.g., human ENTPD2 protein) can be detected by labelling the antibody of interest directly, or the antibody may be unlabeled and binding detected indirectly using various sandwich assay formats known in the art.

[0378] In some embodiments, the ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention block or compete with binding of a reference ENTPD2-binding antibody to ENTPD2 protein (e.g., human ENTPD2 protein). These can be fully human or humanized ENTPD2-binding antibodies described above. They can also be other human, mouse, chimeric or humanized ENTPD2-binding antibodies which bind to the same epitope as the reference antibody. The capacity to block or compete with the reference

antibody binding indicates that ENTPD2-binding antibody under test binds to the same or similar epitope as that defined by the reference antibody, or to an epitope which is sufficiently proximal to the epitope bound by the reference ENTPD2-binding antibody. Such antibodies are especially likely to share the advantageous properties identified for the reference antibody. The capacity to block or compete with the reference antibody may be determined by, e.g., a competition binding assay. With a competition binding assay, the antibody under test is examined for ability to inhibit specific binding of the reference antibody to a common antigen, such as ENTPD2 protein (e.g., human ENTPD2 protein). A test antibody competes with the reference antibody for specific binding to the antigen if an excess of the test antibody substantially inhibits binding of the reference antibody. Substantial inhibition means that the test antibody reduces specific binding of the reference antibody usually by at least 10%, 25%, 50%, 75%, or 90%.

[0379] There are a number of known competition binding assays that can be used to assess competition of an antibody with a reference antibody for binding to a particular protein, in this case, ENTPD2 (e.g., human ENTPD2 protein). These include, e.g., solid phase direct or indirect radioimmunoassay (RIA), solid phase direct or indirect enzyme immunoassay (EIA), sandwich competition assay (see Stahli et al., Methods in Enzymology 9:242-253, 1983); solid phase direct biotin-avidin EIA (see Kirkland et al., J. Immunol. 137:3614-3619, 1986); solid phase direct labeled assay, solid phase direct labeled sandwich assay (see Harlow & Lane, supra); solid phase direct label RIA using I-125 label (see Morel et al., Molec. Immunol. 25:7-15, 1988); solid phase direct biotin-avidin EIA (Cheung et al., Virology 176:546-552, 1990); and direct labeled RIA (Moldenhauer et al., Scand. J. Immunol. 32:77-82, 1990). Typically, such an assay involves the use of purified antigen bound to a solid surface or cells bearing either of these, an unlabelled test ENTPD2-binding antibody and a labelled reference antibody. Competitive inhibition is measured by determining the amount of label bound to the solid surface or cells in the presence of the test antibody. Usually the test antibody is present in excess. Antibodies identified by competition assay (competing antibodies) include antibodies binding to the same epitope as the reference antibody and antibodies binding to an adjacent epitope sufficiently proximal to the epitope bound by the reference antibody for steric hindrance to occur.

[0380] To determine if the selected ENTPD2-binding monoclonal antibodies bind to unique epitopes, each antibody can be biotinylated using commercially available reagents (e.g., reagents from Pierce, Rockford, Ill.). Competition studies using unlabeled monoclonal antibodies and biotinylated monoclonal antibodies can be performed using ENTPD2 protein

coated-ELISA plates. Biotinylated MAb binding can be detected with a strepavidin-alkaline phosphatase probe. To determine the isotype of a purified ENTPD2-binding antibody, isotype ELISA can be performed. For example, wells of microtiter plates can be coated with 1 μg/ml of anti-human IgG overnight at 4°C. After blocking with 1% BSA, the plates are reacted with 1 μg/ml or less of the monoclonal ENTPD2-binding antibody or purified isotype controls, at ambient temperature for one to two hours. The wells can then be reacted with either human IgG1 or human IgM-specific alkaline phosphatase-conjugated probes. Plates are then developed and analyzed so that the isotype of the purified antibody can be determined.

[0381] To demonstrate binding of monoclonal ENTPD2-binding antibodies to live cells expressing ENTPD2 protein (e.g., human ENTPD2 protein), flow cytometry can be used. Briefly, cell lines expressing ENTPD2 (grown under standard growth conditions) can be mixed with various concentrations of ENTPD2-binding antibody in PBS containing 0.1% BSA and 10% fetal calf serum, and incubated at 37°C for 1 hour. After washing, the cells are reacted with fluorescein-labeled anti-human IgG antibody under the same conditions as the primary antibody staining. The samples can be analyzed by FACScan instrument using light and side scatter properties to gate on single cells. An alternative assay using fluorescence microscopy may be used (in addition to or instead of) the flow cytometry assay. Cells can be stained exactly as described above and examined by fluorescence microscopy. This method allows visualization of individual cells, but may have diminished sensitivity depending on the density of the antigen.

[0382] ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention can be further tested for reactivity with ENTPD2 protein (e.g., human ENTPD2 protein) or antigenic fragment by Western blotting. Briefly, purified ENTPD2 protein (e.g., human ENTPD2 protein) or fusion proteins, or cell extracts from cells expressing ENTPD2 can be prepared and subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis. After electrophoresis, the separated antigens are transferred to nitrocellulose membranes, blocked with 10% fetal calf serum, and probed with the monoclonal antibodies to be tested. Human IgG binding can be detected using anti-human IgG alkaline phosphatase and developed with BCIP/NBT substrate tablets (Sigma Chem. Co., St. Louis, Mo.).

[0383] ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention can be further tested for their abilities to modulate one or more ENTPD2 activities/functions.

[0384] ENTPD2-binding antibodies and antigen-binding fragments thereof of the

invention can also be tested using any of the methods or assays described in the Examples.

Methods of Treatment and Therapeutic Use

[0385] The antibodies of the present invention have numerous in vitro and *in vivo* diagnostic and therapeutic utilities involving the diagnosis and treatment of disorders with ENTPD2-dependent pathophysiology. For example, these molecules can be administered to cells in culture, in vitro or *ex vivo*, or to human subjects, e.g., *in vivo*, to treat, prevent and to diagnose a variety disorders with ENTPD2-dependent pathophysiology. Accordingly, in one aspect provided herein are methods of treating a cancer in a subject in need thereof by administering to the subject a therapeutically effective amount of an antibody or antigen binding fragment thereof described herein, a nucleic acid encoding such an antibody or antigen binding fragment, a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, a cell comprising such a nucleic acid or vector, or a pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid, vector or cell. In one aspect, the invention provides a method of inhibiting or reducing growth of tumor cells in a subject comprising administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody as disclosed herein.

[0386] In another aspect, a method of treating a subject, *e.g.*, reducing or ameliorating, a hyperproliferative condition or disorder (*e.g.*, a cancer), *e.g.*, solid tumor, a hematological cancer, soft tissue tumor, or a metastatic lesion, in a subject is provided.

[0387] Accordingly, in one embodiment, the invention provides a method of inhibiting growth of tumor cells in a subject, comprising administering to the subject a therapeutically effective amount of one or more anti-human ENTPD2 antibody molecule or functional fragment thereof as described herein alone or in combination with other agents, e.g., therapeutic agents, or therapeutic modalities.

[0388] In some embodiments, such methods can further comprise a step of assaying expression levels of ENTPD2 in a sample obtained from a subject, e.g., tissue biopsy of the subject.

[0389] The term cancer is meant to include all types of cancerous growths or oncogenic processes, metastatic tissues or malignantly transformed cells, tissues, or organs, irrespective of histopathologic type or stage of invasiveness. Examples of cancerous disorders include, but are not limited to, solid tumors, soft tissue tumors, and metastatic lesions. Examples of solid tumors include malignancies, e.g., sarcomas, adenocarcinomas,

and carcinomas, of the various organ systems, such as those affecting liver, lung, breast, lymphoid, gastrointestinal (e.g., colon), genitourinary tract (e.g., renal, urothelial cells), prostate and pharynx. Adenocarcinomas include malignancies such as most colon cancers, rectal cancer, renal-cell carcinoma, liver cancer (hepatocarcinoma, e.g., an advanced hepatocarcinoma, with or without a viral infection, e.g., a chronic viral hepatitis), non-small cell carcinoma of the lung, cancer of the small intestine and cancer of the esophagus. Squamous cell carcinomas include malignancies, e.g., in the lung, esophagus, skin, head and neck region, oral cavity, anus, and cervix.

[0390] Metastatic lesions of the aforementioned cancers can also be treated or prevented using the methods and compositions of the invention.

[0391] Exemplary cancers whose growth can be inhibited using the antibodies molecules disclosed herein include cancers typically responsive to immunotherapy. Non-limiting examples of preferred cancers for treatment include gastrointestinal cancer (e.g. gastric (stomach) cancer, colorectal cancer (CRC)), cancer of the esophagus (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, and cholangiocarcinoma. Additionally, refractory or recurrent malignancies can be treated using the antibody molecules described herein.

[0392] Examples of other cancers that can be treated include lung cancer (e.g., a non-small cell lung cancer (NSCLC) (e.g., a NSCLC with squamous and/or non-squamous histology, or a NSCLC adenocarcinoma)), a melanoma (e.g., an advanced melanoma), a renal cancer (e.g., a renal cell carcinoma, e.g., clear cell renal cell carcinoma), a liver cancer, a myeloma (e.g., a multiple myeloma), a prostate cancer, a breast cancer (e.g., a breast cancer that does not express one, two or all of estrogen receptor, progesterone receptor, or Her2/neu, e.g., a triple negative breast cancer), a pancreatic cancer, a head and neck cancer (e.g., head and neck squamous cell carcinoma (HNSCC), anal cancer, gastro-esophageal cancer, thyroid cancer, cervical cancer, a lymphoproliferative disease (e.g., a post-transplant lymphoproliferative disease) or a hematological cancer, T-cell lymphoma, a non-Hogdkin's lymphoma, or a leukemia (e.g., a myeloid leukemia), bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, anal cancer, gastro-esophageal cancer, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin Disease, non-Hodgkin lymphoma, myeloma (e.g., multiple myeloma) cancer of the

esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumors of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney (e.g. renal cancer, e.g., a renal cell carcinoma (RCC) (e.g., a metastatic RCC or clear cell renal cell carcinoma)), cancer of the ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

[0393] In some embodiments, the therapies here can be used to treat a patient that has (or is identified as having) a cancer associated with an infection, e.g., a viral or bacterial infection. Exemplary cancers include cervical cancer, anal cancer, HPV-associated head and neck squamous cell cancer, HPV-associated esophageal papillomas, HHV6-associated lymphomas, EBV-associated lymphomas (including Burkitt lymphoma), Gastric MALT lymphoma, other infection-associated MALT lymphomas, HCC, and Kaposi's sarcoma.

[0394] In other embodiments, the cancer is a hematological malignancy or cancer including but is not limited to a leukemia or a lymphoma. For example, the anti-human ENTPD2 antibody molecule or a antigen-binding fragment thereof alone or in combination with other agents, e.g., therapeutic agents, can be used to treat cancers and malignancies including, but not limited to, e.g., acute leukemias including but not limited to, e.g., B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, e.g., chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to, e.g., B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a

diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like.

[0395] In one embodiment, the cancer is chosen from a colon cancer (e.g., colorectal cancer (CRC) or colorectal adenocarcinoma), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma) or ovarian cancer.

[0396] In one embodiment, the cancer is colorectal cancer (CRC) or colorectal adenocarcinoma.

[0397] In another embodiment, the cancer is gastric cancer.

[0398] In yet another embodiment, the cancer is esophageal squamous cell carcinoma (ESCC).

[0399] In yet another embodiment, the cancer is overexpressing ENTPD2 (ENTPD2 positive/ENTPD2+) such as ENTPD2+ CRC, ENTPD2+ stomach cancer (e.g. ENTPD2 gastric cancer), ENTPD2+ esophageal squamous cell carcinoma (ENTPD2+ ESCC).

[0400] The antibody or antigen binding fragment thereof described herein, the nucleic acid encoding such an antibody or antigen binding fragment, or the vector or cell comprising a nucleic acid encoding such an antibody or antigen binding fragment, or the pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid, vector, or cell, can be administered to the subject through an intravenous, intratumoral or subcutaneous route. In some embodiments, such an antibody or or fragment thereof, nucleic acid, vector, cell, or pharmaceutical composition, is administered intravenously.

[0401] Also provided is an antibody or antigen binding fragment thereof described herein, a pharmaceutical composition comprising such an antibody or antigen binding fragment, a nucleic acid encoding such an antibody or antigen binding fragment, or a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, for use in the treatment of a cancer.

[0402] The present disclosure also includes uses of an antibody or antigen binding fragment thereof described herein, a pharmaceutical composition comprising such an antibody or antigen binding fragment, a nucleic acid encoding such an antibody or antigen

binding fragment, or a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, in the manufacture of a medicament for treatment of a cancer.

Combination Therapies

[0403] The various treatments described above can be combined with another treatment. The present disclosure also relates to a pharmaceutical composition comprising a combination according to the disclosure described herein, in particular together with instructions for simultaneous, separate or sequential use (especially for being jointly active) thereof in the treatment of a cancer. For example, the ENTPD2 antibodies or antigen-binding fragments thereof described herein can be combined with one or more of standard of care treatment (e.g., for a cancer), another antibody molecule, an immunomodulator (e.g., an activator of a costimulatory molecule or an inhibitor of a coinhibitory molecule); a vaccine, e.g., a therapeutic cancer vaccine; or other forms of cell therapy, as described below.

[0404] Accordingly, the methods of treating a cancer described herein can further include administering at least one additional therapeutic agent to the subject in need of treatment. Also provided herein are methods of treating a cancer comprising administering at least two additional therapeutic agents to the subject in need of treatment.

[0405] The term "combination" refers to either a fixed combination in one dosage unit form, or a combined administration where a compound of the present invention and at least one combination partner (e.g. at least one other drug as explained below, also referred to as "therapeutic agent(s)" or "co-agent(s)") may be administered independently at the same time or separately within time intervals, especially where these time intervals allow that the combination partners show a cooperative, e.g. synergistic effect. The single components may be packaged in a kit or separately. One or both of the components (e.g., powders or liquids) may be reconstituted or diluted to a desired dose prior to administration. The terms "co-administration" or "combined administration" or the like as utilized herein are meant to encompass administration of the selected combination partner to a single subject in need thereof (e.g. a patient), and are intended to include treatment regimens in which the agents are not necessarily administered by the same route of administration or at the same time. The term "pharmaceutical combination" as used herein means a product that results from the mixing or combining of more than one therapeutic agent and includes both fixed and non-fixed combinations of the therapeutic agents. The term "fixed combination" means that the therapeutic agents, e.g. a compound of the present invention and a combination partner, are

both administered to a patient simultaneously in the form of a single entity or dosage. The term "non-fixed combination" means that the therapeutic agents, e.g., a compound of the present invention and at least one combination partner, are administered to a patient as separate entities either simultaneously, concurrently or sequentially with no specific time limits, wherein such administration provides therapeutically effective levels of the at least two compounds in the body of the patient. The latter also applies to cocktail therapy, e.g. the administration of three or more therapeutic agents.

[0406] The term "pharmaceutical combination" as used herein refers to either a fixed combination in one dosage unit form, or non-fixed combination or a kit of parts for the combined administration where two or more therapeutic agents may be administered independently at the same time or separately within time intervals, especially where these time intervals allow that the combination partners show a cooperative, e.g. synergistic effect.

[0407] The term "combination therapy" refers to the administration of two or more therapeutic agents to treat a therapeutic condition or disorder described in the present disclosure. Such administration encompasses co-administration of these therapeutic agents in a substantially simultaneous manner, such as in a single capsule having a fixed ratio of active ingredients. Alternatively, such administration encompasses co-administration in multiple, or in separate containers (e.g., tablets, capsules, powders, and liquids) for each active ingredient. Powders and/or liquids may be reconstituted or diluted to a desired dose prior to administration. In addition, such administration also encompasses use of each type of therapeutic agent in a sequential manner, either at approximately the same time or at different times. In either case, the treatment regimen will provide beneficial effects of the drug combination in treating the conditions or disorders described herein.

[0408] The anti-human ENTPD2 antibody molecules can be used in combination with other therapies. For example, the combination therapy can include a composition of the present invention co-formulated with, and/or co-administered with, one or more additional therapeutic agents, *e.g.*, one or more anti-cancer agents, cytotoxic or cytostatic agents, hormone treatment, vaccines, and/or other immunotherapies. In other embodiments, the antibody molecules are administered in combination with other therapeutic treatment modalities, including surgery, radiation, cryosurgery, and/or thermotherapy. Such combination therapies may advantageously utilize lower dosages of the administered therapeutic agents, thus avoiding possible toxicities or complications associated with the various monotherapies.

[0409] By "in combination with", it is not intended to imply that the therapy or the therapeutic agents must be administered at the same time and/or formulated for delivery together, although these methods of delivery are within the scope described herein.

[0410] The anti-human ENTPD2 antibody molecules can be administered concurrently with, prior to, or subsequent to, at least one or more other additional therapies or therapeutic agents. The anti-human ENTPD2 antibody molecule and the other at least one agent or therapeutic protocol can be administered in any order. In general, each agent will be administered at a dose and/or on a time schedule determined for that agent. It will further be appreciated that the at least one additional therapeutic agent utilized in this combination may be administered together in a single composition or administered separately in different compositions. In general, it is expected that additional therapeutic agents utilized in combination be utilized at levels that do not exceed the levels at which they are utilized individually. In some embodiments, the levels utilized in combination will be lower than those utilized individually.

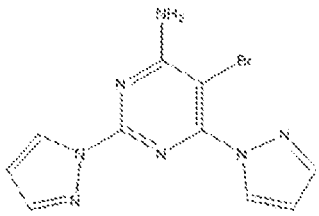
[0411] The present disclosure thus inter alia pertains to a combination product for simultaneous, separate or sequential use, such as a combined preparation or a pharmaceutical fixed combination, or a combination of such preparation and combination.

Exemplary Adenosine A2A Receptor Antagonists

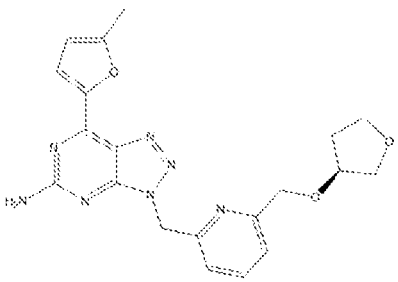
[0412] In certain embodiments, the anti-human ENTPD2 molecules described herein are administered in combination with at least one adenosine A2A receptor (A2AR) antagonist. In certain embodiments, the anti-human ENTPD2 molecules described herein are administered in combination with at least two adenosine A2A receptor (A2AR) antagonists. Exemplary A2AR antagonists include, but are not limited to, e.g., PBF509/NIR178 (Palobiofarma/Novartis), CPI444/V81444 (Corvus/Genentech), AZD4635/HTL-1071 (AstraZeneca/Heptares), Vipadenant (Redox/Juno), GBV-2034 (Globavir), AB928 (Arcus Biosciences), Theophylline, Istradefylline (Kyowa Hakko Kogyo), Tozadenant/SYN-115 (Acorda), KW-6356 (Kyowa Hakko Kogyo), ST-4206 (Leadiant Biosciences), and Preladenant/SCH 420814 (Merck/Schering).

[0413] In certain embodiments, the A2AR antagonist is PBF509/NIR178. PBF509/NIR178 and other A2AR antagonists are disclosed in US 8,796,284 and WO 2017/025918, herein incorporated by reference in their entirety. In certain embodiments, the A2AR antagonist is 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine, or a

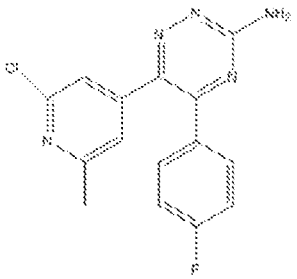
pharmaceutically acceptable salt thereof. In certain embodiments, the A2AR antagonist has the following structure:


, or a pharmaceuticaly acceptable salt thereof.

[0414] In certain embodiments, the A2AR antagonist is CPI444/V81444. CPI-444 and other A2AR antagonists are disclosed in WO 2009/156737, herein incorporated by reference in its entirety. In certain embodiments, the A2AR antagonist is (*S*)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptbale salt thereof. In certain embodiments, the A2AR antagonist is (*R*)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof, or a pharmaceutically acceptbale salt thereof. In certain embodiments, the A2AR antagonist is 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptbale salt thereof. In certain embodiments, the A2AR antagonist has the following structure:

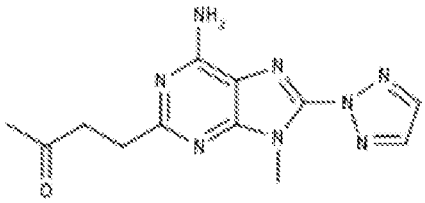

, or a pharmaceuticaly acceptable salt thereof.

[0415] In certain embodiments, the A2AR antagonist is AZD4635/HTL-1071. A2AR antagonists are disclosed in WO 2011/095625, herein incorporated by reference in its entirety. In certain embodiments, the A2AR antagonist is 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine, or a pharmaceuticaly acceptable salt thereof.. In certain embodiments, the A2AR antagonist has the following structure:



, or a pharmaceuticaly acceptable salt thereof.

[0416] In certain embodiments, the A2AR antagonist is ST-4206 (Leadiant Biosciences). In certain embodiments, the A2AR antagonist is an A2AR antagonist described in US 9,133,197, herein incorporated by reference in its entirety. In certain embodiments, the A2AR antagonist has the following structure:



, or a pharmaceuticaly acceptable salt thereof.

[0417] In certain embodiments, the A2AR antagonist is an A2AR antagonist described in US8114845, US9029393, US20170015758, or US20160129108, herein incorporated by reference in their entirety.

[0418] In certain embodiments, the A2AR antagonist is istradefylline (CAS Registry Number: 155270-99-8). Istradefylline is also known as KW-6002 or 8-[(E)-2-(3,4-dimethoxyphenyl)vinyl]-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione. Istradefylline is disclosed, *e.g.,* in LeWitt *et al.* (2008) *Annals of Neurology* 63 (3): 295–302).

[0419] In certain embodiments, the A2aR antagonist is tozadenant (Biotie). Tozadenant is also known as SYN115 or 4-hydroxy-N-(4-methoxy-7-morpholin-4-yl-1,3-benzothiazol-2-yl)-4-methylpiperidine-1-carboxamide. Tozadenant blocks the effect of endogenous adenosine at the A2a receptors, resulting in the potentiation of the effect of dopamine at the D2 receptor and inhibition of the effect of glutamate at the mGluR5 receptor. In some embodiments, the A2aR antagonist is preladenant (CAS Registry Number: 377727-87-2). Preladenant is also known as SCH 420814 or 2-(2-Furanyl)-7-[2-[4-[4-(2-

methoxyethoxy)phenyl]-1-piperazinyl]ethyl]7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-5-amine. Preladenant was developed as a drug that acted as a potent and selective antagonist at the adenosine A2A receptor.

[0420] In certain embodiments, the A2aR antagonist is vipadenant. Vipadenant is also known as BIIB014, V2006, or 3-[(4-amino-3-methylphenyl)methyl]-7-(furan-2-yl)triazolo[4,5-d]pyrimidin-5-amine.

[0421] Other exemplary A2aR antagonists include, *e.g.,* ATL-444, MSX-3, SCH-58261, SCH-412,348, SCH-442,416, VER-6623, VER-6947, VER-7835, CGS-15943, or ZM-241,385.

[0422] In some embodiments, the A2aR antagonist is an A2aR pathway antagonist, *e.g.,* a CD-73 inhibitor, *e.g.,* an anti-CD73 antibody. Targeting the extracellular production of adenosine by CD73 may reduce the immunosuppressive effects of adenosine. Anti-CD73 antibodies have a range of activities, *e.g.,* inhibition of CD73 ectonucleotidase activity, relief from AMP-mediated lymphocyte suppression, and inhibition of syngeneic tumor growth. Anti-CD73 antibodies can drive changes in both myeloid and lymphoid infiltrating leukocyte populations within the tumor microenvironment. These changes include, *e.g.,* increases in CD8 effector cells and activated macrophages, as well as a reduction in the proportions of myeloid-derived suppressor cells (MDSC) and regulatory T lymphocytes. In one embodiment, an anti-CD73 antibody molecule is a full antibody molecule or an antigen-binding fragment thereof. In some embodiments, the anti-CD73 antibody molecule is chosen from any of the antibody molecules listed in Table 2. In other embodiments, the anti-CD73 antibody molecule comprises a heavy chain variable domain sequence, a light chain variable domain sequence, or both, as disclosed in Table 2. In certain embodiments, the anti-CD73 antibody molecule binds to a CD73 protein and reduces, e.g., inhibits or antagonizes, an activity of CD73, e.g., human CD73.

[0423] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/075099, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is MEDI 9447, e.g., as disclosed in WO2016/075099. Alternative names for MEDI 9447 include clone 10.3 or 73combo3. MEDI 9447 is an IgG1 antibody that inhibits, e.g., antagonizes, an activity of CD73. MEDI 9447 and other anti-CD73 antibody molecules are also disclosed in WO2016/075176 and US2016/0129108, the entire contents of which are herein incorporated by reference in their entirety.

[0424] In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of MEDI 9477. The amino acid sequence of the heavy chain variable domain of MEDI 9477 is disclosed as SEQ ID NO: 295 (see Table 2). The amino acid sequence of the light chain variable domain of MEDI 9477 is disclosed as SEQ ID NO: 296 (see Table 2).

[0425] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/081748, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is 11F11, e.g., as disclosed in WO2016/081748. 11F11 is an IgG2 antibody that inhibits, e.g., antagonizes, an activity of CD73. Antibodies derived from 11F11, e.g., CD73.4, and CD73.10; clones of 11F11, e.g., 11F11-1 and 11F11-2; and other anti-CD73 antibody molecules are disclosed in WO2016/081748 and US 9,605,080, the entire contents of which are herein incorporated by reference in their entirety.

[0426] In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of 11F11-1 or 11F11-2. The amino acid sequence of the heavy chain variable domain of 11F11-1 is disclosed as SEQ ID NO: 302 (see Table 2). The amino acid sequence of the light chain variable domain of 11F11-1 is disclosed as SEQ ID NO: 303 (see Table 2). The amino acid sequence of the heavy chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 299 (see Table 2). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 300 (see Table 2). In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain, a light chain, or both, of 11F11-1 or 11F11-2. The heavy and light chain amino acid sequences of 11F11-1 are disclosed as SEQ ID NO: 297 and SEQ ID NO: 301, respectively (see Table 2). The heavy and light chain amino acid sequences of 11F11-2 are disclosed as SEQ ID NO: 294 and SEQ ID NO: 298, respectively (see Table 2).

[0427] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in e.g., US 9,605,080, herein incorporated by reference in its entirety.

[0428] In one embodiment, the anti-CD73 antibody molecule is CD73.4, e.g., as disclosed in US 9,605,080. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of CD73.4. The amino acid sequence of the heavy chain variable domain of CD73.4 is disclosed as SEQ ID NO: 304 (see Table 2). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 305 (see Table 2).

[0429] In one embodiment, the anti-CD73 antibody molecule is CD73.10, e.g., as disclosed in US 9,605,080. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of CD73.10. The amino acid sequence of the heavy chain variable domain of CD73.10 is disclosed as SEQ ID NO: 306 (see Table 2). The amino acid sequence of the light chain variable domain of CD73.10 is disclosed as SEQ ID NO: 307 (see Table 2).

[0430] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2009/0203538, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is 067-213, e.g., as disclosed in WO2009/0203538.

[0431] In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of 067-213. The amino acid sequence of the heavy chain variable domain of 067-213 is disclosed as SEQ ID NO: 308 (see Table 2). The amino acid sequence of the light chain variable domain of 067-213 is disclosed as SEQ ID NO: 309 (see Table 2).

[0432] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US 9,090,697, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is TY/23, e.g., as disclosed in US 9,090,697. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of TY/23.

[0433] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/055609, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2016/055609.

[0434] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/146818, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2016/146818.

[0435] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2004/079013, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain,

a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2004/079013.

[0436] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2012/125850, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2012/125850.

[0437] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2015/004400, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2015/004400.

[0438] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2007/146968, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2007146968.

[0439] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US2007/0042392, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in US2007/0042392.

[0440] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US2009/0138977, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in US2009/0138977.

[0441] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in Flocke *et al.,* Eur J Cell Biol. 1992 Jun;58(1):62-70, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in Flocke *et al.,* Eur J Cell Biol. 1992 Jun;58(1):62-70.

[0442] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in Stagg *et al.*, PNAS. 2010 Jan 107(4): 1547-1552, herein incorporated

by reference in its entirety. In some embodiments, the anti-CD73 antibody molecule is TY/23 or TY11.8, as disclosed in Stagg *et al*. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in Stagg *et al*.

[0443] In one embodiment, the anti-human ENTPD2 antibody as described herein is administered in combination with an anti-CD73 antibody molecule, for example as described herein, and an A2AR antagonist, optionally selected from the group comprising PBF509/NIR178, CPI444/V81444, AZD4635/HTL-1071, Vipadenant, GBV-2034, AB928, Theophylline, Istradefylline, Tozadenant/SYN-115, KW-6356, ST-4206, and Preladenant/SCH 420814.

Table 2. Sequences of exemplary anti-CD73 antibody molecules

WO2016075099 **MEDI 9447**		
SEQ ID NO: 295	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAYSWV RQAPGKGLEWVSAISGSGGRTYYADSVKGRFTISRDNS KNTLYLQMNSLRAEDTAVYYCARLGYGRVDEWGRG TLVTVSS
SEQ ID NO: 296	VL	QSVLTQPPSASGTPGQRVTISCSGSLSNIGRNPVNWYQ QLPGTAPKLLIYLDNLRLSGVPDRFSGSKSGTSASLAIS GLQSEDEADYYCATWDDSHPGWTFGGGTKLTVL
WO2016/081748 **11F11-2**		
SEQ ID NO: 297	HC	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPDSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKC CVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNS TFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 298	LC	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQYNSYPLTFGGGTKVEIKRTVAAPSVF IFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 299	VH	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPDSVKGRFTISRD

		NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMVTVSS
SEQ ID NO: 300	VL kappa	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQYNSYPLTFGGGTKVEIK
WO2016/081748 **11F11-1**		
SEQ ID NO: 297	HC	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPDSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKC CVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNS TFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 301	LC	EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAWYQQ KPGQAPRLLIYDASNRATGIPARFSGSGPGTDFTLTISSL EPEDFAVYYCQQRSNWHLTFGGGTKVEIKRTVAAPSV FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 302	VH	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPDSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMVTVSS
SEQ ID NO: 303	VL kappa	EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAWYQQ KPGQAPRLLIYDASNRATGIPARFSGSGPGTDFTLTISSL EPEDFAVYYCQQRSNWHLTFGGGTKVEIK
US9605080 **CD73.4**		
SEQ ID NO: 304	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPDSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMVTVSS
SEQ ID NO: 305	VL kappa	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQYNSYPLTFGGGTKVEIK
US9605080 **CD73.10**		
SEQ ID NO: 306	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHW VRQAPGKGLEWVAVIWYDESNKYYPDSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMVTVSS
SEQ ID NO: 307	VL kappa	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQYNSYPLTFGGGTKVEIK

US9388249 **067-213**		
SEQ ID NO: 308	VH	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHW VRQAPGKGLEWVSGISWNSGSIGYADSVKGRFTISRDN AKNSLYLQMNSLRAEDTALYYCVRSGSYNYYYYGMD VWGQGTTVTVSR
SEQ ID NO: 309	VL	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQ QLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAIS GLQSEDEADYYCAAWDDSLNGWVFGGGTKLTVLG

[0444] The anti-CD73 antibody molecules used in the combination therapies disclosed herein can include any of the VH/VL sequences disclosed in Table 2, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical thereto). Exemplary sequences for CD73 antibodies include:

(i) the VH and VL amino acid sequences for MEDI 9447, SEQ ID NOs: 295-296, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 295-296);

(ii) the HC and LC amino acid sequences for 11F11-2, SEQ ID NOs: 297-298, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 297-298);

(iii) the VH and VL amino acid sequences for 11F11-2, SEQ ID NOs: 299-300, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 299-300);

(iv) the HC and LC amino acid sequences for 11F11-1, SEQ ID NOs: 297 and 301, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 297 and 301);

(v) the VH and VL amino acid sequences for 11F11-1, SEQ ID NOs: 302-303, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 302-303);

(vi) the VH and VL amino acid sequences for CD73.4, SEQ ID NOs: 304-305, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 304-305);

(vii) the VH and VL amino acid sequences for CD73.10, SEQ ID NOs: 306-307, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 306-307); or

(viii) the VH and VL amino acid sequences for 067-213, SEQ ID NOs: 308-309, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 308-309).

[0445] The anti-human ENTPD2 antibody as described herein can be combined with an inhibitor of a co-inhibitory molecule (e.g., a PD-1 inhibitor (e.g., an anti-PD-1 antibody molecule), a PD-L1 inhibitor (e.g., an anti-PD-L1 antibody molecule), a PD-L2 inhibitor (e.g., an anti-PD-L2 antibody molecule), a LAG-3 inhibitor (e.g., an anti-LAG-3 antibody molecule), a TIM-3 inhibitor (e.g., an anti-TIM-3 antibody molecule)), an activator of a co-stimulatory molecule (e.g., a GITR agonist (e.g., an anti-GITR antibody molecule)), a cytokine (e.g., IL-15 complexed with a soluble form of IL-15 receptor alpha (IL-15Ra)), or any combination thereof.

PD-1 Inhibitors

[0446] In certain embodiments, the ENTPD2 antibody as described herein is administered in combination with a PD-1 inhibitor. In some embodiments, the PD-1 inhibitor is chosen from PDR001 (Novartis), Nivolumab (Bristol-Myers Squibb), Pembrolizumab (Merck & Co), Pidilizumab (CureTech), MEDI0680 (Medimmune), REGN2810 (Regeneron), TSR-042 (Tesaro), PF-06801591 (Pfizer), BGB-A317 (Beigene), BGB-108 (Beigene), INCSHR1210 (Incyte), or AMP-224 (Amplimmune).

Exemplary PD-1 Inhibitors

[0447] In one embodiment, the PD-1 inhibitor is an anti-PD-1 antibody molecule. In one embodiment, the PD-1 inhibitor is an anti-PD-1 antibody molecule as described in US 2015/0210769, published on July 30, 2015, entitled "Antibody Molecules to PD-1 and Uses Thereof," incorporated by reference in its entirety.

[0448] In one embodiment, the anti-PD-1 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 3 (*e.g.*, from the heavy and light chain variable region sequences of BAP049-Clone-E or BAP049-Clone-B disclosed in Table 3), or encoded by a nucleotide sequence shown in Table 3. In some embodiments, the CDRs are according to the Kabat

definition (*e.g.*, as set out in Table 3). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 3). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 3). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GYTFTTYWMH (SEQ ID NO: 541). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 3, or encoded by a nucleotide sequence shown in Table 3.

[0449] In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 501, a VHCDR2 amino acid sequence of SEQ ID NO: 502, and a VHCDR3 amino acid sequence of SEQ ID NO: 503; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 510, a VLCDR2 amino acid sequence of SEQ ID NO: 511, and a VLCDR3 amino acid sequence of SEQ ID NO: 512, each disclosed in Table 3.

[0450] In one embodiment, the antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 524, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 525, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 526; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 529, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 530, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 531, each disclosed in Table 3.

[0451] In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 506. In one embodiment, the anti-PD-1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 520, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 520. In one embodiment, the anti-PD-1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 516, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 516. In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506 and a VL comprising the amino acid sequence of SEQ ID NO: 520. In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid

sequence of SEQ ID NO: 506 and a VL comprising the amino acid sequence of SEQ ID NO: 516.

[0452] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 507, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 507. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 521 or 517, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 521 or 517. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 507 and a VL encoded by the nucleotide sequence of SEQ ID NO: 521 or 517.

[0453] In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 508. In one embodiment, the anti-PD-1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 522, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 522. In one embodiment, the anti-PD-1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 518, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 518. In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508 and a light chain comprising the amino acid sequence of SEQ ID NO: 522. In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508 and a light chain comprising the amino acid sequence of SEQ ID NO: 518.

[0454] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 509, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 509. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 523 or 519, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 523 or 519. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 509 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 523 or 519.

[0455] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0210769, incorporated by reference in its entirety.

Table 3. Amino acid and nucleotide sequences of exemplary anti-PD-1 antibody molecules

BAP049-Clone-B HC		
SEQ ID NO: 501 (Kabat)	HCDR1	TYWMH
SEQ ID NO: 502 (Kabat)	HCDR2	NIYPGTGGSNFDEKFKN
SEQ ID NO: 503 (Kabat)	HCDR3	WTTGTGAY
SEQ ID NO: 504 (Chothia)	HCDR1	GYTFTTY
SEQ ID NO: 505 (Chothia)	HCDR2	YPGTGG
SEQ ID NO: 503 (Chothia)	HCDR3	WTTGTGAY
SEQ ID NO: 506	VH	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTTGTGAYWGQGTTVTVSS
SEQ ID NO: 507	DNA VH	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTCAGGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAACTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGC
SEQ ID NO: 508	Heavy chain	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTTGTGAYWGQGTTVTVSSASTKGPSVFPLAPCSRS TSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPP CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRL TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG
SEQ ID NO: 509	DNA heavy chain	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTCAGGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAACTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGCGCTAGCACTAAGGGCCCGTCCGTGTTCCCCCTGGCACC TTGTAGCCGGAGCACTAGCGAATCCACCGCTGCCCTCGGCTGCC TGGTCAAGGATTACTTCCCGGAGCCCGTGACCGTGTCCTGGAAC AGCGGAGCCCTGACCTCCGGAGTGCACACCTTCCCCGCTGTGCT GCAGAGCTCCGGGCTGTACTCGCTGTCGTCGGTGGTCACGGTGC CTTCATCTAGCCTGGGTACCAAGACCTACACTTGCAACGTGGAC CACAAGCCTTCCAACACTAAGGTGGACAAGCGCGTCGAATCGA AGTACGGCCCACCGTGCCCGCCTTGTCCCGCGCCGGAGTTCCTC

		GGCGGTCCCTCGGTCTTTCTGTTCCCACCGAAGCCCAAGGACAC TTTGATGATTTCCCGCACCCCTGAAGTGACATGCGTGGTCGTGG ACGTGTCACAGGAAGATCCGGAGGTGCAGTTCAATTGGTACGT GGATGGCGTCGAGGTGCACAACGCCAAAACCAAGCCGAGGGA GGAGCAGTTCAACTCCACTTACCGCGTCGTGTCCGTGCTGACGG TGCTGCATCAGGACTGGCTGAACGGGAAGGAGTACAAGTGCAA AGTGTCCAACAAGGGACTTCCTAGCTCAATCGAAAAGACCATC TCGAAAGCCAAGGGACAGCCCCGGGAACCCCAAGTGTATACCC TGCCACCGAGCCAGGAAGAAATGACTAAGAACCAAGTCTCATT GACTTGCCTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGG AATGGGAGTCCAACGGCCAGCCGGAAAACAACTACAAGACCA CCCCTCCGGTGCTGGACTCAGACGGATCCTTCTTCCTCTACTCG CGGCTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGTGT TCAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTACACT CAGAAGTCCCTGTCCCTCTCCCTGGGA
BAP049-Clone-B LC		
SEQ ID NO: 510 (Kabat)	LCDR1	KSSQSLLDSGNQKNFLT
SEQ ID NO: 511 (Kabat)	LCDR2	WASTRES
SEQ ID NO: 512 (Kabat)	LCDR3	QNDYSYPYT
SEQ ID NO: 513 (Chothia)	LCDR1	SQSLLDSGNQKNF
SEQ ID NO: 514 (Chothia)	LCDR2	WAS
SEQ ID NO: 515 (Chothia)	LCDR3	DYSYPY
SEQ ID NO: 516	VL	EIVLTQSPATLSLSPGERATLSCKSSQSLLDSGNQKNFLTWYQQKP GKAPKLLIYWASTRESGVPSRFSGSGSGTDFTFTISSLQPEDIATYY CQNDYSYPYTFGQGTKVEIK
SEQ ID NO: 517	DNA VL	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCCTGACCTGGTATCAGC AGAAGCCCGGTAAAGCCCCTAAGCTGCTGATCTACTGGGCCTC TACTAGAGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCTTCACTATCTCTAGCCTGCAGCCCGA GGATATCGCTACCTACTACTGTCAGAACGACTATAGCTACCCCT ACACCTTCGGTCAAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 518	Light chain	EIVLTQSPATLSLSPGERATLSCKSSQSLLDSGNQKNFLTWYQQKP GKAPKLLIYWASTRESGVPSRFSGSGSGTDFTFTISSLQPEDIATYY CQNDYSYPYTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSST LTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 519	DNA light chain	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCCTGACCTGGTATCAGC AGAAGCCCGGTAAAGCCCCTAAGCTGCTGATCTACTGGGCCTC TACTAGAGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCTTCACTATCTCTAGCCTGCAGCCCGA GGATATCGCTACCTACTACTGTCAGAACGACTATAGCTACCCCT ACACCTTCGGTCAAGGCACTAAGGTCGAGATTAAGCGTACGGT GGCCGCTCCCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAGC TGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTT

		CTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCC CTGCAGAGCGGCAACAGCCAGGAGAGCGTCACCGAGCAGGAC AGCAAGGACTCCACCTACAGCCTGAGCAGCACCCTGACCCTGA GCAAGGCCGACTACGAGAAGCATAAGGTGTACGCCTGCGAGGT GACCCACCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
BAP049-Clone-E HC		
SEQ ID NO: 501 (Kabat)	HCDR1	TYWMH
SEQ ID NO: 502 (Kabat)	HCDR2	NIYPGTGGSNFDEKFKN
SEQ ID NO: 503 (Kabat)	HCDR3	WTTGTGAY
SEQ ID NO: 504 (Chothia)	HCDR1	GYTFTTY
SEQ ID NO: 505 (Chothia)	HCDR2	YPGTGG
SEQ ID NO: 503 (Chothia)	HCDR3	WTTGTGAY
SEQ ID NO: 506	VH	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTTGTGAYWGQGTTVTVSS
SEQ ID NO: 507	DNA VH	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTCAGGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAACTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGC
SEQ ID NO: 508	Heavy chain	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTTGTGAYWGQGTTVTVSSASTKGPSVFPLAPCSRS TSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPP CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRL TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG
SEQ ID NO: 509	DNA heavy chain	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTCAGGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAACTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGCGCTAGCACTAAGGGCCCGTCCGTGTTCCCCCTGGCACC TTGTAGCCGGAGCACTAGCGAATCCACCGCTGCCCTCGGCTGCC TGGTCAAGGATTACTTCCCGGAGCCCGTGACCGTGTCCTGGAAC AGCGGAGCCCTGACCTCCGGAGTGCACACCTTCCCCGCTGTGCT GCAGAGCTCCGGGCTGTACTCGCTGTCGTCGGTGGTCACGGTGC

		CTTCATCTAGCCTGGGTACCAAGACCTACACTTGCAACGTGGAC CACAAGCCTTCCAACACTAAGGTGGACAAGCGCGTCGAATCGA AGTACGGCCCACCGTGCCCGCCTTGTCCCGCGCCGGAGTTCCTC GGCGGTCCCTCGGTCTTTCTGTTCCCACCGAAGCCCAAGGACAC TTTGATGATTTCCCGCACCCCTGAAGTGACATGCGTGGTCGTGG ACGTGTCACAGGAAGATCCGGAGGTGCAGTTCAATTGGTACGT GGATGGCGTCGAGGTGCACAACGCCAAAACCAAGCCGAGGGA GGAGCAGTTCAACTCCACTTACCGCGTCGTGTCCGTGCTGACGG TGCTGCATCAGGACTGGCTGAACGGGAAGGAGTACAAGTGCAA AGTGTCCAACAAGGGACTTCCTAGCTCAATCGAAAAGACCATC TCGAAAGCCAAGGGACAGCCCCGGGAACCCCAAGTGTATACCC TGCCACCGAGCCAGGAAGAAATGACTAAGAACCAAGTCTCATT GACTTGCCTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGG AATGGGAGTCCAACGGCCAGCCGGAAAACAACTACAAGACCA CCCCTCCGGTGCTGGACTCAGACGGATCCTTCTTCCTCTACTCG CGGCTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGTGT TCAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTACACT CAGAAGTCCCTGTCCCTCTCCCTGGGA
BAP049-Clone-E LC		
SEQ ID NO: 510 (Kabat)	LCDR1	KSSQSLLDSGNQKNFLT
SEQ ID NO: 511 (Kabat)	LCDR2	WASTRES
SEQ ID NO: 512 (Kabat)	LCDR3	QNDYSYPYT
SEQ ID NO: 513 (Chothia)	LCDR1	SQSLLDSGNQKNF
SEQ ID NO: 514 (Chothia)	LCDR2	WAS
SEQ ID NO: 515 (Chothia)	LCDR3	DYSYPY
SEQ ID NO: 520	VL	EIVLTQSPATLSLSPGERATLSCKSSQSLLDSGNQKNFLTWYQQKP GQAPRLLIYWASTRESGVPSRFSGSGSGTDFTFTISSLEAEDAATYY CQNDYSYPYTFGQGTKVEIK
SEQ ID NO: 521	DNA VL	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCCTGACCTGGTATCAGC AGAAGCCCGGTCAAGCCCCTAGACTGCTGATCTACTGGGCCTCT ACTAGAGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGTA GTGGCACCGACTTCACCTTCACTATCTCTAGCCTGGAAGCCGAG GACGCCGCTACCTACTACTGTCAGAACGACTATAGCTACCCCTA CACCTTCGGTCAAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 522	Light chain	EIVLTQSPATLSLSPGERATLSCKSSQSLLDSGNQKNFLTWYQQKP GQAPRLLIYWASTRESGVPSRFSGSGSGTDFTFTISSLEAEDAATYY CQNDYSYPYTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSST LTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 523	DNA light chain	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCCTGACCTGGTATCAGC AGAAGCCCGGTCAAGCCCCTAGACTGCTGATCTACTGGGCCTCT ACTAGAGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGTA GTGGCACCGACTTCACCTTCACTATCTCTAGCCTGGAAGCCGAG GACGCCGCTACCTACTACTGTCAGAACGACTATAGCTACCCCTA

		CACCTTCGGTCAAGGCACTAAGGTCGAGATTAAGCGTACGGTG GCCGCTCCCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAGCT GAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACTTC TACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCC TGCAGAGCGGCAACAGCCAGGAGAGCGTCACCGAGCAGGACA GCAAGGACTCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCCTGCGAGGTG ACCCACCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACA GGGGCGAGTGC
BAP049-Clone-B HC		
SEQ ID NO: 524 (Kabat)	HCDR1	ACCTACTGGATGCAC
SEQ ID NO: 525 (Kabat)	HCDR2	AATATCTACCCCGGCACCGGCGGCTCTAACTTCGACGAGAAGT TTAAGAAT
SEQ ID NO: 526 (Kabat)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
SEQ ID NO: 527 (Chothia)	HCDR1	GGCTACACCTTCACTACCTAC
SEQ ID NO: 528 (Chothia)	HCDR2	TACCCCGGCACCGGCGGC
SEQ ID NO: 526 (Chothia)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
BAP049-Clone-B LC		
SEQ ID NO: 529 (Kabat)	LCDR1	AAATCTAGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACT TCCTGACC
SEQ ID NO: 530 (Kabat)	LCDR2	TGGGCCTCTACTAGAGAATCA
SEQ ID NO: 531 (Kabat)	LCDR3	CAGAACGACTATAGCTACCCCTACACC
SEQ ID NO: 532 (Chothia)	LCDR1	AGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACTTC
SEQ ID NO: 533 (Chothia)	LCDR2	TGGGCCTCT
SEQ ID NO: 534 (Chothia)	LCDR3	GACTATAGCTACCCCTAC
BAP049-Clone-E HC		
SEQ ID NO: 524 (Kabat)	HCDR1	ACCTACTGGATGCAC
SEQ ID NO: 525 (Kabat)	HCDR2	AATATCTACCCCGGCACCGGCGGCTCTAACTTCGACGAGAAGT TTAAGAAT
SEQ ID NO: 526 (Kabat)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
SEQ ID NO: 527 (Chothia)	HCDR1	GGCTACACCTTCACTACCTAC
SEQ ID NO: 528 (Chothia)	HCDR2	TACCCCGGCACCGGCGGC
SEQ ID NO: 526 (Chothia)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
BAP049-Clone-E LC		
SEQ ID NO: 529 (Kabat)	LCDR1	AAATCTAGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACT TCCTGACC
SEQ ID NO: 530 (Kabat)	LCDR2	TGGGCCTCTACTAGAGAATCA
SEQ ID NO: 531 (Kabat)	LCDR3	CAGAACGACTATAGCTACCCCTACACC
SEQ ID NO: 532 (Chothia)	LCDR1	AGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACTTC

SEQ ID NO: 533 (Chothia)	LCDR2	TGGGCCTCT
SEQ ID NO: 534 (Chothia)	LCDR3	GACTATAGCTACCCCTAC

Other Exemplary PD-1 Inhibitors

[0456] In one embodiment, the anti-PD-1 antibody molecule is Nivolumab (Bristol-Myers Squibb), also known as MDX-1106, MDX-1106-04, ONO-4538, BMS-936558, or OPDIVO®. Nivolumab (clone 5C4) and other anti-PD-1 antibodies are disclosed in US 8,008,449 and WO 2006/121168, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Nivolumab, *e.g.*, as disclosed in Table 4.

[0457] In one embodiment, the anti-PD-1 antibody molecule is Pembrolizumab (Merck & Co), also known as Lambrolizumab, MK-3475, MK03475, SCH-900475, or KEYTRUDA®. Pembrolizumab and other anti-PD-1 antibodies are disclosed in Hamid, O. *et al.* (2013) *New England Journal of Medicine* 369 (2): 134–44, US 8,354,509, and WO 2009/114335, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Pembrolizumab, *e.g.*, as disclosed in Table 4.

[0458] In one embodiment, the anti-PD-1 antibody molecule is Pidilizumab (CureTech), also known as CT-011. Pidilizumab and other anti-PD-1 antibodies are disclosed in Rosenblatt, J. *et al.* (2011) *J Immunotherapy* 34(5): 409-18, US 7,695,715, US 7,332,582, and US 8,686,119, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Pidilizumab, *e.g.*, as disclosed in Table 4.

[0459] In one embodiment, the anti-PD-1 antibody molecule is MEDI0680 (Medimmune), also known as AMP-514. MEDI0680 and other anti-PD-1 antibodies are disclosed in US 9,205,148 and WO 2012/145493, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR

sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MEDI0680.

[0460] In one embodiment, the anti-PD-1 antibody molecule is REGN2810 (Regeneron). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of REGN2810.

[0461] In one embodiment, the anti-PD-1 antibody molecule is PF-06801591 (Pfizer). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of PF-06801591.

[0462] In one embodiment, the anti-PD-1 antibody molecule is BGB-A317 or BGB-108 (Beigene). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BGB-A317 or BGB-108.

[0463] In one embodiment, the anti-PD-1 antibody molecule is INCSHR1210 (Incyte), also known as INCSHR01210 or SHR-1210. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INCSHR1210.

[0464] In one embodiment, the anti-PD-1 antibody molecule is TSR-042 (Tesaro), also known as ANB011. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-042.

[0465] Further known anti-PD-1 antibodies include those described, *e.g.*, in WO 2015/112800, WO 2016/092419, WO 2015/085847, WO 2014/179664, WO 2014/194302, WO 2014/209804, WO 2015/200119, US 8,735,553, US 7,488,802, US 8,927,697, US 8,993,731, and US 9,102,727, incorporated by reference in their entirety.

[0466] In one embodiment, the anti-PD-1 antibody is an antibody that competes for binding with, and/or binds to the same epitope on PD-1 as, one of the anti-PD-1 antibodies described herein.

[0467] In one embodiment, the PD-1 inhibitor is a peptide that inhibits the PD-1 signaling pathway, *e.g.*, as described in US 8,907,053, incorporated by reference in its

entirety. In one embodiment, the PD-1 inhibitor is an immunoadhesin (*e.g.*, an immunoadhesin comprising an extracellular or PD-1 binding portion of PD-L1 or PD-L2 fused to a constant region (*e.g.*, an Fc region of an immunoglobulin sequence). In one embodiment, the PD-1 inhibitor is AMP-224 (B7-DCIg (Amplimmune), *e.g.*, disclosed in WO 2010/027827 and WO 2011/066342, incorporated by reference in their entirety).

Table 4. Amino acid sequences of other exemplary anti-PD-1 antibody molecules

Nivolumab		
SEQ ID NO: 535	Heavy chain	QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAV IWYDGSKRYYADSVKGRFTISRDNSKNTLFLQMNSLRAEDTAVYYCATND DYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSN TKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSR WQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 536	Light chain	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASN RATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQSSNWPRTFGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC
Pembrolizumab		
SEQ ID NO: 537	Heavy chain	QVQLVQSGVEVKKPGASVKVSCKASGYTFTNYYMYWVRQAPGQGLEWM GGINPSNGGTNFNEKFKNRVTLTTDSSTTTAYMELKSLQFDDTAVYYCARR DYRFDMGFDYWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYT CNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS RLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 538	Light chain	EIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLI YLASYLESGVPARFSGSGSGTDFTLTISSLEPEDFAVYYCQHSRDLPLTFGGG TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC
Pidilizumab		
SEQ ID NO: 539	Heavy chain	QVQLVQSGSELKKPGASVKISCKASGYTFTNYGMNWVRQAPGQGLQWMG WINTDSGESTYAEEFKGRFVFSLDTSVNTAYLQITSLTAEDTGMYFCVRVGY DALDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHK PSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 540	Light chain	EIVLTQSPSSLSASVGDRVTITCSARSSVSYMHWFQQKPGKAPKLWIYRTSN LASGVPSRFSGSGSGTSYCLTINSLQPEDFATYYCQQRSSFPLTFGGGTKLEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC

[0468] In one embodiment the anti-human ENTPD2 antibody as described herein is administered in combination with at least one PD1 inhibitor as described herein and at least one A2A receptor antagonist as described herein.

PD-L1 Inhibitors

[0469] In certain embodiments, the anti-human ENTPD2 antibody as described herein is administered in combination with a PD-L1 inhibitor. The PD-L1 inhibitor may be an antibody, an antigenbinding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the PD-L1 inhibitor is chosen from FAZ053 (Novartis), Atezolizumab, also known as Tecentriq® (Genentech/Roche), Avelumab, also known as Bavencio® (Merck Serono and Pfizer), Durvalumab, also known as Imfinzi® (MedImmune/AstraZeneca), or BMS-936559 (Bristol-Myers Squibb).

Exemplary PD-L1 Inhibitors

[0470] In one embodiment, the PD-L1 inhibitor is an anti-PD-L1 antibody molecule. In one embodiment, the PD-L1 inhibitor is an anti-PD-L1 antibody molecule as disclosed in US 2016/0108123, published on April 21, 2016, entitled "Antibody Molecules to PD-L1 and Uses Thereof," incorporated by reference in its entirety.

[0471] In one embodiment, the anti-PD-L1 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 5 (*e.g.*, from the heavy and light chain variable region sequences of BAP058-Clone O or BAP058-Clone N disclosed in Table 5), or encoded by a nucleotide sequence shown in Table 5. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 5). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 5). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 5). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GYTFTSYWMY (SEQ ID NO: 647). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three,

four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 5, or encoded by a nucleotide sequence shown in Table 5.

[0472] In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 601, a VHCDR2 amino acid sequence of SEQ ID NO: 602, and a VHCDR3 amino acid sequence of SEQ ID NO: 603; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 609, a VLCDR2 amino acid sequence of SEQ ID NO: 610, and a VLCDR3 amino acid sequence of SEQ ID NO: 611, each disclosed in Table 5.

[0473] In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 628, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 629, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 630; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 633, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 634, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 635, each disclosed in Table 5.

[0474] In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 606, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 606. In one embodiment, the anti-PD-L1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 616, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 616. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 620, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 620. In one embodiment, the anti-PD-L1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 624, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 624. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 606 and a VL comprising the amino acid sequence of SEQ ID NO: 616. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 620 and a VL comprising the amino acid sequence of SEQ ID NO: 624.

[0475] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 607, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 607. In one embodiment, the antibody molecule

comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 617, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 617. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 621, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 621. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 625, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 625. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 607 and a VL encoded by the nucleotide sequence of SEQ ID NO: 617. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 621 and a VL encoded by the nucleotide sequence of SEQ ID NO: 625.

[0476] In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 608, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 608. In one embodiment, the anti-PD-L1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 618, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 618. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 622, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 622. In one embodiment, the anti-PD-L1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 626, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 626. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 608 and a light chain comprising the amino acid sequence of SEQ ID NO: 618. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 622 and a light chain comprising the amino acid sequence of SEQ ID NO: 626.

[0477] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 615, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 615. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 619, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 619. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 623, or a nucleotide sequence at least 85%, 90%, 95%,

or 99% identical or higher to SEQ ID NO: 623. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 627, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 627. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 615 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 619. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 623 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 627.

[0478] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2016/0108123, incorporated by reference in its entirety.

Table 5. Amino acid and nucleotide sequences of exemplary anti-PD-L1 antibody molecules

BAP058-Clone O HC		
SEQ ID NO: 601 (Kabat)	HCDR1	SYWMY
SEQ ID NO: 602 (Kabat)	HCDR2	RIDPNSGSTKYNEKFKN
SEQ ID NO: 603 (Kabat)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 604 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 605 (Chothia)	HCDR2	DPNSGS
SEQ ID NO: 603 (Chothia)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 606	VH	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQARGQ RLEWIGRIDPNSGSTKYNEKFKNRFTISRDNSKNTLYLQMNSLRA EDTAVYYCARDYRKGLYAMDYWGQGTTVTVSS
SEQ ID NO: 607	DNA VH	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGCTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTAGAGGGCA AAGACTGGAGTGGATCGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGGTTCACTATTAGT AGGGATAACTCTAAGAACACCCTGTACCTGCAGATGAATAGC CTGAGAGCCGAGGACACCGCCGTCTACTACTGCGCTAGAGACT ATAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCA CTACCGTGACCGTGTCTTCA
SEQ ID NO: 608	Heavy chain	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQARGQ RLEWIGRIDPNSGSTKYNEKFKNRFTISRDNSKNTLYLQMNSLRA EDTAVYYCARDYRKGLYAMDYWGQGTTVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSL SLG

SEQ ID NO: 615	DNA heavy chain	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGCTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTAGAGGGCA AAGACTGGAGTGGATCGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGGTTCACTATTAGT AGGGATAACTCTAAGAACACCCTGTACCTGCAGATGAATAGC CTGAGAGCCGAGGACACCGCCGTCTACTACTGCGCTAGAGACT ATAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCA CTACCGTGACCGTGTCTTCAGCTAGCACTAAGGGCCCGTCCGT GTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCACC GCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCCCG TGACCGTGTCCTGGAACAGCGGAGCCCTGACCTCCGGAGTGCA CACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTCGCTG TCGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTACCAAGA CCTACACTTGCAACGTGGACCACAAGCCTTCCAACACTAAGGT GGACAAGCGCGTCGAATCGAAGTACGGCCCACCGTGCCCGCC TTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTTCTGT TCCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCACCCC TGAAGTGACATGCGTGGTCGTGGACGTGTCACAGGAAGATCC GGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGCA CAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCGTGTCCGTGCTGACGGTGCTGCATCAGGACTGG CTGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGA CTTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGA CAGCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAG GAAGAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGA AGGGCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAA CGGCCAGCCGGAAAACAACTACAAGACCACCCCTCCGGTGCT GGACTCAGACGGATCCTTCTTCCTCTACTCGCGGCTGACCGTG GATAAGAGCAGATGGCAGGAGGGAAATGTGTTCAGCTGTTCT GTGATGCATGAAGCCCTGCACAACCACTACACTCAGAAGTCCC TGTCCCTCTCCCTGGGA
BAP058-Clone O LC		
SEQ ID NO: 609 (Kabat)	LCDR1	KASQDVGTAVA
SEQ ID NO: 610 (Kabat)	LCDR2	WASTRHT
SEQ ID NO: 611(Kabat)	LCDR3	QQYNSYPLT
SEQ ID NO: 612 (Chothia)	LCDR1	SQDVGTA
SEQ ID NO: 613 (Chothia)	LCDR2	WAS
SEQ ID NO: 614 (Chothia)	LCDR3	YNSYPL
SEQ ID NO: 616	VL	AIQLTQSPSSLSASVGDRVTITCKASQDVGTAVAWYLQKPGQSPQ LLIYWASTRHTGVPSRFSGSGSGTDFTFTISSLEAEDAATYYCQQY NSYPLTFGQGTKVEIK
SEQ ID NO: 617	DNA VL	GCTATTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGTG TGGGCGATAGAGTGACTATCACCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCTGCAGAAGCCTGGTCAATCA CCTCAGCTGCTGATCTACTGGGCCTCTACTAGACACACCGGCG TGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGACTTCAC CTTCACTATCTCTTCACTGGAAGCCGAGGACGCCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAG
SEQ ID NO: 618	Light chain	AIQLTQSPSSLSASVGDRVTITCKASQDVGTAVAWYLQKPGQSPQ LLIYWASTRHTGVPSRFSGSGSGTDFTFTISSLEAEDAATYYCQQY NSYPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 619	DNA light chain	GCTATTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGTG TGGGCGATAGAGTGACTATCACCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCTGCAGAAGCCTGGTCAATCA CCTCAGCTGCTGATCTACTGGGCCTCTACTAGACACACCGGCG TGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGACTTCAC CTTCACTATCTCTTCACTGGAAGCCGAGGACGCCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAGCGTACGGTGGCCGCTCCCAGCGT GTTCATCTTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACC GCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCCGGGAGG CCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCA ACAGCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCA CCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACT ACGAGAAGCATAAGGTGTACGCCTGCGAGGTGACCCACCAGG GCCTGTCCAGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGT GC
BAP058-Clone N HC		
SEQ ID NO: 601 (Kabat)	HCDR1	SYWMY
SEQ ID NO: 602 (Kabat)	HCDR2	RIDPNSGSTKYNEKFKN
SEQ ID NO: 603 (Kabat)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 604 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 605 (Chothia)	HCDR2	DPNSGS
SEQ ID NO: 603 (Chothia)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 620	VH	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQATGQ GLEWMGRIDPNSGSTKYNEKFKNRVTITADKSTSTAYMELSSLRS EDTAVYYCARDYRKGLYAMDYWGQGTTVTVSS
SEQ ID NO: 621	DNA VH	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGCTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTACCGGTCA AGGCCTGGAGTGGATGGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGAGTGACTATCACC GCCGATAAGTCTACTAGCACCGCCTATATGGAACTGTCTAGCC TGAGATCAGAGGACACCGCCGTCTACTACTGCGCTAGAGACTA TAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTTCA
SEQ ID NO: 622	Heavy chain	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQATGQ GLEWMGRIDPNSGSTKYNEKFKNRVTITADKSTSTAYMELSSLRS EDTAVYYCARDYRKGLYAMDYWGQGTTVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSL SLG
SEQ ID NO: 623	DNA heavy chain	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGCTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTACCGGTCA AGGCCTGGAGTGGATGGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGAGTGACTATCACC GCCGATAAGTCTACTAGCACCGCCTATATGGAACTGTCTAGCC TGAGATCAGAGGACACCGCCGTCTACTACTGCGCTAGAGACTA TAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTTCAGCTAGCACTAAGGGCCCGTCCGTG

		TTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCACCG CTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCCCGT GACCGTGTCCTGGAACAGCGGAGCCCTGACCTCCGGAGTGCA CACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTCGCTG TCGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTACCAAGA CCTACACTTGCAACGTGGACCACAAGCCTTCCAACACTAAGGT GGACAAGCGCGTCGAATCGAAGTACGGCCCACCGTGCCCGCC TTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTTCTGT TCCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCACCCC TGAAGTGACATGCGTGGTCGTGGACGTGTCACAGGAAGATCC GGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGCA CAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCGTGTCCGTGCTGACGGTGCTGCATCAGGACTGG CTGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGA CTTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGA CAGCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAG GAAGAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGA AGGGCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAA CGGCCAGCCGGAAAACAACTACAAGACCACCCCTCCGGTGCT GGACTCAGACGGATCCTTCTTCCTCTACTCGCGGCTGACCGTG GATAAGAGCAGATGGCAGGAGGGAAATGTGTTCAGCTGTTCT GTGATGCATGAAGCCCTGCACAACCACTACACTCAGAAGTCCC TGTCCCTCTCCCTGGGA
BAP058-Clone N LC		
SEQ ID NO: 609 (Kabat)	LCDR1	KASQDVGTAVA
SEQ ID NO: 610 (Kabat)	LCDR2	WASTRHT
SEQ ID NO: 611(Kabat)	LCDR3	QQYNSYPLT
SEQ ID NO: 612 (Chothia)	LCDR1	SQDVGTA
SEQ ID NO: 613 (Chothia)	LCDR2	WAS
SEQ ID NO: 614 (Chothia)	LCDR3	YNSYPL
SEQ ID NO: 624	VL	DVVMTQSPLSLPVTLGQPASISCKASQDVGTAVAWYQQKPGQAP RLLIYWASTRHTGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ YNSYPLTFGQGTKVEIK
SEQ ID NO: 625	DNA VL	GACGTCGTGATGACTCAGTCACCCCTGAGCCTGCCCGTGACCC TGGGGCAGCCCGCCTCTATTAGCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCAGCAGAAGCCAGGGCAAGC CCCTAGACTGCTGATCTACTGGGCCTCTACTAGACACACCGGC GTGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCA CCCTGACTATCTCTTCACTGCAGCCCGACGACTTCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAG
SEQ ID NO: 626	Light chain	DVVMTQSPLSLPVTLGQPASISCKASQDVGTAVAWYQQKPGQAP RLLIYWASTRHTGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ YNSYPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 627	DNA light chain	GACGTCGTGATGACTCAGTCACCCCTGAGCCTGCCCGTGACCC TGGGGCAGCCCGCCTCTATTAGCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCAGCAGAAGCCAGGGCAAGC CCCTAGACTGCTGATCTACTGGGCCTCTACTAGACACACCGGC GTGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCA CCCTGACTATCTCTTCACTGCAGCCCGACGACTTCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAGCGTACGGTGGCCGCTCCCAGCGT GTTCATCTTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACC

		GCCAGCGTGGTGTGCCTGCTGAACAACTTCTACCCCCGGGAGG CCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCA ACAGCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCA CCTACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACT ACGAGAAGCATAAGGTGTACGCCTGCGAGGTGACCCACCAGG GCCTGTCCAGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGT GC
BAP058-Clone O HC		
SEQ ID NO: 628 (Kabat)	HCDR1	agctactggatgtac
SEQ ID NO: 629 (Kabat)	HCDR2	agaatcgaccctaatagcggctctactaagtataacgagaagtttaagaat
SEQ ID NO: 630 (Kabat)	HCDR3	gactatagaaagggcctgtacgctatggactac
SEQ ID NO: 631 (Chothia)	HCDR1	ggctacaccttcactagctac
SEQ ID NO: 632 (Chothia)	HCDR2	gaccctaatagcggctct
SEQ ID NO: 630 (Chothia)	HCDR3	gactatagaaagggcctgtacgctatggactac
BAP058-Clone O LC		
SEQ ID NO: 633 (Kabat)	LCDR1	aaagcctctcaggacgtgggcaccgccgtggcc
SEQ ID NO: 634 (Kabat)	LCDR2	tgggcctctactagacacacc
SEQ ID NO: 635 (Kabat)	LCDR3	cagcagtataatagctacccccctgacc
SEQ ID NO: 636 (Chothia)	LCDR1	tctcaggacgtgggcaccgcc
SEQ ID NO: 637 (Chothia)	LCDR2	tgggcctct
SEQ ID NO: 638 (Chothia)	LCDR3	tataatagctacccccctg
BAP058-Clone N HC		
SEQ ID NO: 628 (Kabat)	HCDR1	agctactggatgtac
SEQ ID NO: 629 (Kabat)	HCDR2	agaatcgaccctaatagcggctctactaagtataacgagaagtttaagaat
SEQ ID NO: 630 (Kabat)	HCDR3	gactatagaaagggcctgtacgctatggactac
SEQ ID NO: 631 (Chothia)	HCDR1	ggctacaccttcactagctac
SEQ ID NO: 632 (Chothia)	HCDR2	gaccctaatagcggctct
SEQ ID NO: 630 (Chothia)	HCDR3	gactatagaaagggcctgtacgctatggactac
BAP058-Clone N LC		
SEQ ID NO: 633 (Kabat)	LCDR1	aaagcctctcaggacgtgggcaccgccgtggcc
SEQ ID NO: 634 (Kabat)	LCDR2	tgggcctctactagacacacc
SEQ ID NO: 635 (Kabat)	LCDR3	cagcagtataatagctacccccctgacc
SEQ ID NO: 636 (Chothia)	LCDR1	tctcaggacgtgggcaccgcc
SEQ ID NO: 637 (Chothia)	LCDR2	tgggcctct
SEQ ID NO: 638 (Chothia)	LCDR3	tataatagctacccccctg

Other Exemplary PD-L1 Inhibitors

[0479] In one embodiment, the anti-PD-L1 antibody molecule is Atezolizumab (Genentech/Roche), also known as MPDL3280A, RG7446, RO5541267, YW243.55.S70, or TECENTRIQ™. Atezolizumab and other anti-PD-L1 antibodies are disclosed in US 8,217,149, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Atezolizumab, *e.g.*, as disclosed in Table 6.

[0480] In one embodiment, the anti-PD-L1 antibody molecule is Avelumab (Merck Serono and Pfizer), also known as MSB0010718C or Bavencio®. Avelumab and other anti-PD-L1 antibodies are disclosed in WO 2013/079174, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Avelumab, *e.g.*, as disclosed in Table 6.

[0481] In one embodiment, the anti-PD-L1 antibody molecule is Durvalumab (MedImmune/AstraZeneca), also known as MEDI4736 or Imfinzi®. Durvalumab and other anti-PD-L1 antibodies are disclosed in US 8,779,108, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Durvalumab, *e.g.*, as disclosed in Table 6.

[0482] In one embodiment, the anti-PD-L1 antibody molecule is BMS-936559 (Bristol-Myers Squibb), also known as MDX-1105 or 12A4. BMS-936559 and other anti-PD-L1 antibodies are disclosed in US 7,943,743 and WO 2015/081158, incorporated by reference in their entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-936559, *e.g.*, as disclosed in Table 6.

[0483] Further known anti-PD-L1 antibodies include those described, *e.g.*, in WO 2015/181342, WO 2014/100079, WO 2016/000619, WO 2014/022758, WO 2014/055897, WO 2015/061668, WO 2013/079174, WO 2012/145493, WO 2015/112805, WO 2015/109124, WO 2015/195163, US 8,168,179, US 8,552,154, US 8,460,927, and US 9,175,082, incorporated by reference in their entirety.

[0484] In one embodiment, the anti-PD-L1 antibody is an antibody that competes for binding with, and/or binds to the same epitope on PD-L1 as, one of the anti-PD-L1 antibodies described herein.

Table 6. Amino acid sequences of other exemplary anti-PD-L1 antibody molecules

Atezolizumab		
SEQ ID NO: 639	Heavy chain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWVRQAPGKGLEWVAWI SPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWP GGFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKP SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 640	Light chain	DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASF LYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYLYHPATFGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
Avelumab		
SEQ ID NO: 641	Heavy chain	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYIMMWVRQAPGKGLEWVSSIY PSGGITFYADTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARIKLGTV TTVDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKP SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 642	Light chain	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYD VSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTRVFGTGT KVTVLGQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGS PVKAGVETTKPSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKT VAPTECS
Durvalumab		
SEQ ID NO: 643	Heavy chain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSRYWMSWVRQAPGKGLEWVANI KQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGG WFGELAFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEFEGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSK LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 644	Light chain	EIVLTQSPGTLSLSPGERATLSCRASQRVSSSYLAWYQQKPGQAPRLLIYDAS SRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSLPWTFGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

		SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
BMS-936559		
SEQ ID NO: 645	VH	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTYAISWVRQAPGQGLEWMGGII PIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSG SPFGMDVWGQGTTVTVSS
SEQ ID NO: 646	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASN RATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPTFGQGTKVEIK

[0485] In one embodiment the anti-human ENTPD2 antibody as described herein is administered in combination with at least one PD-L1 inhibitor as described herein and at least one A2A receptor antagonist as described herein.

LAG-3 Inhibitors

[0486] In certain embodiments, the anti-human ENTPD2 antibody described herein is administered in combination with a LAG-3 inhibitor. The LAG-3 inhibitor may be an antibody, an antigen-binding fragment thereof, an immunoadhesin, a fusion protein, or oligopeptide. In some embodiments, the LAG-3 inhibitor is chosen from LAG525 (Novartis), BMS-986016 (Bristol-Myers Squibb), TSR-033 (Tesaro), MK-4280 (Merck & Co), or REGN3767 (Regeneron).

Exemplary LAG-3 Inhibitors

[0487] In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule. In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule as disclosed in US 2015/0259420, published on September 17, 2015, entitled "Antibody Molecules to LAG-3 and Uses Thereof," incorporated by reference in its entirety.

[0488] In one embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 7 (*e.g.*, from the heavy and light chain variable region sequences of BAP050-Clone I or BAP050-Clone J disclosed in Table 7), or encoded by a nucleotide sequence shown in Table 7. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 7). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 7). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 7). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1

comprises the amino acid sequence GFTLTNYGMN (SEQ ID NO: 766). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 7, or encoded by a nucleotide sequence shown in Table 7.

[0489] In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 701, a VHCDR2 amino acid sequence of SEQ ID NO: 702, and a VHCDR3 amino acid sequence of SEQ ID NO: 703; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 710, a VLCDR2 amino acid sequence of SEQ ID NO: 711, and a VLCDR3 amino acid sequence of SEQ ID NO: 712, each disclosed in Table 7.

[0490] In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 736 or 737, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 738 or 739, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 740 or 741; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 746 or 747, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 748 or 749, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 750 or 751, each disclosed in Table 7. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 758 or 737, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 759 or 739, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 760 or 741; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 746 or 747, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 748 or 749, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 750 or 751, each disclosed in Table 7.

[0491] In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 706, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 706. In one embodiment, the anti-LAG-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 718, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 718. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 724, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 724. In one embodiment, the anti-LAG-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ

ID NO: 730, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 730. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 706 and a VL comprising the amino acid sequence of SEQ ID NO: 718. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 724 and a VL comprising the amino acid sequence of SEQ ID NO: 730.

[0492] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 707 or 708, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 707 or 708. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 719 or 720, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 719 or 720. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 725 or 726, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 725 or 726. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 731 or 732, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 731 or 732. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 707 or 708 and a VL encoded by the nucleotide sequence of SEQ ID NO: 719 or 720. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 725 or 726 and a VL encoded by the nucleotide sequence of SEQ ID NO: 731 or 732.

[0493] In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 709, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 709. In one embodiment, the anti-LAG-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 721, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 721. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 727, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 727. In one embodiment, the anti-LAG-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 733, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 733. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 709 and a light chain comprising the amino acid sequence of SEQ ID NO:

721. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 727 and a light chain comprising the amino acid sequence of SEQ ID NO: 733.

[0494] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 716 or 717, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 716 or 717. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 722 or 723, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 722 or 723. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 728 or 729, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 728 or 729. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 734 or 735, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 734 or 735. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 716 or 717 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 722 or 723. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 728 or 729 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 734 or 735.

[0495] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0259420, incorporated by reference in its entirety.

Table 7. Amino acid and nucleotide sequences of exemplary anti-LAG-3 antibody molecules

BAP050-Clone I HC		
SEQ ID NO: 701 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 702 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 703 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 704 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 705 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 703 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO:706	VH	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQARGQ RLEWIGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKAE DTAVYYCARNPPYYYGTNNAEAMDYWGQGTTVTVSS

SEQ ID NO: 707	DNA VH	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAAGAAGCCTG GAGCCTCGGTGAAGGTGTCGTGCAAGGCATCCGGATTCACCCT CACCAATTACGGGATGAACTGGGTCAGACAGGCCCGGGGTCAA CGGCTGGAGTGGATCGGATGGATTAACACCGACACCGGGGAGC CTACCTACGCGGACGATTTCAAGGGACGGTTCGTGTTCTCCCTC GACACCTCCGTGTCCACCGCCTACCTCCAAATCTCCTCACTGAA AGCGGAGGACACCGCCGTGTACTATTGCGCGAGGAACCCGCCC TACTACTACGGAACCAACAACGCCGAAGCCATGGACTACTGGG GCCAGGGCACCACTGTGACTGTGTCCAGC
SEQ ID NO: 708	DNA VH	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCCTGCAAGGCCTCTGGCTTCACCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCAGGGGCCAGC GGCTGGAATGGATCGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCACCGTGACCGTGTCCTCT
SEQ ID NO: 709	Heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQARGQ RLEWIGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKAE DTAVYYCARNPPYYYGTNNAEAMDYWGQGTTVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLS LG
SEQ ID NO: 716	DNA heavy chain	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAAGAAGCCTG GAGCCTCGGTGAAGGTGTCGTGCAAGGCATCCGGATTCACCCT CACCAATTACGGGATGAACTGGGTCAGACAGGCCCGGGGTCAA CGGCTGGAGTGGATCGGATGGATTAACACCGACACCGGGGAGC CTACCTACGCGGACGATTTCAAGGGACGGTTCGTGTTCTCCCTC GACACCTCCGTGTCCACCGCCTACCTCCAAATCTCCTCACTGAA AGCGGAGGACACCGCCGTGTACTATTGCGCGAGGAACCCGCCC TACTACTACGGAACCAACAACGCCGAAGCCATGGACTACTGGG GCCAGGGCACCACTGTGACTGTGTCCAGCGCGTCCACTAAGGG CCCGTCCGTGTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCG AATCCACCGCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCG GAGCCCGTGACCGTGTCCTGGAACAGCGGAGCCCTGACCTCCG GAGTGCACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTAC TCGCTGTCGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTAC CAAGACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACT AAGGTGGACAAGCGCGTCGAATCGAAGTACGGCCCACCGTGCC CGCCTTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTT CTGTTCCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCAC CCCTGAAGTGACATGCGTGGTCGTGGACGTGTCACAGGAAGAT CCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGC ACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCGTGTCCGTGCTGACGGTGCTGCATCAGGACTGGC TGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGAC

		TTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGACA GCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAGGAA GAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGAAGG GCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAACGG CCAGCCGGAAAACAACTACAAGACCACCCCTCCGGTGCTGGAC TCAGACGGATCCTTCTTCCTCTACTCGCGGCTGACCGTGGATAA GAGCAGATGGCAGGAGGGAAATGTGTTCAGCTGTTCTGTGATG CATGAAGCCCTGCACAACCACTACACTCAGAAGTCCCTGTCCCT CTCCCTGGGA
SEQ ID NO: 717	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCCTGCAAGGCCTCTGGCTTCACCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCAGGGGCCAGC GGCTGGAATGGATCGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCACCGTGACCGTGTCCTCTGCTTCTACCAAGGGGC CCAGCGTGTTCCCCCTGGCCCCCTGCTCCAGAAGCACCAGCGA GAGCACAGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCC GAGCCCGTGACCGTGTCCTGGAACAGCGGAGCCCTGACCAGCG GCGTGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCTGTA CAGCCTGAGCAGCGTGGTGACCGTGCCCAGCAGCAGCCTGGGC ACCAAGACCTACACCTGTAACGTGGACCACAAGCCCAGCAACA CCAAGGTGGACAAGAGGGTGGAGAGCAAGTACGGCCCACCCT GCCCCCCCTGCCCAGCCCCCGAGTTCCTGGGCGGACCCAGCGT GTTCCTGTTCCCCCCCAAGCCCAAGGACACCCTGATGATCAGCA GAACCCCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGA GGACCCCGAGGTCCAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCCAGAGAGGAGCAGTTTAACA GCACCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGA CTGGCTGAACGGCAAAGAGTACAAGTGTAAGGTCTCCAACAAG GGCCTGCCAAGCAGCATCGAAAAGACCATCAGCAAGGCCAAG GGCCAGCCTAGAGAGCCCCAGGTCTACACCCTGCCACCCAGCC AAGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGTCTGGT GAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGC AACGGCCAGCCCGAGAACAACTACAAGACCACCCCCCCAGTGC TGGACAGCGACGGCAGCTTCTTCCTGTACAGCAGGCTGACCGT GGACAAGTCCAGATGGCAGGAGGGCAACGTCTTTAGCTGCTCC GTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCC TGAGCCTGTCCCTGGGC
BAP050-Clone I LC		
SEQ ID NO: 710 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 711 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 712 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 713 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 714 (Chothia)	LCDR2	YTS
SEQ ID NO: 715 (Chothia)	LCDR3	YYNLPW

SEQ ID NO: 718	VL	DIQMTQSPSSLSASVGDRVTITCSSSQDISNYLNWYLQKPGQSPQL LIYYTSTLHLGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYYN LPWTFGQGTKVEIK
SEQ ID NO: 719	DNA VL	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCTGCAGAAGCCCGGTCAATCACCT CAGCTGCTGATCTACTACACTAGCACCCTGCACCTGGGCGTGCC CTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCACCCTGA CTATCTCTAGCCTGCAGCCCGACGACTTCGCTACCTACTACTGT CAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAG
SEQ ID NO: 720	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCTGCAGAAGCCCGGCCAGTCCCC TCAGCTGCTGATCTACTACACCTCCACCCTGCACCTGGGCGTGC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAGTTTACCCTG ACCATCAGCTCCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCACC AAGGTGGAAATCAAG
SEQ ID NO: 721	Light chain	DIQMTQSPSSLSASVGDRVTITCSSSQDISNYLNWYLQKPGQSPQL LIYYTSTLHLGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYYN LPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNF YPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 722	DNA light chain	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCTGCAGAAGCCCGGTCAATCACCT CAGCTGCTGATCTACTACACTAGCACCCTGCACCTGGGCGTGCC CTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCACCCTGA CTATCTCTAGCCTGCAGCCCGACGACTTCGCTACCTACTACTGT CAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAGCGTACGGTGGCCGCTCCCAGCGTGTTCAT CTTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGC GTGGTGTGCCTGCTGAACAACTTCTACCCCCGGGAGGCCAAGG TGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCA GGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACAGC CTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGC ATAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAG CCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
SEQ ID NO: 723	DNA light chain	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCTGCAGAAGCCCGGCCAGTCCCC TCAGCTGCTGATCTACTACACCTCCACCCTGCACCTGGGCGTGC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAGTTTACCCTG ACCATCAGCTCCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCACC AAGGTGGAAATCAAGCGTACGGTGGCCGCTCCCAGCGTGTTCA TCTTCCCCCCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAG CGTGGTGTGTCTGCTGAACAACTTCTACCCCAGGGAGGCCAAG GTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCC AGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACA GCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAA

		GCACAAGGTGTACGCCTGTGAGGTGACCCACCAGGGCCTGTCC AGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
BAP050-Clone J HC		
SEQ ID NO: 701 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 702 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 703 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 704 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 705 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 703 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 724	VH	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQAPGQ GLEWMGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKA EDTAVYYCARNPPYYYGTNNAEAMDYWGQGTTVTVSS
SEQ ID NO: 725	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCCG GCGCTAGTGTGAAAGTCAGCTGTAAAGCTAGTGGCTTCACCCT GACTAACTACGGGATGAACTGGGTCCGCCAGGCCCCAGGTCAA GGCCTCGAGTGGATGGGCTGGATTAACACCGACACCGGCGAGC CTACCTACGCCGACGACTTTAAGGGCAGATTCGTGTTTAGCCTG GACACTAGTGTGTCTACCGCCTACCTGCAGATCTCTAGCCTGAA GGCCGAGGACACCGCCGTCTACTACTGCGCTAGAAACCCCCCC TACTACTACGGCACTAACAACGCCGAGGCTATGGACTACTGGG GTCAAGGCACTACCGTGACCGTGTCTAGC
SEQ ID NO: 726	DNA VH	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCCTGCAAGGCCTCTGGCTTCACCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCCCTGGACAGG GCCTGGAATGGATGGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCACCGTGACCGTGTCCTCT
SEQ ID NO: 727	Heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQAPGQ GLEWMGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKA EDTAVYYCARNPPYYYGTNNAEAMDYWGQGTTVTVSSASTKGP SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLS LG
SEQ ID NO: 728	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCCG GCGCTAGTGTGAAAGTCAGCTGTAAAGCTAGTGGCTTCACCCT GACTAACTACGGGATGAACTGGGTCCGCCAGGCCCCAGGTCAA GGCCTCGAGTGGATGGGCTGGATTAACACCGACACCGGCGAGC CTACCTACGCCGACGACTTTAAGGGCAGATTCGTGTTTAGCCTG GACACTAGTGTGTCTACCGCCTACCTGCAGATCTCTAGCCTGAA GGCCGAGGACACCGCCGTCTACTACTGCGCTAGAAACCCCCCC

		TACTACTACGGCACTAACAACGCCGAGGCTATGGACTACTGGG GTCAAGGCACTACCGTGACCGTGTCTAGCGCTAGCACTAAGGG CCCGTCCGTGTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCG AATCCACCGCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCG GAGCCCGTGACCGTGTCCTGGAACAGCGGAGCCCTGACCTCCG GAGTGCACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTAC TCGCTGTCGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTAC CAAGACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACT AAGGTGGACAAGCGCGTCGAATCGAAGTACGGCCCACCGTGCC CGCCTTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTT CTGTTCCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCAC CCCTGAAGTGACATGCGTGGTCGTGGACGTGTCACAGGAAGAT CCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGC ACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCGTGTCCGTGCTGACGGTGCTGCATCAGGACTGGC TGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGAC TTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGACA GCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAGGAA GAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGAAGG GCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAACGG CCAGCCGGAAAACAACTACAAGACCACCCCTCCGGTGCTGGAC TCAGACGGATCCTTCTTCCTCTACTCGCGGCTGACCGTGGATAA GAGCAGATGGCAGGAGGGAAATGTGTTCAGCTGTTCTGTGATG CATGAAGCCCTGCACAACCACTACACTCAGAAGTCCCTGTCCCT CTCCCTGGGA
SEQ ID NO: 729	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCCTGCAAGGCCTCTGGCTTCACCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCCCTGGACAGG GCCTGGAATGGATGGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCACCGTGACCGTGTCCTCTGCTTCTACCAAGGGGC CCAGCGTGTTCCCCCTGGCCCCCTGCTCCAGAAGCACCAGCGA GAGCACAGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCC GAGCCCGTGACCGTGTCCTGGAACAGCGGAGCCCTGACCAGCG GCGTGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCTGTA CAGCCTGAGCAGCGTGGTGACCGTGCCCAGCAGCAGCCTGGGC ACCAAGACCTACACCTGTAACGTGGACCACAAGCCCAGCAACA CCAAGGTGGACAAGAGGGTGGAGAGCAAGTACGGCCCACCCT GCCCCCCCTGCCCAGCCCCCGAGTTCCTGGGCGGACCCAGCGT GTTCCTGTTCCCCCCCAAGCCCAAGGACACCCTGATGATCAGCA GAACCCCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGA GGACCCCGAGGTCCAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCCAGAGAGGAGCAGTTTAACA GCACCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGA CTGGCTGAACGGCAAAGAGTACAAGTGTAAGGTCTCCAACAAG GGCCTGCCAAGCAGCATCGAAAAGACCATCAGCAAGGCCAAG GGCCAGCCTAGAGAGCCCCAGGTCTACACCCTGCCACCCAGCC AAGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGTCTGGT GAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGC

		AACGGCCAGCCCGAGAACAACTACAAGACCACCCCCCCAGTGC TGGACAGCGACGGCAGCTTCTTCCTGTACAGCAGGCTGACCGT GGACAAGTCCAGATGGCAGGAGGGCAACGTCTTTAGCTGCTCC GTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCC TGAGCCTGTCCCTGGGC
BAP050-Clone J LC		
SEQ ID NO: 710 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 711 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 712 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 713 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 714 (Chothia)	LCDR2	YTS
SEQ ID NO: 715 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 730	VL	DIQMTQSPSSLSASVGDRVTITCSSSQDISNYLNWYQQKPGKAPKL LIYYTSTLHLGIPPRFSGSGYGTDFTLTINNIESEDAAYYFCQQYYN LPWTFGQGTKVEIK
SEQ ID NO: 731	DNA VL	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCAGCAGAAGCCCGGTAAAGCCCC TAAGCTGCTGATCTACTACACTAGCACCCTGCACCTGGGAATCC CCCCTAGGTTTAGCGGTAGCGGCTACGGCACCGACTTCACCCTG ACTATTAACAATATCGAGTCAGAGGACGCCGCCTACTACTTCTG TCAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAG
SEQ ID NO: 732	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCAGCAGAAGCCCGGCAAGGCCC CCAAGCTGCTGATCTACTACACCTCCACCCTGCACCTGGGCATC CCCCCTAGATTCTCCGGCTCTGGCTACGGCACCGACTTCACCCT GACCATCAACAACATCGAGTCCGAGGACGCCGCCTACTACTTC TGCCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCA CCAAGGTGGAAATCAAG
SEQ ID NO: 733	Light chain	DIQMTQSPSSLSASVGDRVTITCSSSQDISNYLNWYQQKPGKAPKL LIYYTSTLHLGIPPRFSGSGYGTDFTLTINNIESEDAAYYFCQQYYN LPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNF YPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 734	DNA light chain	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCAGCAGAAGCCCGGTAAAGCCCC TAAGCTGCTGATCTACTACACTAGCACCCTGCACCTGGGAATCC CCCCTAGGTTTAGCGGTAGCGGCTACGGCACCGACTTCACCCTG ACTATTAACAATATCGAGTCAGAGGACGCCGCCTACTACTTCTG TCAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAGCGTACGGTGGCCGCTCCCAGCGTGTTCAT CTTCCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGC GTGGTGTGCCTGCTGAACAACTTCTACCCCCGGGAGGCCAAGG TGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCA GGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACAGC

		CTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAGAAGC ATAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAG CCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
SEQ ID NO: 735	DNA light chain	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCAGCAGAAGCCCGGCAAGGCCC CCAAGCTGCTGATCTACTACACCTCCACCCTGCACCTGGGCATC CCCCCTAGATTCTCCGGCTCTGGCTACGGCACCGACTTCACCCT GACCATCAACAACATCGAGTCCGAGGACGCCGCCTACTACTTC TGCCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCA CCAAGGTGGAAATCAAGCGTACGGTGGCCGCTCCCAGCGTGTT CATCTTCCCCCCAAGCGACGAGCAGCTGAAGAGCGGCACCGCC AGCGTGGTGTGTCTGCTGAACAACTTCTACCCCAGGGAGGCCA AGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACA GCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTA CAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACTACGAG AAGCACAAGGTGTACGCCTGTGAGGTGACCCACCAGGGCCTGT CCAGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
BAP050-Clone I HC		
SEQ ID NO: 736 (Kabat)	HCDR1	AATTACGGGATGAAC
SEQ ID NO: 737 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 738 (Kabat)	HCDR2	TGGATTAACACCGACACCGGGGAGCCTACCTACGCGGACGATT TCAAGGGA
SEQ ID NO: 739 (Kabat)	HCDR2	TGGATCAACACCGACACCGGCGAGCCTACCTACGCCGACGACT TCAAGGGC
SEQ ID NO: 740 (Kabat)	HCDR3	AACCCGCCCTACTACTACGGAACCAACAACGCCGAAGCCATGG ACTAC
SEQ ID NO: 741 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGG ACTAT
SEQ ID NO: 742 (Chothia)	HCDR1	GGATTCACCCTCACCAATTAC
SEQ ID NO: 743 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 744 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 745 (Chothia)	HCDR2	AACACCGACACCGGCGAG
SEQ ID NO: 740 (Chothia)	HCDR3	AACCCGCCCTACTACTACGGAACCAACAACGCCGAAGCCATGG ACTAC
SEQ ID NO: 741 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGG ACTAT
BAP050-Clone I LC		
SEQ ID NO: 746 (Kabat)	LCDR1	AGCTCTAGTCAGGATATCTCTAACTACCTGAAC
SEQ ID NO: 747 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACTACCTGAAC
SEQ ID NO: 748 (Kabat)	LCDR2	TACACTAGCACCCTGCACCTG
SEQ ID NO: 749 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 750 (Kabat)	LCDR3	CAGCAGTACTATAACCTGCCCTGGACC
SEQ ID NO: 751 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 752 (Chothia)	LCDR1	AGTCAGGATATCTCTAACTAC

SEQ ID NO: 753 (Chothia)	LCDR1	AGCCAGGACATCTCCAACTAC
SEQ ID NO: 754 (Chothia)	LCDR2	TACACTAGC
SEQ ID NO: 755 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 756 (Chothia)	LCDR3	TACTATAACCTGCCCTGG
SEQ ID NO: 757 (Chothia)	LCDR3	TACTACAACCTGCCCTGG
BAP050-Clone J HC		
SEQ ID NO: 758 (Kabat)	HCDR1	AACTACGGGATGAAC
SEQ ID NO: 737 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 759 (Kabat)	HCDR2	TGGATTAACACCGACACCGGCGAGCCTACCTACGCCGACGACTTTAAGGGC
SEQ ID NO: 739 (Kabat)	HCDR2	TGGATCAACACCGACACCGGCGAGCCTACCTACGCCGACGACTTCAAGGGC
SEQ ID NO: 760 (Kabat)	HCDR3	AACCCCCCCTACTACTACGGCACTAACAACGCCGAGGCTATGGACTAC
SEQ ID NO: 741 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGGACTAT
SEQ ID NO: 761 (Chothia)	HCDR1	GGCTTCACCCTGACTAACTAC
SEQ ID NO: 743 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 744 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 745 (Chothia)	HCDR2	AACACCGACACCGGCGAG
SEQ ID NO: 760 (Chothia)	HCDR3	AACCCCCCCTACTACTACGGCACTAACAACGCCGAGGCTATGGACTAC
SEQ ID NO: 741 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGGACTAT
BAP050-Clone J LC		
SEQ ID NO: 746 (Kabat)	LCDR1	AGCTCTAGTCAGGATATCTCTAACTACCTGAAC
SEQ ID NO: 747 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACTACCTGAAC
SEQ ID NO: 748 (Kabat)	LCDR2	TACACTAGCACCCTGCACCTG
SEQ ID NO: 749 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 750 (Kabat)	LCDR3	CAGCAGTACTATAACCTGCCCTGGACC
SEQ ID NO: 751 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 752 (Chothia)	LCDR1	AGTCAGGATATCTCTAACTAC
SEQ ID NO: 753 (Chothia)	LCDR1	AGCCAGGACATCTCCAACTAC
SEQ ID NO: 754 (Chothia)	LCDR2	TACACTAGC
SEQ ID NO: 755 (Chothia)	LCDR2	TACACCTCC

SEQ ID NO: 756 (Chothia)	LCDR3	TACTATAACCTGCCCTGG
SEQ ID NO: 757 (Chothia)	LCDR3	TACTACAACCTGCCCTGG

Other Exemplary LAG-3 Inhibitors

[0496] In one embodiment, the anti-LAG-3 antibody molecule is BMS-986016 (Bristol-Myers Squibb), also known as BMS986016. BMS-986016 and other anti-LAG-3 antibodies are disclosed in WO 2015/116539 and US 9,505,839, incorporated by reference in their entirety. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-986016, *e.g.*, as disclosed in Table 8.

[0497] In one embodiment, the anti-LAG-3 antibody molecule is TSR-033 (Tesaro). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-033.

[0498] In one embodiment, the anti-LAG-3 antibody molecule is MK-4280 (Merck & Co). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MK-4280.

[0499] In one embodiment, the anti-LAG-3 antibody molecule is REGN3767 (Regeneron). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of REGN3767.

[0500] In one embodiment, the anti-LAG-3 antibody molecule is IMP731 or GSK2831781 (GSK and Prima BioMed). IMP731 and other anti-LAG-3 antibodies are disclosed in WO 2008/132601 and US 9,244,059, incorporated by reference in their entirety. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of IMP731, *e.g.*, as disclosed in Table 8. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of GSK2831781.

[0501] In one embodiment, the anti-LAG-3 antibody molecule is IMP761 (Prima BioMed). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of IMP761.

[0502] Further known anti-LAG-3 antibodies include those described, *e.g.*, in WO 2008/132601, WO 2010/019570, WO 2014/140180, WO 2015/116539, WO 2015/200119, WO 2016/028672, US 9,244,059, US 9,505,839, incorporated by reference in their entirety.

[0503] In one embodiment, the anti-LAG-3 antibody is an antibody that competes for binding with, and/or binds to the same epitope on LAG-3 as, one of the anti-LAG-3 antibodies described herein.

[0504] In one embodiment, the anti-LAG-3 inhibitor is a soluble LAG-3 protein, *e.g.*, IMP321 (Prima BioMed), *e.g.*, as disclosed in WO 2009/044273, incorporated by reference in its entirety.

Table 8. Amino acid sequences of other exemplary anti-LAG-3 antibody molecules

BMS-986016		
SEQ ID NO: 762	Heavy chain	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSDYYWNWIRQPPGKGLE WIGEINHRGSTNSNPSLKSRVTLSLDTSKNQFSLKLRSVTAADTAVYYC AFGYSDYEYNWFDPWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV PSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA KTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKT ISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHE ALHNHYTQKSLSLSLGK
SEQ ID NO: 763	Light chain	EIVLTQSPATLSLSPGERATLSCRASQSISSYLAWYQQKPGQAPRLLIYD ASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPLTFG QGTNLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC
IMP731		
SEQ ID NO: 764	Heavy chain	QVQLKESGPGLVAPSQSLSITCTVSGFSLTAYGVNWVRQPPGKGLEWL GMIWDDGSTDYNSALKSRLSISKDNSKSQVFLKMNSLQTDDTARYYC AREGDVAFDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK

SEQ ID NO: 765	Light chain	DIVMTQSPSSLAVSVGQKVTMSCKSSQSLLNGSNQKNYLAWYQQKPG QSPKLLVYFASTRDSGVPDRFIGSGSGTDFTLTISSVQAEDLADYFCLQ HFGTPPTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC

TIM-3 Inhibitors

[0505] In certain embodiments, the anti-human ENTPD2 antibody as described herein is administered in combination with a TIM-3 inhibitor. The TIM-3 inhibitor may be an antibody, an antigen-binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the TIM-3 inhibitor is chosen from MBG453 (Novartis), TSR-022 (Tesaro) or LY3321367 (Eli Lilly).

Exemplary TIM-3 Inhibitors

[0506] In one embodiment, the TIM-3 inhibitor is an anti-TIM-3 antibody molecule. In one embodiment, the TIM-3 inhibitor is an anti-TIM-3 antibody molecule as disclosed in US 2015/0218274, published on August 6, 2015, entitled "Antibody Molecules to TIM-3 and Uses Thereof," incorporated by reference in its entirety.

[0507] In one embodiment, the anti-TIM-3 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 9 (*e.g.*, from the heavy and light chain variable region sequences of ABTIM3-hum11 or ABTIM3-hum03 disclosed in Table 9), or encoded by a nucleotide sequence shown in Table 9. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 9). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 9). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 9, or encoded by a nucleotide sequence shown in Table 9.

[0508] In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 801, a VHCDR2 amino acid sequence of SEQ ID NO: 802, and a VHCDR3 amino acid sequence of SEQ ID NO: 803; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 810, a VLCDR2 amino acid sequence of SEQ ID NO: 811,

and a VLCDR3 amino acid sequence of SEQ ID NO: 812, each disclosed in Table 9. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 801, a VHCDR2 amino acid sequence of SEQ ID NO: 820, and a VHCDR3 amino acid sequence of SEQ ID NO: 803; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 810, a VLCDR2 amino acid sequence of SEQ ID NO: 811, and a VLCDR3 amino acid sequence of SEQ ID NO: 812, each disclosed in Table 9.

[0509] In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 806, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 806. In one embodiment, the anti-TIM-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 816, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 816. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 822, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 822. In one embodiment, the anti-TIM-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 826, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 826. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 806 and a VL comprising the amino acid sequence of SEQ ID NO: 816. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 822 and a VL comprising the amino acid sequence of SEQ ID NO: 826.

[0510] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 807, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 807. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 817, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 817. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 823, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 823. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 827, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 827. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 807 and a VL encoded by the nucleotide sequence of SEQ ID NO: 817. In one embodiment, the

antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 823 and a VL encoded by the nucleotide sequence of SEQ ID NO: 827.

[0511] In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 808, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 808. In one embodiment, the anti-TIM-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 818, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 818. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 824, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 824. In one embodiment, the anti-TIM-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 828, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 828. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 808 and a light chain comprising the amino acid sequence of SEQ ID NO: 818. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 824 and a light chain comprising the amino acid sequence of SEQ ID NO: 828.

[0512] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 809, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 809. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 819, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 819. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 825, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 825. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 829, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 829. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 809 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 819. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 825 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 829.

[0513] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0218274, incorporated by reference in its entirety.

Table 9. Amino acid and nucleotide sequences of exemplary anti-TIM-3 antibody molecules

ABTIM3-hum11		
SEQ ID NO: 801 (Kabat)	HCDR1	SYNMH
SEQ ID NO: 802 (Kabat)	HCDR2	DIYPGNGDTSYNQKFKG
SEQ ID NO: 803 (Kabat)	HCDR3	VGGAFPMDY
SEQ ID NO: 804 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 805 (Chothia)	HCDR2	YPGNGD
SEQ ID NO: 803 (Chothia)	HCDR3	VGGAFPMDY
SEQ ID NO: 806	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAPG QGLEWMGDIYPGNGDTSYNQKFKGRVTITADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMDYWGQGTTVTVSS
SEQ ID NO: 807	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCTCTAGCGTGAAAGTTTCTTGTAAAGCTAGTGGCTACAC CTTCACTAGCTATAATATGCACTGGGTTCGCCAGGCCCCAGG GCAAGGCCTCGAGTGGATGGGCGATATCTACCCCGGGAACGG CGACACTAGTTATAATCAGAAGTTTAAGGGTAGAGTCACTAT CACCGCCGATAAGTCTACTAGCACCGTCTATATGGAACTGAG TTCCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAG AGTGGGCGGAGCCTTCCCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTAGC
SEQ ID NO: 808	Heavy chain	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAPG QGLEWMGDIYPGNGDTSYNQKFKGRVTITADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMDYWGQGTTVTVSSASTKGPSVFP LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLG
SEQ ID NO: 809	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCTCTAGCGTGAAAGTTTCTTGTAAAGCTAGTGGCTACAC CTTCACTAGCTATAATATGCACTGGGTTCGCCAGGCCCCAGG GCAAGGCCTCGAGTGGATGGGCGATATCTACCCCGGGAACGG CGACACTAGTTATAATCAGAAGTTTAAGGGTAGAGTCACTAT CACCGCCGATAAGTCTACTAGCACCGTCTATATGGAACTGAG TTCCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAG AGTGGGCGGAGCCTTCCCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTAGCGCTAGCACTAAGGGCCCGTCCGT GTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCAC CGCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCC CGTGACCGTGTCCTGGAACAGCGGAGCCCTGACCTCCGGAGT GCACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTC GCTGTCGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTACC AAGACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACT AAGGTGGACAAGCGCGTCGAATCGAAGTACGGCCCACCGTG CCCGCCTTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTC TTTCTGTTCCCACCGAAGCCCAAGGACACTTTGATGATTTCCC GCACCCCTGAAGTGACATGCGTGGTCGTGGACGTGTCACAGG AAGATCCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCG AGGTGCACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTC

		AACTCCACTTACCGCGTCGTGTCCGTGCTGACGGTGCTGCATC AGGACTGGCTGAACGGGAAGGAGTACAAGTGCAAAGTGTCC AACAAGGGACTTCCTAGCTCAATCGAAAAGACCATCTCGAAA GCCAAGGGACAGCCCCGGGAACCCCAAGTGTATACCCTGCCA CCGAGCCAGGAAGAAATGACTAAGAACCAAGTCTCATTGACT TGCCTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGGAA TGGGAGTCCAACGGCCAGCCGGAAAACAACTACAAGACCAC CCCTCCGGTGCTGGACTCAGACGGATCCTTCTTCCTCTACTCG CGGCTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGT GTTCAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTA CACTCAGAAGTCCCTGTCCCTCTCCCTGGGA
SEQ ID NO: 810 (Kabat)	LCDR1	RASESVEYYGTSLMQ
SEQ ID NO: 811 (Kabat)	LCDR2	AASNVES
SEQ ID NO: 812 (Kabat)	LCDR3	QQSRKDPST
SEQ ID NO: 813 (Chothia)	LCDR1	SESVEYYGTSL
SEQ ID NO: 814 (Chothia)	LCDR2	AAS
SEQ ID NO: 815 (Chothia)	LCDR3	SRKDPS
SEQ ID NO: 816	VL	AIQLTQSPSSLSASVGDRVTITCRASESVEYYGTSLMQWYQQKP GKAPKLLIYAASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATY FCQQSRKDPSTFGGGTKVEIK
SEQ ID NO: 817	DNA VL	GCTATTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGT GTGGGCGATAGAGTGACTATCACCTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCGGGAAAGCCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATCTCTAGCCTGCAGCCC GAGGACTTCGCTACCTACTTCTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGGCGGAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 818	Light chain	AIQLTQSPSSLSASVGDRVTITCRASESVEYYGTSLMQWYQQKP GKAPKLLIYAASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATY FCQQSRKDPSTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 819	DNA light chain	GCTATTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGT GTGGGCGATAGAGTGACTATCACCTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCGGGAAAGCCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATCTCTAGCCTGCAGCCC GAGGACTTCGCTACCTACTTCTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGGCGGAGGCACTAAGGTCGAGATTAAGCGT ACGGTGGCCGCTCCCAGCGTGTTCATCTTCCCCCCCAGCGAC GAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTG AACAACTTCTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTG GACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCA CCCTGACCCTGAGCAAGGCCGACTACGAGAAGCATAAGGTGT ACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGTGA CCAAGAGCTTCAACAGGGGCGAGTGC
ABTIM3-hum03		
SEQ ID NO: 801 (Kabat)	HCDR1	SYNMH
SEQ ID NO: 820 (Kabat)	HCDR2	DIYPGQGDTSYNQKFKG
SEQ ID NO: 803 (Kabat)	HCDR3	VGGAFPMDY
SEQ ID NO: 804 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 821 (Chothia)	HCDR2	YPGQGD
SEQ ID NO: 803 (Chothia)	HCDR3	VGGAFPMDY
SEQ ID NO: 822	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPG QGLEWIGDIYPGQGDTSYNQKFKGRATMTADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMDYWGQGTLVTVSS

SEQ ID NO: 823	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCGCTAGTGTGAAAGTTAGCTGTAAAGCTAGTGGCTATAC TTTCACTTCTTATAATATGCACTGGGTCCGCCAGGCCCCAGGT CAAGGCCTCGAGTGGATCGGCGATATCTACCCCGGTCAAGGC GACACTTCCTATAATCAGAAGTTTAAGGGTAGAGCTACTATG ACCGCCGATAAGTCTACTTCTACCGTCTATATGGAACTGAGTT CCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAGAG TGGGCGGAGCCTTCCCAATGGACTACTGGGGTCAAGGCACCC TGGTCACCGTGTCTAGC
SEQ ID NO: 824	Heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPG QGLEWIGDIYPGQGDTSYNQKFKGRATMTADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMDYWGQGTLVTVSSASTKGPSVFP LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLG
SEQ ID NO: 825	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCGCTAGTGTGAAAGTTAGCTGTAAAGCTAGTGGCTATAC TTTCACTTCTTATAATATGCACTGGGTCCGCCAGGCCCCAGGT CAAGGCCTCGAGTGGATCGGCGATATCTACCCCGGTCAAGGC GACACTTCCTATAATCAGAAGTTTAAGGGTAGAGCTACTATG ACCGCCGATAAGTCTACTTCTACCGTCTATATGGAACTGAGTT CCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAGAG TGGGCGGAGCCTTCCCAATGGACTACTGGGGTCAAGGCACCC TGGTCACCGTGTCTAGCGCTAGCACTAAGGGCCCGTCCGTGT TCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCACCG CTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCCCGT GACCGTGTCCTGGAACAGCGGAGCCCTGACCTCCGGAGTGCA CACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTCGCTG TCGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTACCAAG ACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACTAAG GTGGACAAGCGCGTCGAATCGAAGTACGGCCCACCGTGCCCG CCTTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTTC TGTTCCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCA CCCCTGAAGTGACATGCGTGGTCGTGGACGTGTCACAGGAAG ATCCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGG TGCACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAAC TCCACTTACCGCGTCGTGTCCGTGCTGACGGTGCTGCATCAGG ACTGGCTGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAAC AAGGGACTTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCC AAGGGACAGCCCCGGGAACCCCAAGTGTATACCCTGCCACCG AGCCAGGAAGAAATGACTAAGAACCAAGTCTCATTGACTTGC CTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGGAATGG GAGTCCAACGGCCAGCCGGAAAACAACTACAAGACCACCCC TCCGGTGCTGGACTCAGACGGATCCTTCTTCCTCTACTCGCGG CTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGTGTT CAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTACAC TCAGAAGTCCCTGTCCCTCTCCCTGGGA
SEQ ID NO: 810 (Kabat)	LCDR1	RASESVEYYGTSLMQ
SEQ ID NO: 811 (Kabat)	LCDR2	AASNVES
SEQ ID NO: 812 (Kabat)	LCDR3	QQSRKDPST
SEQ ID NO: 813 (Chothia)	LCDR1	SESVEYYGTSL
SEQ ID NO: 814 (Chothia)	LCDR2	AAS
SEQ ID NO: 815 (Chothia)	LCDR3	SRKDPS

SEQ ID NO: 826	VL	DIVLTQSPDSLAVSLGERATINCRASESVEYYGTSLMQWYQQKP GQPPKLLIYAASNVESGVPDRFSGSGSGTDFTLTISSLQAEDVAV YYCQQSRKDPSTFGGGTKVEIK
SEQ ID NO: 827	DNA VL	GATATCGTCCTGACTCAGTCACCCGATAGCCTGGCCGTCAGC CTGGGCGAGCGGGCTACTATTAACTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCGGTCAACCCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCGATAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATTAGTAGCCTGCAGGCC GAGGACGTGGCCGTCTACTACTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGGCGGAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 828	Light chain	DIVLTQSPDSLAVSLGERATINCRASESVEYYGTSLMQWYQQKP GQPPKLLIYAASNVESGVPDRFSGSGSGTDFTLTISSLQAEDVAV YYCQQSRKDPSTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTA SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 829	DNA light chain	GATATCGTCCTGACTCAGTCACCCGATAGCCTGGCCGTCAGC CTGGGCGAGCGGGCTACTATTAACTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCGGTCAACCCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCGATAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATTAGTAGCCTGCAGGCC GAGGACGTGGCCGTCTACTACTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGGCGGAGGCACTAAGGTCGAGATTAAGCGT ACGGTGGCCGCTCCCAGCGTGTTCATCTTCCCCCCCAGCGAC GAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTG AACAACTTCTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTG GACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCA CCCTGACCCTGAGCAAGGCCGACTACGAGAAGCATAAGGTGT ACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGTGA CCAAGAGCTTCAACAGGGGCGAGTGC

Other Exemplary TIM-3 Inhibitors

[0514] In one embodiment, the anti-TIM-3 antibody molecule is TSR-022 (AnaptysBio/Tesaro). In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-022. In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of APE5137 or APE5121, *e.g.*, as disclosed in Table 10. APE5137, APE5121, and other anti-TIM-3 antibodies are disclosed in WO 2016/161270, incorporated by reference in its entirety.

[0515] In one embodiment, the anti-TIM-3 antibody molecule is LY3321367 (Eli Lilly). In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of LY3321367.

[0516] In one embodiment, the anti-TIM-3 antibody molecule is the antibody clone F38-2E2. In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of F38-2E2.

[0517] Further known anti-TIM-3 antibodies include those described, *e.g.*, in WO 2016/111947, WO 2016/071448, WO 2016/144803, US 8,552,156, US 8,841,418, and US 9,163,087, incorporated by reference in their entirety.

[0518] In one embodiment, the anti-TIM-3 antibody is an antibody that competes for binding with, and/or binds to the same epitope on TIM-3 as, one of the anti-TIM-3 antibodies described herein.

Table 10. Amino acid sequences of other exemplary anti-TIM-3 antibody molecules

APE5137		
SEQ ID NO: 830	VH	EVQLLESGGGLVQPGGSLRLSCAAASGFTFSSYDMSWVRQAPGKGLDWVS TISGGGTYTYYQDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASMD YWGQGTTVTVSSA
SEQ ID NO: 831	VL	DIQMTQSPSSLSASVGDRVTITCRASQSIRRYLNWYHQKPGKAPKLLIYGAS TLQSGVPSRFSGSGSGTDFTLTISSLQPEDFAVYYCQQSHSAPLTFGGGTKVE IKR
APE5121		
SEQ ID NO: 832	VH	EVQVLESGGGLVQPGGSLRLYCVASGFTFSGSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKKY YVGPADYWGQGTLVTVSSG
SEQ ID NO: 833	VL	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQHKPGQPPK LLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSSPLTF GGGTKIEVK

CTLA-4 Inhibitors

[0519] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a CTLA-4 inhibitor. The CTLA-4 inhibitor may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the CTLA-4 inhibitor is Ipilimumab (Yervoy®, Bristol-Myers Squibb) or Tremelimumab (Pfizer). The antibody Ipilimumab and other anti-CTLA-4 antibodies are disclosed in US 6,984,720, herein incorporated by reference. The antibody Tremelimumab and other anti-CTLA-4 antibodies are disclosed in US 7,411,057, herein incorporated by reference.

GITR Agonists

[0520] In certain embodiments, the anti-human ENTPD2 antibody as decribed herein is administered in combination with a GITR agonist. The GITR agonist may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the GITR agonist is GWN323 (Novartis), BMS-986156 (BMS), MK-4166 or MK-1248 (Merck), TRX518 (Leap Therapeutics), INCAGN1876 (Incyte/Agenus), AMG 228 (Amgen) or INBRX-110 (Inhibrx).

Exemplary Anti-GITR Antibody Molecules

[0521] In one embodiment, the GITR agonist is an anti-GITR antibody molecule. In one embodiment, the GITR agonist is an anti-GITR antibody molecule as described in WO 2016/057846, published on April 14, 2016, entitled "Compositions and Methods of Use for Augmented Immune Response and Cancer Therapy," incorporated by reference in its entirety.

[0522] In one embodiment, the anti-GITR antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 11 (*e.g.*, from the heavy and light chain variable region sequences of MAB7 disclosed in Table 11), or encoded by a nucleotide sequence shown in Table 11. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 11). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 11). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 11, or encoded by a nucleotide sequence shown in Table 11.

[0523] In one embodiment, the anti-GITR antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 909, a VHCDR2 amino acid sequence of SEQ ID NO: 911, and a VHCDR3 amino acid sequence of SEQ ID NO: 913; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 914, a VLCDR2 amino acid sequence of SEQ ID NO: 916, and a VLCDR3 amino acid sequence of SEQ ID NO: 918, each disclosed in Table 11.

[0524] In one embodiment, the anti-GITR antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 901, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 901. In one embodiment, the

anti-GITR antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 902, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 902. In one embodiment, the anti-GITR antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 901 and a VL comprising the amino acid sequence of SEQ ID NO: 902.

[0525] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 905, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 905. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 906, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 906. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 905 and a VL encoded by the nucleotide sequence of SEQ ID NO: 906.

[0526] In one embodiment, the anti-GITR antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 903, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 903. In one embodiment, the anti-GITR antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 904, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 904. In one embodiment, the anti-GITR antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 903 and a light chain comprising the amino acid sequence of SEQ ID NO: 904.

[0527] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 907, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 907. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 908, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 908. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 907 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 908.

[0528] The antibody molecules described herein can be made by vectors, host cells, and methods described in WO 2016/057846, incorporated by reference in its entirety.

Table 11. Amino acid and nucleotide sequences of exemplary anti-GITR antibody molecule

MAB7		

SEQ ID NO: 901	VH	EVQLVESGGGLVQSGGSLRLSCAASGFSLSSYGVDWVRQAP GKGLEWVGVIWGGGGTYYASSLMGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARHAYGHDGGFAMDYWGQGTLVTVS S
SEQ ID NO: 902	VL	EIVMTQSPATLSVSPGERATLSCRASESVSSNVAWYQQRPGQ APRLLIYGASNRATGIPARFSGSGSGTDFTLTISRLEPEDFAVY YCGQSYSYPFTFGQGTKLEIK
SEQ ID NO: 903	Heavy Chain	EVQLVESGGGLVQSGGSLRLSCAASGFSLSSYGVDWVRQAP GKGLEWVGVIWGGGGTYYASSLMGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARHAYGHDGGFAMDYWGQGTLVTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSK LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 904	Light Chain	EIVMTQSPATLSVSPGERATLSCRASESVSSNVAWYQQRPGQ APRLLIYGASNRATGIPARFSGSGSGTDFTLTISRLEPEDFAVY YCGQSYSYPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
SEQ ID NO: 905	DNA VH	GAGGTGCAGCTGGTGGAATCTGGCGGCGGACTGGTGCAG TCCGGCGGCTCTCTGAGACTGTCTTGCGCTGCCTCCGGCTT CTCCCTGTCCTCTTACGGCGTGGACTGGGTGCGACAGGCC CCTGGCAAGGGCCTGGAATGGGTGGGAGTGATCTGGGGC GGAGGCGGCACCTACTACGCCTCTTCCCTGATGGGCCGGT TCACCATCTCCCGGGACAACTCCAAGAACACCCTGTACCT GCAGATGAACTCCCTGCGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGACACGCCTACGGCCACGACGGCGGCTTCG CCATGGATTATTGGGGCCAGGGCACCCTGGTGACAGTGTC CTCC
SEQ ID NO: 906	DNA VL	GAGATCGTGATGACCCAGTCCCCCGCCACCCTGTCTGTGT CTCCCGGCGAGAGAGCCACCCTGAGCTGCAGAGCCTCCGA GTCCGTGTCCTCCAACGTGGCCTGGTATCAGCAGAGACCT GGTCAGGCCCCTCGGCTGCTGATCTACGGCGCCTCTAACC GGGCCACCGGCATCCCTGCCAGATTCTCCGGCTCCGGCAG CGGCACCGACTTCACCCTGACCATCTCCCGGCTGGAACCC GAGGACTTCGCCGTGTACTACTGCGGCCAGTCCTACTCAT ACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAAATCAA G

SEQ ID NO: 907	DNA Heavy Chain	GAGGTGCAGCTGGTGGAATCTGGCGGCGGACTGGTGCAG TCCGGCGGCTCTCTGAGACTGTCTTGCGCTGCCTCCGGCTT CTCCCTGTCCTCTTACGGCGTGGACTGGGTGCGACAGGCC CCTGGCAAGGGCCTGGAATGGGTGGGAGTGATCTGGGGC GGAGGCGGCACCTACTACGCCTCTTCCCTGATGGGCCGGT TCACCATCTCCCGGGACAACTCCAAGAACACCCTGTACCT GCAGATGAACTCCCTGCGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGACACGCCTACGGCCACGACGGCGGCTTCG CCATGGATTATTGGGGCCAGGGCACCCTGGTGACAGTGTC CTCCGCTAGCACCAAGGGCCCAAGTGTGTTTCCCCTGGCC CCCAGCAGCAAGTCTACTTCCGGCGGAACTGCTGCCCTGG GTTGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGACAGT GTCCTGGAACTCTGGGGCTCTGACTTCCGGCGTGCACACC TTCCCCGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGA GCAGCGTGGTGACAGTGCCCTCCAGCTCTCTGGGAACCCA GACCTATATCTGCAACGTGAACCACAAGCCCAGCAACACC AAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGCGACAAG ACCCACACCTGCCCCCCCTGCCCAGCTCCAGAACTGCTGG GAGGGCCTTCCGTGTTCCTGTTCCCCCCCAAGCCCAAGGA CACCCTGATGATCAGCAGGACCCCCGAGGTGACCTGCGTG GTGGTGGACGTGTCCCACGAGGACCCAGAGGTGAAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAG ACCAAGCCCAGAGAGGAGCAGTACAACAGCACCTACAGG GTGGTGTCCGTGCTGACCGTGCTGCACCAGGACTGGCTGA ACGGCAAAGAATACAAGTGCAAAGTCTCCAACAAGGCCC TGCCAGCCCCAATCGAAAAGACAATCAGCAAGGCCAAGG GCCAGCCACGGGAGCCCCAGGTGTACACCCTGCCCCCCAG CCGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTG TCTGGTGAAGGGCTTCTACCCCAGCGATATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCGAGAACAACTACAAGACC ACCCCCCCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGT ACAGCAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTCAGCTGCAGCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGTCCCTGAGCCTGAGCCCCGGC AAG
SEQ ID NO: 908	DNA Light Chain	GAGATCGTGATGACCCAGTCCCCCGCCACCCTGTCTGTGT CTCCCGGCGAGAGAGCCACCCTGAGCTGCAGAGCCTCCGA GTCCGTGTCCTCCAACGTGGCCTGGTATCAGCAGAGACCT GGTCAGGCCCCTCGGCTGCTGATCTACGGCGCCTCTAACC GGGCCACCGGCATCCCTGCCAGATTCTCCGGCTCCGGCAG CGGCACCGACTTCACCCTGACCATCTCCCGGCTGGAACCC GAGGACTTCGCCGTGTACTACTGCGGCCAGTCCTACTCAT ACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAAATCAA GCGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCCCCCCC AGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTG TGCCTGCTGAACAACTTCTACCCCCGGGAGGCCAAGGTGC AGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCC AGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCT ACAGCCTGAGCAGCACCCTGACCCTGAGCAAGGCCGACT ACGAGAAGCATAAGGTGTACGCCTGCGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACAGGG GCGAGTGC
SEQ ID NO: 909 (KABAT)	HCDR1	SYGVD
SEQ ID NO: 910 (CHOTHIA)	HCDR1	GFSLSSY
SEQ ID NO: 911 (KABAT)	HCDR2	VIWGGGGTYYASSLMG
SEQ ID NO: 912 (CHOTHIA)	HCDR2	WGGGG
SEQ ID NO: 913 (KABAT)	HCDR3	HAYGHDGGFAMDY
SEQ ID NO: 913 (CHOTHIA)	HCDR3	HAYGHDGGFAMDY
SEQ ID NO: 914 (KABAT)	LCDR1	RASESVSSNVA
SEQ ID NO: 915 (CHOTHIA)	LCDR1	SESVSSN

SEQ ID NO: 916 (KABAT)	LCDR2	GASNRAT
SEQ ID NO: 917 (CHOTHIA)	LCDR2	GAS
SEQ ID NO: 918 (KABAT)	LCDR3	GQSYSYPFT
SEQ ID NO: 919 (CHOTHIA)	LCDR3	SYSYPF

Other Exemplary anti-GITR Antibodies and Agonists

[0529] In one embodiment, the anti-GITR antibody molecule is BMS-986156 (Bristol-Myers Squibb), also known as BMS 986156 or BMS986156. BMS-986156 and other anti-GITR antibodies are disclosed, *e.g.*, in US 9,228,016 and WO 2016/196792, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-986156, *e.g.*, as disclosed in Table 12Table 12.

[0530] In one embodiment, the anti-GITR antibody molecule is MK-4166 or MK-1248 (Merck). MK-4166, MK-1248, and other anti-GITR antibodies are disclosed, *e.g.*, in US 8,709,424, WO 2011/028683, WO 2015/026684, and Mahne *et al. Cancer Res.* 2017; 77(5):1108-1118, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MK-4166 or MK-1248.

[0531] In one embodiment, the anti-GITR antibody molecule is TRX518 (Leap Therapeutics). TRX518 and other anti-GITR antibodies are disclosed, *e.g.*, in US 7,812,135, US 8,388,967, US 9,028,823, WO 2006/105021, and Ponte J *et al.* (2010) *Clinical Immunology*; 135:S96, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TRX518.

[0532] In one embodiment, the anti-GITR antibody molecule is INCAGN1876 (Incyte/Agenus). INCAGN1876 and other anti-GITR antibodies are disclosed, *e.g.*, in US 2015/0368349 and WO 2015/184099, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INCAGN1876.

[0533] In one embodiment, the anti-GITR antibody molecule is AMG 228 (Amgen). AMG 228 and other anti-GITR antibodies are disclosed, *e.g.*, in US 9,464,139 and WO

2015/031667, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of AMG 228.

[0534] In one embodiment, the anti-GITR antibody molecule is INBRX-110 (Inhibrx). INBRX-110 and other anti-GITR antibodies are disclosed, *e.g.*, in US 2017/0022284 and WO 2017/015623, incorporated by reference in their entirety. In one embodiment, the GITR agonist comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INBRX-110.

[0535] In one embodiment, the GITR agonist (*e.g.*, a fusion protein) is MEDI 1873 (MedImmune), also known as MEDI1873. MEDI 1873 and other GITR agonists are disclosed, *e.g.*, in US 2017/0073386, WO 2017/025610, and Ross *et al. Cancer Res* 2016; 76(14 Suppl): Abstract nr 561, incorporated by reference in their entirety. In one embodiment, the GITR agonist comprises one or more of an IgG Fc domain, a functional multimerization domain, and a receptor binding domain of a glucocorticoid-induced TNF receptor ligand (GITRL) of MEDI 1873.

[0536] Further known GITR agonists (*e.g.*, anti-GITR antibodies) include those described, *e.g.*, in WO 2016/054638, incorporated by reference in its entirety.

[0537] In one embodiment, the anti-GITR antibody is an antibody that competes for binding with, and/or binds to the same epitope on GITR as, one of the anti-GITR antibodies described herein.

[0538] In one embodiment, the GITR agonist is a peptide that activates the GITR signaling pathway. In one embodiment, the GITR agonist is an immunoadhesin binding fragment (*e.g.*, an immunoadhesin binding fragment comprising an extracellular or GITR binding portion of GITRL) fused to a constant region (*e.g.*, an Fc region of an immunoglobulin sequence).

Table 12. Amino acid sequences of other exemplary anti-GITR antibody molecules

BMS-986156		
SEQ ID NO: 920	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGL EWVAVIWYEGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAED TAVYYCARGGSMVRGDYYYGMDVWGQGTTVTVSS
SEQ ID NO: 921	VL	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLI YDASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPY TFGQGTKLEIK

Exemplary anti-CD3 multispecific antibody molecules

[0539] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an anti-CD3 multispecific antibody molecule (e.g., an anti-CD3 bispecific antibody molecule). In one embodiment, the anti-CD3 multispecific antibody molecule binds to CD3 and a target tumor antigen (TTA). In one embodiment, the TTA is chosen from CD19, CD20, CD38, or CD123. In one embodiment, the anti-CD3 multispecific antibody molecule is in a format disclosed in FIGs 1A, 1B, 1C, and 125 of WO 2016/182751, herein incorporated by reference in its entirety.

[0540] In one embodiment, the anti-CD3 multispecific antibody molecule is an anti-CD3 x anti-CD123 bispecific antibody molecule, e.g., XENP14045 (e.g., as set out in Table 15) or an anti-CD3 x anti-CD123 bispecific antibody molecule disclosed in WO 2016/086189 or WO 2016/182751, herein incorporated by reference in their entirety. In one embodiment, the anti-CD3 x anti-CD123 bispecific antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of XENP14045, or an amino acid sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

[0541] In one embodiment, the anti-CD3 multispecific antibody is an anti-CD3 x anti-CD20 bispecific antibody molecule, e.g., XENP13676 (e.g., as set out in Table 13) or an anti-CD3 x anti-CD20 bispecific antibody molecule disclosed in WO 2016/086189 or WO 2016/182751, herein incorporated by reference in their entirety. In one embodiment, the anti-CD3 x anti-CD20 bispecific antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of XENP13676, or an amino acid sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

Table 13. Amino acid sequences of exemplary anti-CD3 bispecific antibody molecules

XENP14045 (anti-CD123 x anti-CD3 Fab-scFv-Fc)		
SEQ ID NO: 314	Heavy chain 1 (anti-CD123 Fab-Fc)	QVQLQQSGAEVKKPGASVKVSCKASGYTFTDYYMKWVKQSHGKS LEWMGDIIPSNGATFYNQKFKGKATLTVDRSTSTAYMELSSLRSED TAVYYCARSHLLRASWFAYWGQGTLVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHT CPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV KFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVS

		LTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLT VDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 315	Heavy chain 2 (anti-CD3 scFv-Fc)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGL EWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRA EDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPG SGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYA NWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQ PEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAP PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 316	Light chain	DFVMTQSPDSLAVSLGERATINCKSSQSLLNTGNQKNYLTWYQQKP GQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSLQAEDVAVYY CQNDYSYPYTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
XENP13676 (anti-CD20 x anti-CD3 Fab-scFv-Fc)		
SEQ ID NO: 317	Heavy chain 1 (Fab-Fc)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQG LEWMGAIYPGNGDTSYNQKFQGRVTITADKSISTAYMELSSLRSED TAVYYCARSTYYGGDWYFNVWGAGTLVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKT HTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDP EVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 318	Heavy chain 2 (scFv-Fc)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGL EWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRA EDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPG SGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYA NWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQ PEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAP PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 319	Light chain	QIVLTQSPSSLSASVGDRVTITCRASSSVSYIHWFQQKPGKSPKPLIY ATSNLASGVPVRFSGSGSGTDYTLTISSLQPEDFATYYCQQWTSNPP TFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC

IL15/IL-15Ra complexes

[0542] In certain embodiments, the anti-human ENTPD2 antibody as decribed herein is administered in combination with an IL-15/IL-15Ra complex. In some embodiments, the IL-15/IL-15Ra complex is chosen from NIZ985 (Novartis), ATL-803 (Altor) or CYP0150 (Cytune).

Exemplary IL-15/IL-15Ra complexes

[0543] In one embodiment, the IL-15/IL-15Ra complex comprises human IL-15 complexed with a soluble form of human IL-15Ra. The complex may comprise IL-15 covalently or noncovalently bound to a soluble form of IL-15Ra. In a particular embodiment, the human IL-15 is noncovalently bonded to a soluble form of IL-15Ra. In a particular embodiment, the human IL-15 of the composition comprises an amino acid sequence of SEQ ID NO: 1001 in Table 14 and the soluble form of human IL-15Ra comprises an amino acid sequence of SEQ ID NO:1002 in Table 14, as described in WO 2014/066527, incorporated by reference in its entirety. The molecules described herein can be made by vectors, host cells, and methods described in WO 2007/084342, incorporated by reference in its entirety.

Table 14. Amino acid and nucleotide sequences of exemplary IL-15/IL-15Ra complexes

NIZ985		
SEQ ID NO: 1001	Human IL-15	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLEL QVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNI KEFLQSFVHIVQMFINTS
SEQ ID NO: 1002	Human Soluble IL-15Ra	ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLN KATNVAHWTTPSLKCIRDPALVHQRPAPPSTVTTAGVTPQPESLSPSG KEPAASSPSSNNTAATTAAIVPGSQLMPSKSPSTGTTEISSHESSHGTPS QTTAKNWELTASASHQPPGVYPQG

Other exemplary IL-15/IL-15Ra complexes

[0544] In one embodiment, the IL-15/IL-15Ra complex is ALT-803, an IL-15/IL-15Ra Fc fusion protein (IL-15N72D:IL-15RaSu/Fc soluble complex). ALT-803 is disclosed in WO 2008/143794, incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra Fc fusion protein comprises the sequences as disclosed in Table 15.

[0545] In one embodiment, the IL-15/IL-15Ra complex comprises IL-15 fused to the sushi domain of IL-15Ra (CYP0150, Cytune). The sushi domain of IL-15Ra refers to a domain beginning at the first cysteine residue after the signal peptide of IL-15Ra, and ending at the fourth cysteine residue after said signal peptide. The complex of IL-15 fused to the sushi domain of IL-15Ra is disclosed in WO 2007/04606 and WO 2012/175222, incorporated by reference in their entirety. In one embodiment, the IL-15/IL-15Ra sushi domain fusion comprises the sequences as disclosed in Table 15.

[0546] In one embodiment, the IL-15/IL-15Ra complex comprises a fusion protein of IL-15 and IL-15Ra, which may further comprise a linker, particularly a glycine-serine linker,

connecting the IL-15 and IL-15Ra as disclosed in WO 2014/186469 (Board of Regents, the University of Texas System), incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra fusion protein comprises the sequence as disclosed in Table 15.

[0547] In one embodiment, the IL-15/IL-15Ra complex comprises a fusion protein of a sushi domain of IL-15Ra and IL-15, linked by a glycine-serine linker, as disclosed in WO 2015/109124 (Kadmon Corp.), incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra fusion protein comprises the sequence as disclosed in Table 15.

[0548] In one embodiment, the IL-15/IL-15Ra complex comprises a fusion protein of IL-15, IL-15Ra, a Fc domain and a RGD peptide, preferably configured as RGD polypeptide-Fc domain-IL-15 polypeptide-IL-15Ra polypeptide, as disclosed in WO 2017/000913 (Numab Biopharmaceuticals), incorporated by reference in its entirety. In one embodiment, the RGD -Fc-IL-15-IL-15Ra fusion protein comprises the sequence as disclosed in Table 15.

[0549] In one embodiment, the IL-15/IL-15Ra complex comprises a heterodimeric protein comprising IL-15 linked to a first Fc domain and IL-15Ra linked to a second Fc domain. The IL-15 is the mature form of human IL-15 and the IL-15Ra is the extracellular domain of human IL-15Ra or a truncated variant thereof such as IL-15Ra-sushi. The two Fc domains may comprise mutations to enable heterodimer formation via “Knob-into-Hole” interactions and exemplary constructs are disclosed in WO 2015/103928 (Jiangsu Hendrui Medicine Co), incorporated by reference in its entirety.

[0550] In one embodiment, the IL-15/IL-15Ra complex comprises a combination of IL-15 comprising a cys amino acid mutation and IL-15Ra (extracellular or sushi domain thereof) comprising a cys mutation to facilitate the formation of intramolecular disulfide bonds between the polypeptides. Sequences of IL-15 and IL-15Ra with mutation combinations are disclosed in WO 2016/095642 (Jiangsu Hendrui Medicine Co), incorporated by reference in its entirety.

[0551] In one embodiment, the IL-15/IL-15Ra complex comprises a heterodimeric protein comprising IL-15 linked to a first Fc domain and IL-15Ra linked to a second Fc domain. The first and second Fc domains may have a set of amino acid substitutions as listed: S267K/L368D/K370S: S267K/LS364K/E357Q; S364K/E357Q: L36HD/K370S; L36HD/K370S; S364K; L36HE/K370S: S364K; T411T/E360E/Q362E: D401K; L368D/K370S: S364K/E357L and K370S; S364K/E357Q, according to EU numbering, and in addition may comprise further amino acid substitutions and substitutions to ablate Fcgamma receptor binding as disclosed in WO 2018/071919 (Xencor, Inc.), incorporated by reference in its entirety.

Table 15. Amino acid sequences of other exemplary IL-15/IL-15Ra complexes

ALT-803 (Altor)		
SEQ ID NO: 1003	IL-15N72D	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLEL QVISLESGDASIHDTVENLIILANDSLSSNGNVTESGCKECEELEEKNI KEFLQSFVHIVQMFINTS
SEQ ID NO: 1004	IL-15RaSu/ Fc	ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLN KATNVAHWTTPSLKCIREPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
IL-15 / IL-15Ra sushi domain fusion (Cytune)		
SEQ ID NO:1005	Human IL-15	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLEL QVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEXKNI KEFLQSFVHIVQMFINTS Where X is E or K
SEQ ID NO:1006	Human IL-15Ra sushi and hinge domains	ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLN KATNVAHWTTPSLKCIRDPALVHQRPAPP
IL-15 / IL-15Ra fusion protein (University of Texas)		
SEQ ID NO: 1007	IL-15/IL-15Ra fusion protein with Gly-Ser linker	MDWTWILFLVAAATRVHSNWVNVISDLKKIEDLIQSMHI DATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHD TVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQS FVHIVQMFINTSSGGGSGGGGSGGGGSGGGGSGGGSLQI TCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSS LTECVLNKATNVAHWTTPSLKCIRDPALVHQRPAPPSTV TTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGSQ LMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASH QPPGVYPQGHSDTTVAISTSTVLLCGLSAVSLLACYLKSR QTPPLASVEMEAMEALPVTWGTSSRDEDLENCSHHLSR MDYKDDDDKDYKDDDDKDYKDDDDK
IL-15Ra / IL-15 fusion protein (Kadmon Corp.)		
SEQ ID NO: 1008	Sushi-IL-15Ra/ IL-15 fusion protein with Gly-Ser linker	CPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSL TECVLNKATNVAHWTTPSLKCIRDPALVHQRPAPPSGGS GGGGSGGGSGGGGSLQNWVNVISDLKKIEDLIQSMHIDA TLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTV ENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFV HIVQMFINTS
RGD -Fc-IL-15-IL-15Ra fusion protein (Numab Biopharmaceuticals)		
SEQ ID NO: 1009	RGD-Fc-IL-15-IL-15Ra	ACDCRGDCFCGGGGGSDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGKGGGGSPPPMSVEHADIWVKSYSLYSRERYICNSG FKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPALVH

		QRPAPPSTVSGGSGGGGSGGGSGGGGSLQNWVNVISDL KKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQV ISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE LEEKNIKEFLQSFVHIVQMFINTS

Exemplary CSF-1/1R Binding Agents

[0552] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a CSF-1/1R binding agent.

[0553] In some embodiments, the CSF-1/1R binding agent is an inhibitor of macrophage colony-stimulating factor (M-CSF). M-CSF is also sometimes known as CSF-1.

[0554] In another embodiment, the CSF-1/1R binding agent is a CSF-1R tyrosine kinase inhibitor, 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15), or a compound disclosed in PCT Publication No. WO 2005/073224. In some embodiments, the CSF-1/1R binding agent is an M-CSF inhibitor, Compound A33, or a binding agent to CSF-1 disclosed in PCT Publication No. WO 2004/045532 or PCT Publication No WO 2005/068503 including RX1 or 5H4 (*e.g.*, an antibody molecule or Fab fragment against M-CSF).

[0555] In some embodiments, the CSF-1/1R binding agent is a CSF1R inhibitor or 4-(2-((1R, 2R)-2-hydroxycyclohexylamino)benzothiazol-6-yloxy)-N-methylpicolinamide. 4-(2-((1R, 2R)-2-hydroxycyclohexylamino)benzothiazol-6-yloxy)-N-methylpicolinamide is disclosed as example 157 at page 117 of PCT Publication No. WO 2007/121484.

[0556] In some embodiments, the CSF-1/1R binding agent is pexidartinib (CAS Registry Number 1029044-16-3). Pexidartinib is also known as PLX3397 or 5-((5-chloro-1H-pyrrolo[2,3-b]pyridin-3-yl)methyl)-N-((6-(trifluoromethyl)pyridin-3-yl)methyl)pyridin-2-amine. Pexidartinib is a small-molecule receptor tyrosine kinase (RTK) inhibitor of KIT, CSF1R and FLT3.

[0557] In some embodiments, the CSF-1/1R binding agent is emactuzumab. Emactuzumab is also known as RG7155 or RO5509554. Emactuzumab is a humanized IgG1 mAb targeting CSF1R.

[0558] In some embodiments, the CSF-1/1R binding agent is FPA008. FPA008 is a humanized mAb that inhibits CSF1R.

Exemplary IDO/TDO Inhibitors

[0559] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO).

[0560] In some embodiments, the IDO/TDO inhibitor is chosen from (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine (also known as INCB24360 or Epacadostat; CAS Registry Number: 1204669-58-8 (Incyte)), Indoximod (1-methyl-D-tryptophan), α-cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol (also known as NLG919) or BMS-986205 (also known as F001287 or ONO-7701).

[0561] In some embodiments, the IDO/TDO inhibitor is Epacadostat. It is a potent and selective indoleamine 2,3-dioxygenase (IDO1) inhibitor with an IC_{50} of 10 nM. Epacadostat ishighly selective over other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO).

[0562] In some embodiments, the IDO/TDO inhibitor is Indoximod (New Link Genetics). Indoximod, the D isomer of 1-methyl-tryptophan, is an orally administered small-molecule indoleamine 2,3-dioxygenase (IDO) pathway inhibitor that disrupts the mechanisms by which tumors evade immune-mediated destruction. NLG919 is a potent IDO pathway inhibitor with a Ki/EC_{50} of 7nM/75nM, respectively, in cell free assays.

[0563] In some embodiments, the IDO/TDO inhibitor is BMS-986205 (also known as F001287 or ONO-7701) (Flexus/BMS). BMS-986205 is a small molecule inhibitor of indoleamine 2,3-dioxygenase 1 (IDO1).

Exemplary TGF-β Inhibitors

[0564] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a transforming growth factor beta (TGF-β) inhibitor. The TGF-β inhibitor may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the TGF-β inhibitor is chosen from fresolimumab and XOMA 089 (Xoma).

[0565] TGF-β belongs to a large family of structurally-related cytokines including, *e.g.*, bone morphogenetic proteins (BMPs), growth and differentiation factors, activins and inhibins. In some embodiments, the TGF-β inhibitors described herein can bind and/or inhibit one or more isoforms of TGF-β (*e.g.*, one, two, or all of TGF-β1, TGF-β2, or TGF-β3).

[0566] In some embodiments, the TGF-β inhibitor is fresolimumab (CAS Registry Number: 948564-73-6). Fresolimumab is also known as GC1008. Fresolimumab is a human monoclonal antibody that binds to and inhibits TGF-beta isoforms 1, 2 and 3. Fresolimumab is disclosed, *e.g.*, in WO 2006/086469, US 8,383,780, and US 8,591,901.

[0567] The heavy chain of fresolimumab has the amino acid sequence of: QVQLVQSGAEVKKPGSSVKVSCKASGYTFSSNVISWVRQAPGQGLEWMGGVIPIVDI ANYAQRFKGRVTITADESTSTTYMELSSLRSEDTAVYYCASTLGLVLDAMDYWGQG TLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSC PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHN AKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDS DGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK (SEQ ID NO: 1012).

[0568] The light chain of fresolimumab has the amino acid sequence of: ETVLTQSPGTLSLSPGERATLSCRASQSLGSSYLAWYQQKPGQAPRLLIYGASSRAPG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYADSPITFGQGTRLEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 1013).

[0569] In some embodiments, the TGF-β inhibitor is XOMA 089. XOMA 089 is also known as XPA.42.089. XOMA 089 is a fully human monoclonal antibody that binds and neutralizes TGF-beta 1 and 2 ligands while sparing TGF-beta 3.

[0570] The heavy chain variable region of XOMA 089 has the amino acid sequence of:

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGT ANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGLWEVRALPSVYWGQ GTLVTVSS (SEQ ID NO: 310) (disclosed as SEQ ID NO: 6 in WO2012/167143).

[0571] The light chain variable region of XOMA 089 has the amino acid sequence of: SYELTQPPSVSVAPGQTARITCGANDIGSKSVHWYQQKAGQAPVLVVSEDIIRPSGIP ERISGSNSGNTATLTISRVEAGDEADYYCQVWDRDSDQYVFGTGTKVTVLG (SEQ ID NO: 311) (disclosed as SEQ ID NO: 8 in WO2012/167143).

Exemplary VEGFR Inhibitors

[0572] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a vascular endothelial growth factor (VEGF) receptor inhibitor (*e.g.*, an inhibitor of one or more of VEGFR (*e.g.*, VEGFR-1, VEGFR-2, or VEGFR-3) or VEGF).

[0573] In some embodiments, the VEGFR inhibitor is vatalanib succinate (Compound A47) or a compound disclosed in EP 296122.

[0574] In some embodiment, the VEGFR inhibitor is an inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C, 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377.

[0575] Other exemplary VEGFR pathway inhibitors that can be used in the combinations disclosed herein include, *e.g.,* bevacizumab (AVASTIN®), axitinib (INLYTA®); brivanib alaninate (BMS-582664, (S)-((R)-1-(4-(4-Fluoro-2-methyl-1H-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy)propan-2-yl)2-aminopropanoate); sorafenib (NEXAVAR®); pazopanib (VOTRIENT®); sunitinib malate (SUTENT®); cediranib (AZD2171, CAS 288383-20-1); vargatef (BIBF1120, CAS 928326-83-4); Foretinib (GSK1363089); telatinib (BAY57-9352, CAS 332012-40-5); apatinib (YN968D1, CAS 811803-05-1); imatinib (GLEEVEC®); ponatinib (AP24534, CAS 943319-70-8); tivozanib (AV951, CAS 475108-18-0); regorafenib (BAY73-4506, CAS 755037-03-7); vatalanib dihydrochloride (PTK787, CAS 212141-51-0); brivanib (BMS-540215, CAS 649735-46-6); vandetanib (CAPRELSA® or AZD6474); motesanib diphosphate (AMG706, CAS 857876-30-3, N-(2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]-3-pyridinecarboxamide, described in PCT Publication No. WO 02/066470); linfanib (ABT869, CAS 796967-16-3); cabozantinib (XL184, CAS 849217-68-1); lestaurtinib (CAS 111358-88-4); N-[5-[[[5-(1,1-dimethylethyl)-2-oxazolyl]methyl]thio]-2-thiazolyl]-4-piperidinecarboxamide (BMS38703, CAS 345627-80-7); (3R,4R)-4-amino-1-((4-((3-methoxyphenyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)methyl)piperidin-3-ol (BMS690514); N-(3,4-Dichloro-2-fluorophenyl)-6-methoxy-7-[[(3aα,5β,6aα)-octahydro-2-methylcyclopenta[c]pyrrol-5-yl]methoxy]- 4-quinazolinamine (XL647, CAS 781613-23-8); 4-methyl-3-[[1-methyl-6-(3-pyridinyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]amino]-N-[3-(trifluoromethyl)phenyl]-benzamide (BHG712, CAS 940310-85-0); aflibercept (EYLEA®), and endostatin (ENDOSTAR®).

[0576] Exemplary anti-VEGF antibodies that can be used in the combinations disclosed herein include, *e.g.,* a monoclonal antibody that binds to the same epitope as the monoclonal anti-VEGF antibody A4.6.1 produced by hybridoma ATCC HB 10709; a recombinant humanized anti-VEGF monoclonal antibody generated according to Presta *et al.* (1997) Cancer Res. 57:4593-4599. In one embodiment, the anti-VEGF antibody is Bevacizumab (BV), also known as rhuMAb VEGF or AVASTIN®. It comprises mutated

human IgG1 framework regions and antigen-binding complementarity- determining regions from the murine anti-hVEGF monoclonal antibody A.4.6.1 that blocks binding of human VEGF to its receptors. Bevacizumab and other humanized anti-VEGF antibodies are further described in U.S. Pat. No. 6,884,879 issued Feb. 26, 2005. Additional antibodies include the G6 or B20 series antibodies (*e.g.,* G6-31, B20-4.1), as described in PCT Publication No. WO2005/012359, PCT Publication No. WO2005/044853. For additional antibodies, *see* U.S. Pat. Nos. 7,060,269, 6,582,959, 6,703,020, 6,054,297, WO98/45332, WO 96/30046, WO94/10202, EP 0666868B1, U.S. Patent Application Publication Nos. 2006/009360, 2005/0186208, 2003/0206899, 2003/0190317, 2003/0203409, and 2005/0112126; and Popkov *et al, Journal of Immunological Methods* 288: 149-164 (2004). Other antibodies include those that bind to a functional epitope on human VEGF comprising of residues F17, Ml 8, D19, Y21, Y25, Q89, 191 , Kl 01, El 03, and C104 or, alternatively, comprising residues F17, Y21, Q22, Y25, D63, 183 and Q89.

Exemplary EGFR Inhibitors

[0577] In some embodiments, the anti-human ENTPD2 antibody molecule, *e.g.*, the anti- ENTPD2 antibody molecule described herein, is used, in combination with a tyrosine kinase inhibitor (*e.g.*, a receptor tyrosine kinase (RTK) inhibitor). Exemplary tyrosine kinase inhibitor include, but are not limited to, an epidermal growth factor (EGF) pathway inhibitor (*e.g.*, an epidermal growth factor receptor (EGFR) inhibitor), a vascular endothelial growth factor (VEGF) pathway inhibitor (*e.g.*, a vascular endothelial growth factor receptor (VEGFR) inhibitor (*e.g.*, a VEGFR-1 inhibitor, a VEGFR-2 inhibitor, a VEGFR-3 inhibitor)), a platelet derived growth factor (PDGF) pathway inhibitor (*e.g.*, a platelet derived growth factor receptor (PDGFR) inhibitor (*e.g.*, a PDGFR-ß inhibitor)), a RAF-1 inhibitor, a KIT inhibitor and a RET inhibitor. In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of Epidermal Growth Factor Receptor (EGFR).

[0578] In some embodiments, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757.

[0579] In some embodiments, the EGFR inhibitor is chosen from one of more of erlotinib (Tarceva®), gefitinib (Iressa®), cetuximab (Erbitux ®), panitumumab (Vectibix®),

necitumumab (Portrazza®), dacomitinib, nimotuzumab, Imgatuzumab, afatinib, or osimertinib (Tagrisso).

[0580] Other anticancer agents, e.g., tyrosine kinase inhibitors pathway inhibitors, that can be used in the combinations disclosed herein include, but are not limited to, Selected tyrosine kinase inhibitors are chosen from sunitinib (Sutent®), or sorafenib (Nexavar®).

[0581] In some embodiments, the anti-cancer agent used in combination with the hedgehog inhibitor is selected from the group consisting of: axitinib (AG013736), bosutinib (SKI-606), cediranib (RECENTIN™, AZD2171), dasatinib (SPRYCEL®, BMS-354825), erlotinib (TARCEVA®), gefitinib (IRESSA®), imatinib (Gleevec®, CGP57148B, STI-571), lestaurtinib (CEP-701), neratinib (HKI-272), nilotinib (TASIGNA®), semaxanib (semaxinib, SU5416), sunitinib (SUTENT®, SU11248), toceranib (PALLADIA®), vandetanib (ZACTIMA®, ZD6474), vatalanib (PTK787, PTK/ZK), trastuzumab (HERCEPTIN®), bevacizumab (AVASTIN®), rituximab (RITUXAN®), cetuximab (ERBITUX®), panitumumab (VECTIBIX®), ranibizumab (Lucentis®), nilotinib (TASIGNA®), sorafenib (NEXAVAR®), alemtuzumab (CAMPATH®), gemtuzumab ozogamicin (MYLOTARG®), ENMD-2076, PCI-32765, AC220, BIBW 2992 (TOVOK™), SGX523, PF-04217903, PF-02341066, PF-299804, BMS-777607, ABT-869, MP470, BIBF 1120 (VARGATEF®), AP24534, JNJ-26483327, MGCD265, DCC-2036, BMS-690154, CEP-11981, tivozanib (AV-951), OSI-930, MM-121, XL-184, XL-647, XL228, AEE788, AG-490, AST-6, BMS-599626, CUDC-101, PD153035, pelitinib (EKB-569), vandetanib (zactima), WZ3146, WZ4002, WZ8040, ABT-869 (linifanib), AEE788, AP24534 (ponatinib), AV-951(tivozanib), axitinib, BAY 73-4506 (regorafenib), brivanib alaninate (BMS-582664), brivanib (BMS-540215), cediranib (AZD2171), CP 673451, CYC116, E7080, Ki8751, masitinib (AB1010), MGCD-265, motesanib diphosphate (AMG-706), MP-470, OSI-930, Pazopanib Hydrochloride, PD173074, Sorafenib Tosylate(Bay 43-9006), SU 5402SU 5402, TSU-68 (SU6668)., vatalanib, XL880 (GSK1363089, EXEL-2880).

Exemplary c-MET Inhibitors

[0582] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of c-MET.

[0583] In some embodiments, the c-MET inhibitor is Compound A17 or a compound described in U.S. Patent Nos. 7,767,675 and 8,420,645).

[0584] In some embodiments, the c-MET inhibitor is JNJ-38877605. JNJ-38877605 is an orally available, small molecule inhibitor of c-Met. JNJ-38877605 selectively binds to

c-MET, thereby inhibiting c-MET phosphorylation and disrupting c-Met signal transduction pathways.

[0585] In some embodiments, the c-Met inhibitor is AMG 208. AMG 208 is a selective small-molecule inhibitor of c-MET. AMG 208 inhibits the ligand-dependent and ligand-independent activation of c-MET, inhibiting its tyrosine kinase activity, which may result in cell growth inhibition in tumors that overexpress c-Met.

[0586] In some embodiments, the c-Met inhibitor is AMG 337. AMG 337 is an orally bioavailable inhibitor of c-Met. AMG 337 selectively binds to c-MET, thereby disrupting c-MET signal transduction pathways.

[0587] In some embodiments, the c-Met inhibitor is LY2801653. LY2801653 is an orally available, small molecule inhibitor of c-Met. LY2801653 selectively binds to c-MET, thereby inhibiting c-MET phosphorylation and disrupting c-Met signal transduction pathways.

[0588] In some embodiments, c-Met inhibitor is MSC2156119J. MSC2156119J is an orally bioavailable inhibitor of c-Met. MSC2156119J selectively binds to c-MET, which inhibits c-MET phosphorylation and disrupts c-Met-mediated signal transduction pathways.

[0589] In some embodiments, the c-MET inhibitor is capmatinib. Capmatinib is also known as INCB028060. Capmatinib is an orally bioavailable inhibitor of c-MET. Capmatinib selectively binds to c-Met, thereby inhibiting c-Met phosphorylation and disrupting c-Met signal transduction pathways.

[0590] In some embodiments, the c-MET inhibitor is crizotinib. Crizotinib is also known as PF-02341066. Crizotinib is an orally available aminopyridine-based inhibitor of the receptor tyrosine kinase anaplastic lymphoma kinase (ALK) and the c-Met/hepatocyte growth factor receptor (HGFR). Crizotinib, in an ATP-competitive manner, binds to and inhibits ALK kinase and ALK fusion proteins. In addition, crizotinib inhibits c-Met kinase, and disrupts the c-Met signaling pathway. Altogether, this agent inhibits tumor cell growth.

[0591] In some embodiments, the c-MET inhibitor is golvatinib. Golvatinib is an orally bioavailable dual kinase inhibitor of c-MET and VEGFR-2 with potential antineoplastic activity. Golvatinib binds to and inhibits the activities of both c-MET and VEGFR-2, which may inhibit tumor cell growth and survival of tumor cells that overexpress these receptor tyrosine kinases.

[0592] In some embodiments, the c-MET inhibitor is tivantinib. Tivantinib is also known as ARQ 197. Tivantinib is an orally bioavailable small molecule inhibitor of c-MET. Tivantinib binds to the c-MET protein and disrupts c-Met signal transduction pathways,

which may induce cell death in tumor cells overexpressing c-MET protein or expressing constitutively activated c-Met protein.

Exemplary IAP Inhibitors

[0593] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of Inhibitor of Apoptosis Protein (IAP).

[0594] In some embodiments, the IAP inhibitor is (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in U.S. Patent No. 8,552,003.

Exemplary mTOR Inhibitors

[0595] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of mammalian target of rapamycin (mTOR).

[0596] In some embodiments, the mTOR inhibitor is 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41).

[0597] In some embodiments, the mTOR inhibitor is everolimus (also known as RAD001 or AFINITOR®; Compound A36) or a compound first disclosed in PCT Publication No. WO 94/09010.

[0598] In some embodiments, the mTOR inhibitor is chosen from one or more of temsirolimus (TORISEL®), PF-4691502, GDC0980, OSI-027, GSK1059615, KU-0063794, WYE-354, Palomid 529 (P529), PF-04691502, gedatolisib (PF-05212384, PKI-587), ridaforolimus (formally known as deferolimus, (1R,2R,4S)-4-[(2R)-2 [(1R,9S,12S,15R,16E,18R,19R,21R, 23S,24E,26E,28Z,30S,32S,35R)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.04,9] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669, and described in PCT Publication No. WO 03/064383); rapamycin (AY22989, SIROLIMUS®); simapimod (CAS Registry Number: 164301-51-3); (5-{2,4-Bis[(3S)-3-methylmorpholin-4-yl]pyrido[2,3-d]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-Amino-8-[trans-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-d]pyrimidin-7(8H)-one (PF04691502, CAS Registry Number: 1013101-36-4); N2-[1,4-

dioxo-4-[[4-(4-oxo-8-phenyl-4H-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L-α-aspartylL-serine inner salt (SF1126, CAS Registry Number: 936487-67-1) (SEQ ID NO: 1011), or XL765 (SAR245409).

Exemplary PI3K-γ, -δ Inhibitors

[0599] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K), *e.g.,* phosphatidylinositol-4,5-bisphosphate 3-kinase gamma and/or delta (PI3K-γ,δ).

[0600] In some embodiments, the PI3K inhibitor is an inhibitor of delta and gamma isoforms of PI3K. Exemplary PI3K inhibitors that can be used in combination are described in, *e.g.*, WO 2010/036380, WO 2010/006086, WO 09/114870, WO 05/113556. In some embodiments, the PI3K inhibitor is chosen from one or more of GSK 2126458, GDC-0980, GDC-0941, Sanofi XL147, XL756, XL147, PF-46915032, CAL-101, CAL 263, SF1126, PX-886, and a dual PI3K inhibitor.

[0601] In some embodiments, the PI3K-γ,δ inhibitor is idelalisib (CAS Registry Number: 870281-82-6). Idelalisib is also known as ZYDELIG®, GS-1101, CAL-101, or 5-Fluoro-3-phenyl-2-[(1S)-1-(7H-purin-6-ylamino)propyl]-4(3H)-quinazolinone. Idelalisib blocks P110δ, the delta isoform of PI3K. Idelalisib is disclosed, *e.g.,* in Wu *et al. Journal of Hematology & Oncology* (2013) 6: 36.

[0602] In some embodiments, the PI3K-γ,δ inhibitor is 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41).

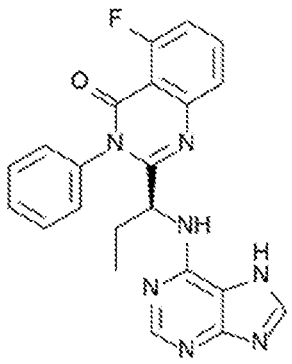
[0603] Other exemplary PI3K-γ,δ inhibitors that can be used in the combination include, *e.g.,* pictilisib (GDC-0941), LY294002, pilaralisib (XL147), PI-3065, PI-103, VS-5584 (SB2343), CZC24832, duvelisib (IPI-145, INK1197), TG100-115, CAY10505, GSK1059615, PF-04691502, AS-605240, voxtalisib (SAR245409, XL765), IC-87114, omipalisib (GSK2126458, GSK458), TG100713, gedatolisib (PF-05212384, PKI-587), PKI-402, XL147 analogue, PIK-90, PIK-293, PIK-294, 3-Methyladenine (3-MA), AS-252424, AS-604850, or apitolisib (GDC-0980, RG7422).

[0604] In some embodiments, the PI3K inhibitor is Compound A8 or a compound described in PCT Publication No. WO2010/029082.

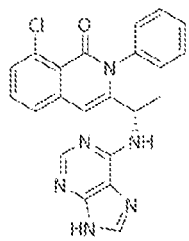
[0605] In some embodiments, the PI3K inhibitor is a pan-PI3K inhibitor, (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-

methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826.

[0606] Exemplary PI3K-γ, -δ inhibitors include, but are not limited to, duvelisib and idelalisib. Idelalisib (also called GS-1101 or CAL-101; Gilead) is a small molecule that blocks the delta isoform of PI3K. The structure of idelalisib (5-Fluoro-3-phenyl-2-[(1*S*)-1-(7*H*-purin-6-ylamino)propyl]-4(3*H*)-quinazolinone) is shown below.



[0607] Duvelisib (also called IPI-145; Infinity Pharmaceuticals and Abbvie) is a small molecule that blocks PI3K-δ,γ. The structure of duvelisib (8-Chloro-2-phenyl-3-[(1S)-1-(9H-purin-6-ylamino)ethyl]-1(2H)-isoquinolinone) is shown below.



[0608] In one embodiment, the inhibitor is a dual phosphatidylinositol 3-kinase (PI3K) and mTOR inhibitor selected from 2-Amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF-04691502); *N*-[4-[[4-(Dimethylamino)-1-piperidinyl]carbonyl]phenyl]-*N'*-[4-(4,6-di-4-morpholinyl-1,3,5-triazin-2-yl)phenyl]urea (PF-05212384, PKI-587); apitolisib (GDC-0980, RG7422); 2,4-Difluoro-N-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide (GSK2126458); 8-(6-methoxypyridin-3-yl)-3-methyl-1-(4-(piperazin-1-yl)-3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-c]quinolin-2(3H)-one Maleic acid (NVP-BGT226); 3-[4-(4-Morpholinylpyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl]phenol

(PI-103); 5-(9-isopropyl-8-methyl-2-morpholino-9H-purin-6-yl)pyrimidin-2-amine (VS-5584, SB2343); or N-[2-[(3,5-Dimethoxyphenyl)amino]quinoxalin-3-yl]-4-[(4-methyl-3-methoxyphenyl)carbonyl]aminophenylsulfonamide (XL765).

Exemplary JAK Inhibitors

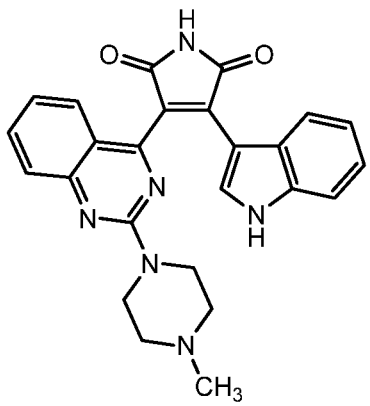
[0609] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of Janus kinase (JAK).

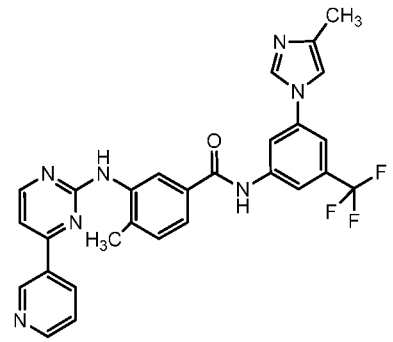
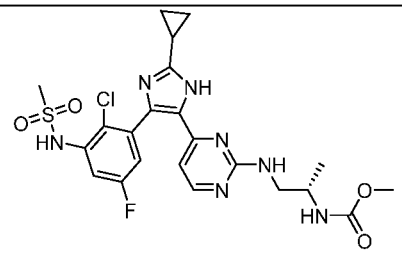
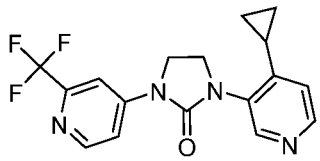
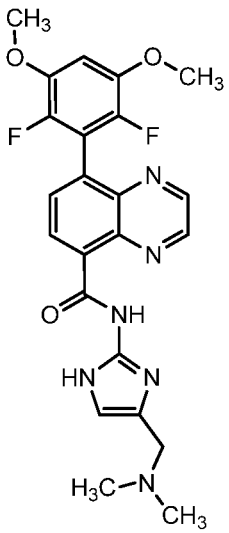
[0610] In some embodiments, the JAK inhibitor is 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514.

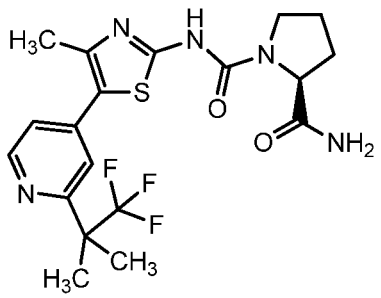
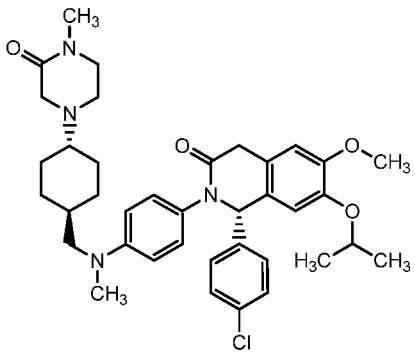
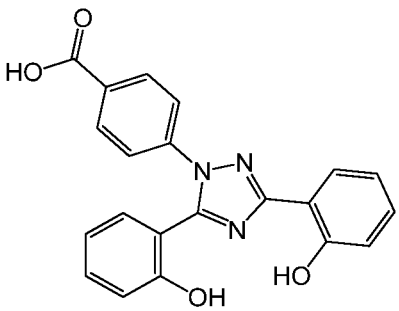
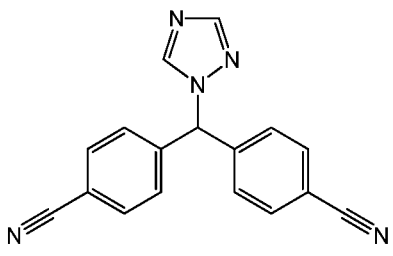
[0611] In some embodiment, the JAK inhibitor is ruxolitinib phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514.

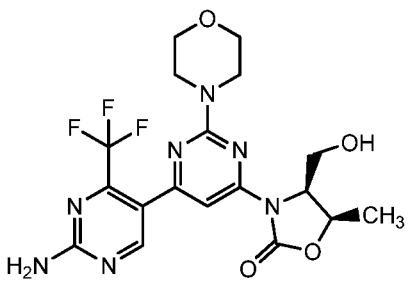
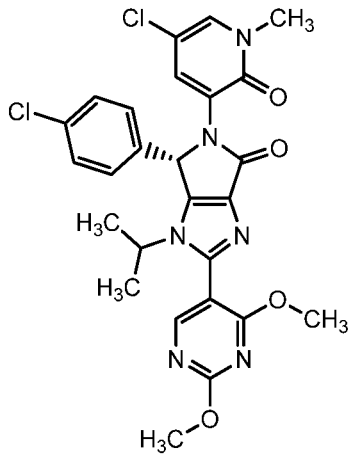
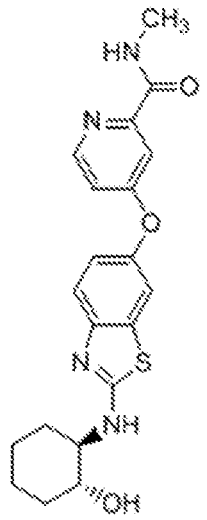
[0612] In certain embodiments, any of the combinations disclosed herein, alternatively or in combination, further includes one or more of the agents described in Table 16.

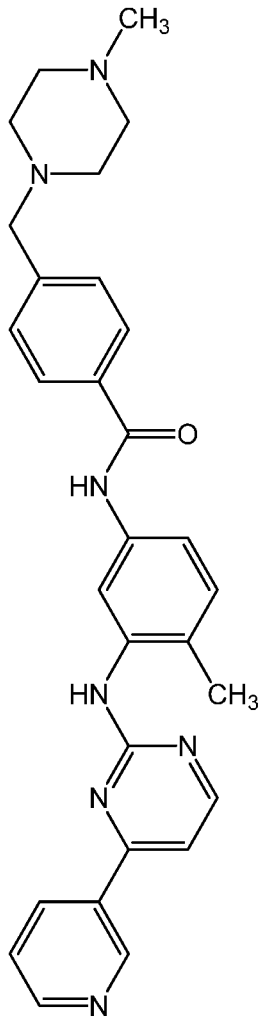
Table 16. Selected therapeutic agents that can be administered in combination with the anti-human ENTPD2 antibody molecules, *e.g.*, as a single agent or in combination with other immunomodulators described herein. Each publication listed in this Table is herein incorporated by reference in its entirety, including all structural formulae therein.

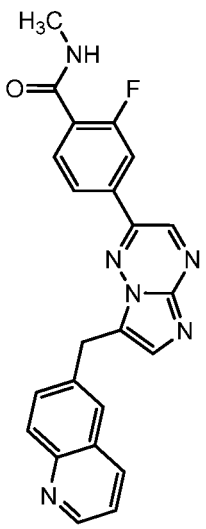
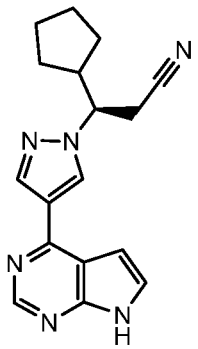
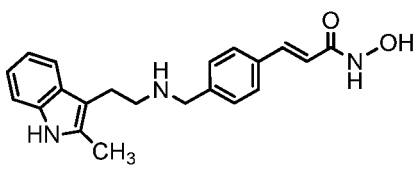
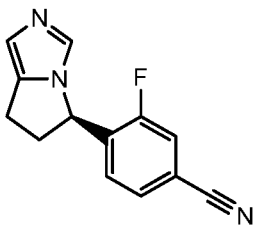
Compound Designation	Generic Name Tradename	Compound Structure	Patents / Patent Application Publications
A1	Sotrastaurin		EP 1682103 US 2007/142401 WO 2005/039549

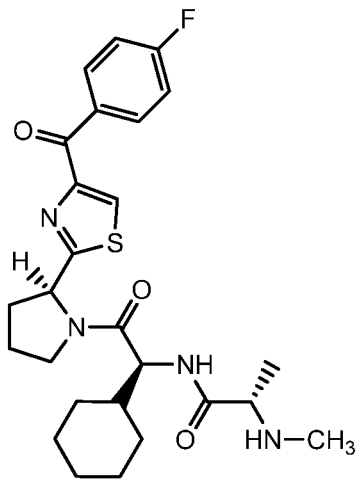
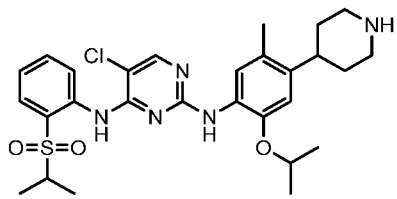
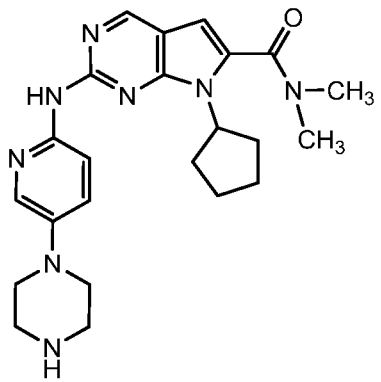
A2	Nilotinib HCl monohydrate TASIGNA®	 HCl • H_20	WO 2004/005281 US 7,169,791
A3			WO2011/023773
A4			WO2012/149413
A7			WO 2009/141386 US 2010/0105667

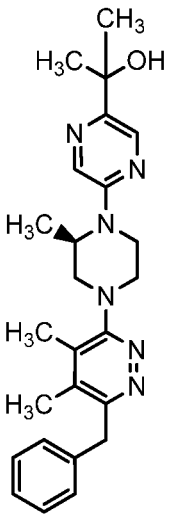
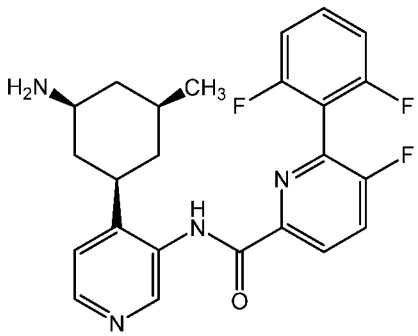
A8			WO 2010/029082
A10			WO 2011/076786
A11	Deferasirox EXJADE®		WO 1997/049395
A12	Letrozole FEMARA®		US 4,978,672

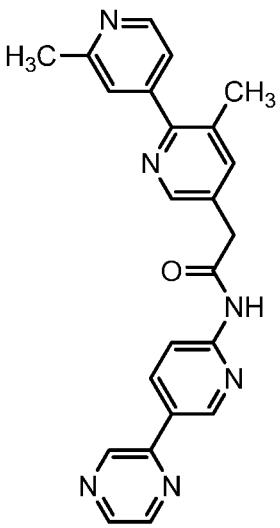
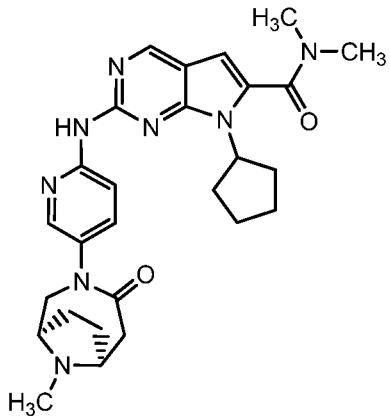
A13			WO 2013/124826 US 2013/0225574
A14			WO 2013/111105
A15			WO2007/121484

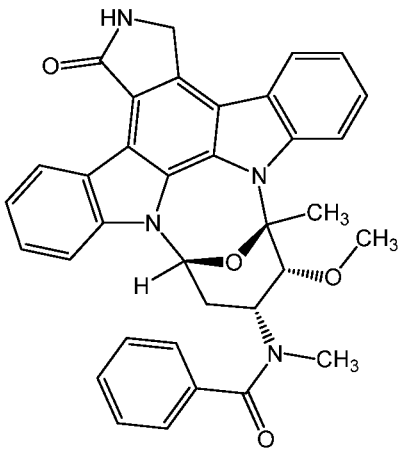
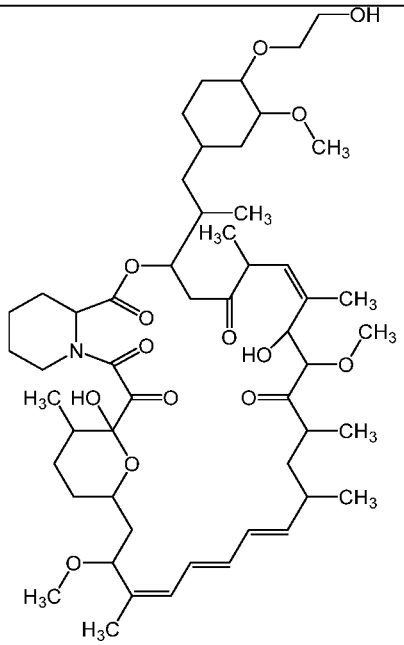
A16	Imatinib mesylate GLEEVEC®	 Mesylate	WO 1999/003854
A17			EP 2099447 US 7,767,675 US 8,420,645

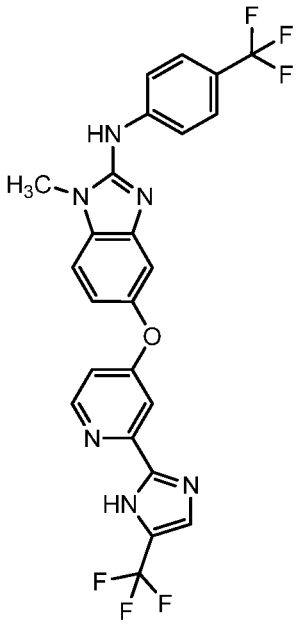
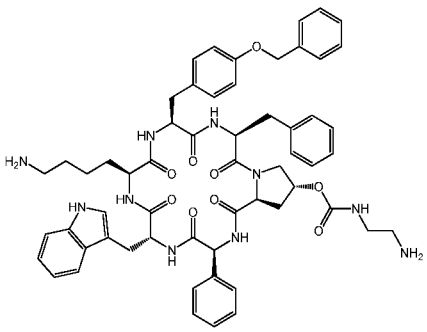
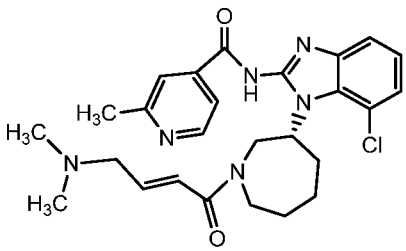
		 Dihydrochloric salt	
A18	Ruxolitinib Phosphate JAKAFI®	 H_3PO_4	WO 2007/070514 EP 2474545 US 7,598,257 WO 2014/018632
A19	Panobinostat		WO 2014/072493 WO 2002/022577 EP 1870399
A20	Osilodrostat		WO 2007/024945

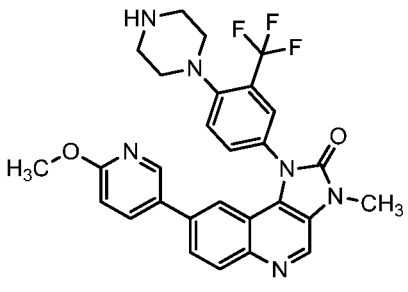
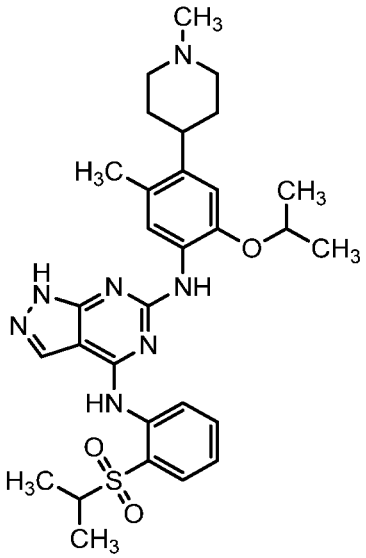
A21			WO 2008/016893 EP 2051990 US 8,546,336
A23	ceritinib ZYKADIA™		WO 2008/073687 US 8,039,479
A24	Ribociclib KISQALI®		US 8,415,355 US 8,685,980

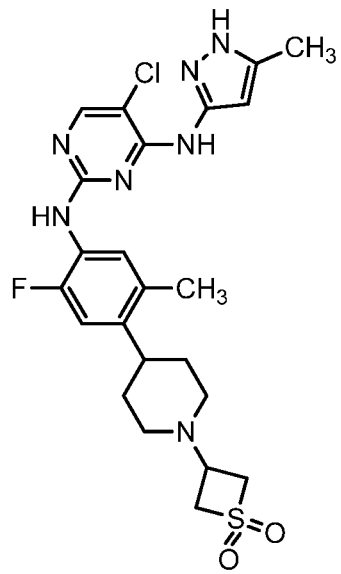
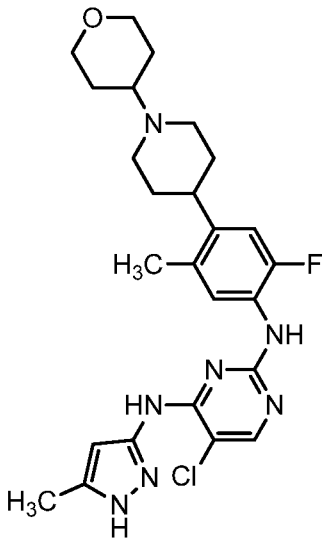
A25			WO 2010/007120
A26		Human monoclonal antibody to PRLR	US 7,867,493
A27			WO 2010/026124 EP 2344474 US 2010/0056576 WO2008/106692

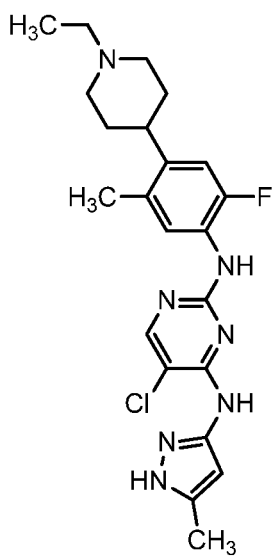
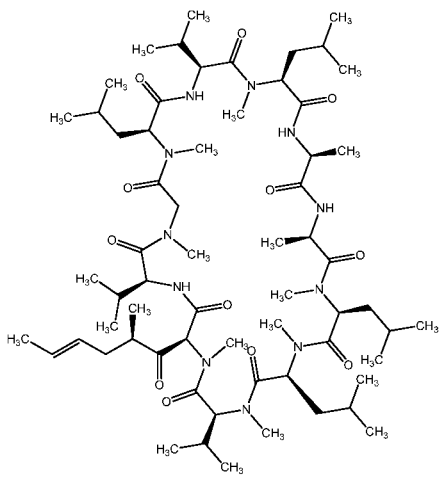
A28			WO 2010/101849
A30			WO 2011/101409
A31		Human monoclonal antibody to HER3	WO 2012/022814 EP 2606070 US 8,735,551
A32		Antibody Drug Conjugate (ADC)	WO 2014/160160 Ab: 12425 (*see* Table 1, paragraph [00191]) Linker: SMCC (*see* paragraph [00117] Payload: DM1 (*see* paragraph

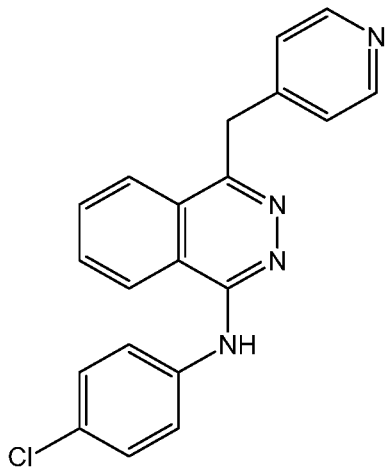
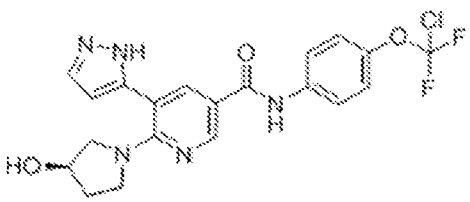
			[00111] *See* also Claim 29
A33		Monoclonal antibody or Fab to M-CSF	WO 2004/045532
A35	Midostaurin		WO 2003/037347 EP 1441737 US 2012/252785
A36	Everolimus AFINITOR ®		WO 1994/009010 WO 2014/085318

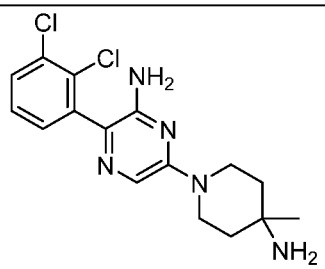
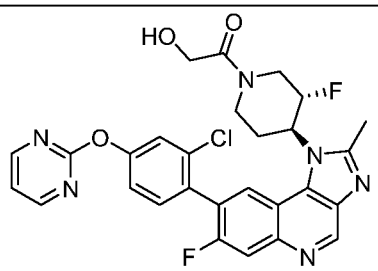
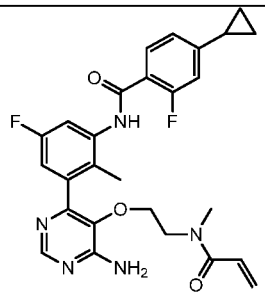
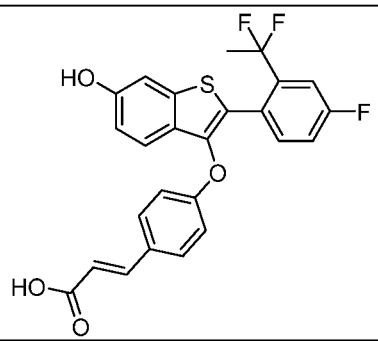
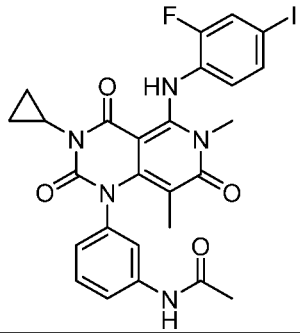
A37			WO 2007/030377 US 7,482,367
A38	Pasireotide diaspartate SIGNIFOR ®		WO2002/010192 US 7,473,761
A40			WO 2013/184757

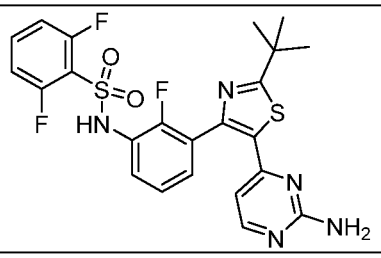
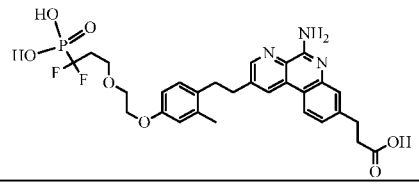
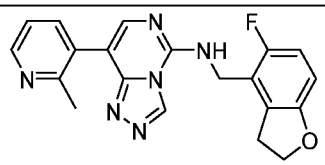
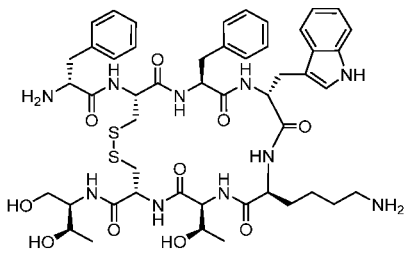
A41			WO 2006/122806
A42			WO 2008/073687 US 8,372,858

A43			WO 2010/002655 US 8,519,129
A44			WO 2010/002655 US 8,519,129

A45			WO 2010/002655
A46	Valspodar AMDRAY™		EP 296122

A47	Vatalanib succinate	 succinate	WO 98/35958
A48		IDH inhibitor	WO2014/141104
A49	Asciminib	BCR-ABL inhibitor 	WO2013/171639 WO2013/171640 WO2013/171641 WO2013/171642
A50		cRAF inhibitor	WO2014/151616
A51		ERK1/2 ATP competitive inhibitor	WO2015/066188
A52		or a choline salt thereof	WO2010/015613 WO2013030803 US 7,989,497
A53			WO2015/107493

			
A54			WO2015/022662
A55			US 9,512,084 WO/2015/079417
A56			WO2014/130310
A57	trametinib		WO2005/121142 US 7,378,423

A58	dabrafenib		WO 2009/137391 US 7,994,185
A59			WO2011/049677
A60			WO 2016/103155 US 9580437 EP 3237418
A61	octreotide		US 4,395,403 EP 0 029 579

[0613] The anti-human ENTPD2 antibody molecules as described herein can be administered in combination with an additional therapeutic agent. In some embodiments, the additional therapeutic agent is chosen from one or more of: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (e.g., a CYP17 inhibitor or a 17alpha-Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, e.g., an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of histamine release, Flt3 (e.g., FLK2/STK1) or PKC; 18) an inhibitor of one

or more of VEGFR-2 (e.g., FLK-1/KDR), PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor, e.g., an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11β-hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, e.g., BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; or 39) an inhibitor of a lipid kinase, e.g., as described herein and in Table 1.

[0614] In one embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PKC inhibitor, Sotrastaurin (Compound A1), or a compound disclosed in PCT Publication No. WO 2005/039549, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PKC inhibitor is Sotrastaurin (Compound A1) or a compound disclosed in PCT Publication No. WO 2005/039549.

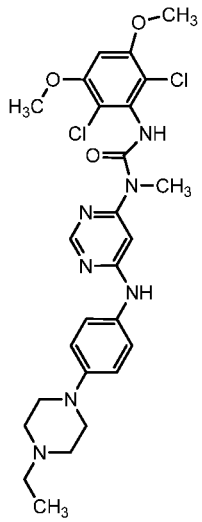
[0615] In one embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a BCR-ABL inhibitor, nilotinib (Compound A2, Tasigna®), or a compound disclosed in PCT Publication No. WO 2004/005281, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the BCR-ABL inhibitor is nilotinib, or a compound disclosed in PCT Publication No. WO 2004/005281.

[0616] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an HSP90 inhibitor, to treat a disorder, *e.g.*, a disorder described herein, e.g., a cancer.

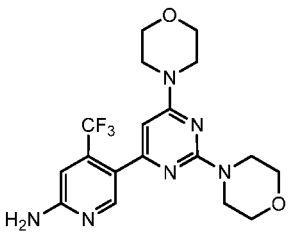
[0617] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, is used in combination with an inhibitor of PI3K and/or mTOR, 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41), to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K and/or mTOR

inhibitor is 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41).

[0618] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an FGFR inhibitor, 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) or a compound disclosed in US Patent 8,552,002, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR inhibitor is 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) or a compound disclosed in US Patent No. 8,552,002. Compound A5 has the following structure:



[0619] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PI3K inhibitor, Buparlisib (Compound A6), or a compound disclosed in PCT Publication No. WO 2007/084786, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is Buparlisib (Compound A6) or a compound disclosed in PCT Publication No. WO 2007/084786. Compound A6 has the following structure:



a.

[0620] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an FGFR inhibitor, 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide (Compound A7) or a compound disclosed in PCT Publication No. WO 2009/141386 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR inhibitor is 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide(Compound A7) or a compound disclosed in a PCT Publication No. WO 2009/141386.

[0621] In another embodiment the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PI3K inhibitor, (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) or a compound disclosed PCT Publication No. WO 2010/029082 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) or a compound disclosed PCT Publication No. WO 2010/029082.

[0622] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an inhibitor of cytochrome P450 (*e.g.*, a CYP17 inhibitor) or a compound disclosed in PCT Publication No. WO 2010/149755, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the cytochrome P450 inhibitor (*e.g.*, the CYP17 inhibitor) is a compound disclosed in PCT Publication No. WO 2010/149755; US 8,263,635 B2; or EP 2445903 B1.

[0623] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an HDM2 inhibitor, (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1r,4S)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-

dihydroisoquinolin-3(4H)-one(Compound A10) or a compound disclosed in PCT Publication No. WO 2011/076786 to treat a disorder, *e.g.*, a disorder described herein). In one embodiment, the HDM2 inhibitor is (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1r,4S)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-dihydroisoquinolin-3(4H)-one (Compound A10) or a compound disclosed in PCT Publication No. WO 2011/076786.

[0624] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an iron chelating agent, Deferasirox (also known as EXJADE; Compound A11), or a compound disclosed in PCT Publication No. WO 1997/049395 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the iron chelating agent is Deferasirox or a compound disclosed in PCT Publication No. WO 1997/049395. In one embodiment, the iron chelating agent is Deferasirox (Compound A11).

[0625] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an aromatase inhibitor, Letrozole (also known as FEMARA; Compound A12), or a compound disclosed in US 4,978,672 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the aromatase inhibitor is Letrozole (Compound A12) or a compound disclosed in US Patent 4,978,672.

[0626] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PI3K inhibitor, *e.g.*, a pan-PI3K inhibitor, (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the PI3K inhibitor is (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826.

[0627] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an inhibitor of p53 and/or a p53/Mdm2 interaction, (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14), or a compound disclosed in PCT Publication No. WO2013/111105 to treat a disorder, *e.g.,* a disorder

described herein. In one embodiment, the p53 and/or a p53/Mdm2 interaction inhibitor is (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14) or a compound disclosed in PCT Publication No. WO2013/111105.

[0628] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a CSF-1R tyrosine kinase inhibitor, 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15), or a compound disclosed in PCT Publication No. WO 2005/073224 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the CSF-1R tyrosine kinase inhibitor is 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15) or a compound disclosed in PCT Publication No. WO 2005/073224.

[0629] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an apoptosis inducer and/or an angiogenesis inhibitor, such as Imatinib mesylate (also known as GLEEVEC®; Compound A16) or a compound disclosed in PCT Publication No. WO1999/003854 to treat a disorder, *e.g.,* a disorder described. In one embodiment, the apoptosis inducer and/or an angiogenesis inhibitor is Imatinib mesylate (Compound A16) or a compound disclosed in PCT Publication No. WO1999/003854.

[0630] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a JAK inhibitor, 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK inhibitor is 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514.

[0631] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a JAK inhibitor, Ruxolitinib Phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK inhibitor is

Ruxolitinib Phosphate (Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514.

[0632] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a deacetylase (DAC) inhibitor, Panobinostat (Compound A19), or a compound disclosed in PCT Publication No. WO 2014/072493 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the DAC inhibitor is Panobinostat (Compound A19) or a compound disclosed in PCT Publication No. WO 2014/072493.

[0633] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an inhibitor of one or more of cytochrome P450 (*e.g.*, 11B2), aldosterone or angiogenesis, Osilodrostat (Compound A20), or a compound disclosed in PCT Publication No. WO2007/024945 to treat a disorder, *e.g.*, a disorder described herein.

[0634] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a IAP inhibitor, (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in US 8,552,003 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the IAP inhibitor is (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in US Patent 8,552,003.

[0635] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a Smoothened (SMO) inhibitor, (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2010/007120 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the SMO inhibitor is (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2010/007120.

[0636] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an Alk inhibitor, ceritinib (also known as ZYKADIA; Compound A23) to treat a disorder, *e.g.*, a disorder described herein.

[0637] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a JAK and/or CDK4/6 inhibitor, 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24), or a compound disclosed in US Patent 8,415,355 or US Patent 8,685,980 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK and/or CDK4/6 inhibitor is 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24) or a compound disclosed in US Patent 8,415,355 or US Patent 8,685,980.

[0638] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a prolactin receptor (PRLR) inhibitor, a human monoclonal antibody molecule (Compound A26) as disclosed in US Patent 7,867,493), to treat a disorder, *e.g.*, a disorder described herein.

[0639] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PIM Kinase inhibitor, N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (Compound A27) or a compound disclosed in PCT Publication No. WO 2010/026124 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PIM Kinase inhibitor is N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (Compound A27) or a compound disclosed in PCT Publication No. WO 2010/026124.

[0640] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a Wnt signaling inhibitor, 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) or a compound disclosed in PCT publication No. WO 2010/101849 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the Wnt signaling inhibitor is 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) or a compound disclosed in PCT publication No. WO 2010/101849. In one embodiment, the Wnt signaling inhibitor is 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28).

[0641] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in

combination with a BRAF inhibitor, to treat a disorder, *e.g.*, a disorder described herein, e.g., a cancer.

[0642] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a CDK4/6 inhibitor, 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30), or a compound disclosed in PCT publication No. WO 2011/101409 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the CDK4/6 inhibitor is 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30) or a compound disclosed in PCT publication No. WO 2011/101409.

[0643] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a HER3 inhibitor, Compound A31, or a compound disclosed in PCT Publication No. WO 2012/022814, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the HER3 inhibitor is Compound A31 or a compound disclosed in PCT Publication WO 2012/022814.

[0644] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an FGFR2 and/or FGFR4 inhibitor, Compound A32, or a compound disclosed in a publication PCT Publication No. WO 2014/160160 (*e.g.*, an antibody molecule drug conjugate against an FGFR2 and/or FGFR4, *e.g.*, mAb 12425), to treat a disorder, *e.g.,* a disorder described herein. In some embodiments, Compound A32 is an antibody molecule drug conjugate against an FGFR2 and/or FGFR4, *e.g.*, mAb 12425.

[0645] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an M-CSF inhibitor, Compound A33, or a compound disclosed in PCT Publication No. WO 2004/045532 (*e.g.*, an antibody molecule or Fab fragment against M-CSF), to treat a disorder, *e.g.,* a disorder described herein.

[0646] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a MEK inhibitor, to treat a disorder, e.g., a cancer as described herein.

[0647] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an inhibitor of one or more of c-KIT, histamine release, Flt3 (*e.g.*, FLK2/STK1) or PKC, Midostaurin (Compound A35) or a compound disclosed in PCT Publication No. WO 2003/037347 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the inhibitor is Midostaurin (Compound A35) or compound disclosed in PCT Publication No. WO 2003/037347.

[0648] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C, 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C is 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377.

[0649] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a somatostatin agonist and/or growth hormone release inhibitor, Pasireotide diaspartate (also known as SIGNIFOR; Compound A38) or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the somatostatin agonist and/or growth hormone release inhibitor is Pasireotide diaspartate (Compound A38) or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761.

[0650] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a signal transduction modulator and/or angiogenesis inhibitor, e.g., to treat a disorder such as a cancer as described herein.

[0651] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757 to treat a disorder, *e.g.*, a

disorder described herein. In one embodiment, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino) but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757. In one embodiment, an anti-human ENTPD2 antibody molecule is used in combination with (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757, to treat a disorder such as a cancer.

[0652] In some embodiments, the EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757, is administered in combination with an inhibitor of ENTPD2 (*e.g.,* an anti-human ENTPD2 antibody molecule) to treat a cancer.

[0653] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an ALK inhibitor, N^6-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N^4-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42) or a compound disclosed in PCT Publication No. WO 2008/073687 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the ALK inhibitor is N^6-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N^4-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42) or a compound disclosed in PCT Publication No. WO 2008/073687.

[0654] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an IGF-1R inhibitor, 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N^2-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N^4-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), or 5-chloro-N2-(4-(1-ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N^4-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45) or a compound disclosed in PCT Publication No. WO 2010/002655 to treat a disorder, *e.g.,* a disorder described. In one embodiment, the IGF-1R inhibitor is 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N^2-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N^4-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), 5-chloro-N2-(4-(1-

ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N^4-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45), or a compound disclosed in PCT Publication No. WO 2010/002655.

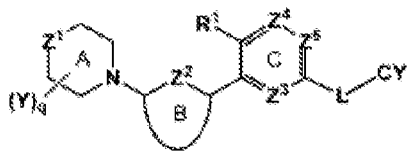
[0655] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a P-Glycoprotein 1 inhibitor, Valspodar (also known as AMDRAY; Compound A46) or a compound disclosed in EP 296122 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the P-Glycoprotein 1 inhibitor is Valspodar (Compound A46) or a compound disclosed in EP 296122.

[0656] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination one or more of a VEGFR inhibitor, Vatalanib succinate (Compound A47) or a compound disclosed in EP 296122 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the VEGFR inhibitor is Vatalanib succinate (Compound A47) or a compound disclosed in EP 296122.

[0657] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an IDH inhibitor or a compound disclosed in WO2014/141104 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the IDH inhibitor is a compound disclosed in PCT Publication No. WO2014/141104.

[0658] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a BCL-ABL inhibitor or a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the BCL-ABL inhibitor is a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642.

[0659] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a c-RAF inhibitor or a compound disclosed in PCT Publication No. WO2014/151616 to treat a disorder, *e.g.,* a disorder described herein. In one embodiment, the c-RAF inhibitor is Compound A50 or a compound disclosed in PCT Publication No. WO2014/151616. In some embodiments, the c-RAF inhibitor or Compound A50 is a compound of formula (I):

b.  (I)

c. or a pharmaceutically acceptable salt thereof, wherein:

d. Z^1 is O, S, S(=O) or SO_2;

e. Z^2 is N, S or CR^a, where R^a is H, halo, C_{1-4} alkyl or C_{1-4} haloalkyl;

f. R^1 is CN, halo, OH, C_{1-4} alkoxy, or C_{1-4} alkyl that is optionally substituted with one to three groups selected from halo, C_{1-4} alkoxy, CN, and hydroxyl;

g. Ring B is selected from phenyl, pyridine, pyrimidine, pyrazine, pyridazine, pyridone, pyrimidone, pyrazinone, pyridazinone, and thiazole, each of which is optionally substituted with up to two groups selected from halo, OH, CN, C_{1-4} alkyl, C_{2-4} alkenyl, -O-(C_{1-4} alkyl), NH_2, NH-(C_{1-4} alkyl), -N(C_{1-4} alkyl)$_2$, -SO_2R^2, $NHSO_2R^2$, $NHC(O)R^2$, $NHCO_2R^2$, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, -O-C_{3-6} cycloalkyl, -O-(5-6-membered heteroaryl), C_{4-8} heterocycloalkyi, and -O-(4-8 membered heterocycloalkyi), where each heterocycloalkyi and heteroaryl contains up to three heteroatoms selected from N, O and S as ring members,

i. where each C_{1-4} alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, and 4-8 membered heterocycloalkyi is each optionally substituted with up to three groups selected from oxo, hydroxyl, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and -$(CH_2)_{1-2}Q$ where Q is OH, C_{1-4} alkoxy, -CN, NH_2, -NHR^3, -$N(R^3)_2$, - SO_2R^3, $NHSO_2R^3$, $NHC(O)OR^3$, or $NHC(O)R^3$; each R^2 and R^3 is independently C_{1-4} alkyl; and

ii. Ring B is optionally fused to a 5-6 membered aromatic or nonaromatic ring containing up to two heteroatoms selected from N, O and S, where the 5-6 membered ring can be substituted with halo, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} alkoxy, and if the fused ring is non-aromatic the substituent options can further include oxo;

h. each Y is independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, CN, halo, oxo, -$(CH_2)_pOR^4$, -(CH_2)p $N(R^4)_2$, -(CH_2)p$NHC(O)R^4$, -$(CH_2)_pNHCOO(C_{1-4}$ alkyl),and imidazole,

i. or two Y groups on Ring A are optionally taken together to form a ring fused to or bridging Ring A, where said fused or bridging ring optionally contains a heteroatom selected from N, O and S as a ring member, and is optionally substituted with up to two groups selected from C_{1-4} alkyl, C_{1-4} alkoxy, CN, halo, oxo, -$(CH_2)_pOR^4$, -$(CH_2)_p$ $N(R^4)_2$, -$(CH_2)_pNHC(O)R^4$, and -$(CH_2)_pNHCOO(C_{1-4}$ alkyl);

j. each R^4 is independently H or C_{1-4} alkyl;

k. each p is independently 0, 1, or 2;

l. q is 0, 1 or 2;

m. Z^3, Z^4, and Z^5 are independently selected from CH and N and optionally NO;

n. L is -C(=O)-NR^4-[CY] or -NR^4-C(=O)-[CY], where [CY] indicates which atom of L is attached to CY; and

o. CY is an aromatic ring selected from phenyl, pyridine, pyrimidine, pyrazine, pyridazine, pyridone, thiazole, isothiazole, oxazole, pyrazole, and isoxazole, wherein the ring is optionally fused to a thiophene, imidazole, oxazolone, or pyrrole ring;

p. and CY is substituted with up to two groups selected from halo, CN, R^5, OR^5, SO_2R^5, -S(=NH)(=O)R^5, OH, NH_2, NHR^5, and -$N(R^5)_2$,

i. wherein each R^5 is independently C_{1-4} alkyl, C_{2-4}. alkenyl, C_{2-6} heterocyclyl, 5-membered heteroaryl containing up to three heteroatoms selected from N, O and S as ring members, or C_{3-8} cycloalkyl, and R^5 is optionally substituted with up to four groups selected from oxo, halo, CN, R^6, OH, OR^6, SO_2R^6, NH_2, NHR^6, $N(R^6)_2$, $NHSO_2R^6$, $NHCOOR^6$, $NHC(=O)R^6$, -CH_2OR^7, -$CH_2N(R^7)_2$, wherein each

q. R^6 is independently C_{1-4} alkyl, and each R^7 is independently H or C_{1-4} alkyl;

r. and two R^4, R^5, R^6, or R^7 on the same nitrogen atom can be taken together to form a 5-6 membered heterocyclic ring optionally containing an additional N, O or S as a ring member and optionally substituted with up to two groups selected from C_{1-4} alkyl, oxo, halo, OH, and C_{1-4} alkoxy.

Exemplary Cell therapies

[0660] Anti-human ENTPD2 antibody molecules can also be combined with a cell therapy, e.g., a chimeric antigen receptor (CAR) therapy, a T cell therapy, a natural killer (NK) cell therapy, or a dendritic cell therapy.

Combinations with CAR therapies

[0661] The anti-human ENTPD2 antibody molecules described herein can be administered in combination with a second therapeutic, e.g., a cell comprising a chimeric antigen receptor (CAR). The CAR may comprise i) an extracellular antigen binding domain, ii) a transmembrane domain, and iii) an intracellular signaling domain (which may comprise one or both of a primary signaling domain and a costimulatory domain). The CAR may further comprise a leader sequence and/or a hinge sequence. In specific embodiments, the

CAR construct comprises a scFv domain, wherein the scFv may be preceded by an optional leader sequence, and followed by an optional hinge sequence, a transmembrane region, and an intracellular signaling domain, e.g., wherein the domains are contiguous with and in the same reading frame to form a single fusion protein.

[0662] In some embodiments, the CAR molecule comprises a CD19 CAR molecule described herein, e.g., a CD19 CAR molecule described in US 2015/0283178, e.g., CTL019. In embodiments, the CD19 CAR comprises an amino acid, or has a nucleotide sequence shown in US 2015/0283178, incorporated herein by reference in its entirety, or a sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

[0663] In one embodiment, the CAR T cell that binds to CD19 has the USAN designation TISAGENLECLEUCEL-T. CTL019 is made by a gene modification of T cells mediated by stable insertion via transduction with a self-inactivating, replication deficient lentiviral (LV) vector containing the CTL019 transgene under the control of the EF-1 alpha promoter. CTL019 can be a mixture of transgene positive and negative T cells that are delivered to the subject on the basis of percent transgene positive T cells.

[0664] In one embodiment, the CD19 CAR comprises an amino acid sequence provided as SEQ ID NO: 12 in PCT publication WO2012/079000. In embodiment, the amino acid sequence is:

MALPVTALLLPLALLLHAARPdiqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliy
htsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqgntlpytfgggtkleitggggsggggsggggsevklqesg
pglvapsqslsvtctvsgvslpdygvswirqpprkglewlgviwgsettyynsalksrltiikdnsksqvflkmnslqtd
dtaiyycakhyyyggsyamdywgqgtsvtvsstttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfacdiyi
waplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqn
qlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglst
atkdtydalhmqalppr (SEQ ID NO: 312),

or a sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto), with or without the signal peptide sequence indicated in capital letters.

[0665] In one embodiment, the amino acid sequence is:

diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliyhtsrlhsgvpsrfsgsgsgtdysltisnleqedi
atyfcqqgntlpytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvsgvslpdygvswirqp

prkglewlgviwgsettyynsalksrltiikdnsksqvflkmnslqtddtaiyycakhyyyggsyamdywgqgtsvt vsstttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkq pfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemggk prrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr (SEQ ID NO: 313),

or a sequence substantially homologous thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

Antigen binding domain of a chimeric antigen receptor (CAR)

[0666] The antigen binding domain can be any domain that binds to the antigen including but not limited to a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, and a functional fragment thereof, including but not limited to a single-domain antibody such as a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) of camelid derived nanobody, and to an alternative scaffold known in the art to function as antigen binding domain, such as a recombinant fibronectin domain, a T cell receptor (TCR), or a fragment there of, e.g., single chain TCR, and the like. In some instances, it is beneficial for the antigen binding domain to be derived from the same species in which the CAR will ultimately be used in. For example, for use in humans, it may be beneficial for the antigen binding domain of the CAR to comprise human or humanized residues for the antigen binding domain of an antibody or antibody fragment.

[0667] In some embodiments, the antigen binding domain of the CAR is a scFv antibody fragment that is humanized compared to the murine sequence of the scFv from which it is derived.

[0668] In some embodiments, the antigen binding domain binds a tumor antigen described herein. In embodiments, the tumor antigen is chosen from: CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38;

CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT);

sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1).

[0669] In one embodiment, the CAR molecule comprises a BCMA CAR molecule, e.g., a BCMA CAR described in US 2016/0046724 or WO 2016/014565, incorporated herein by reference. In embodiments, the BCMA CAR comprises an amino acid, or has a nucleotide sequence of a CAR molecule, or an antigen binding domain according to US 2016/0046724, or Table 1 or 16, SEQ ID NO: 271 or SEQ ID NO: 273 of WO 2016/014565, incorporated herein by reference, or a sequence substantially identical to any of the aforesaid sequences (e.g., having at least about 85%, 90%, or 95% sequence identity to any of the aforesaid BCMA CAR sequences). The amino acid and nucleotide sequences encoding the BCMA CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), are specified in WO 2016/014565.

Transmembrane domain of a chimeric antigen receptor (CAR)

[0670] With respect to the transmembrane domain, in various embodiments, a CAR can be designed to comprise a transmembrane domain that is attached to the extracellular domain of the CAR.

[0671] The transmembrane domain may be derived either from a natural or from a recombinant source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. In one aspect the transmembrane domain is capable of signaling to the intracellular domain(s) whenever the CAR has bound to a target. A transmembrane domain may include at least the transmembrane region(s) of e.g., the alpha, beta or zeta chain of the T-cell receptor, CD28, CD27, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154. In some embodiments, a transmembrane domain may include at least the transmembrane region(s) of, e.g., KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, IL2R beta, IL2R gamma, IL7R-α, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKG2D, or NKG2C.

[0672] In some instances, the transmembrane domain can be attached to the extracellular region of the CAR, e.g., the antigen binding domain of the CAR, via a hinge, e.g., a hinge from a human protein. For example, in one embodiment, the hinge can be a human Ig (immunoglobulin) hinge (e.g., an IgG4 hinge, an IgD hinge), a GS linker (e.g., a GS linker described herein), a KIR2DS2 hinge or a CD8a hinge.

Intracellular signaling domain of a chimeric antigen receptor (CAR)

[0673] The cytoplasmic domain or region of the CAR includes an intracellular signaling domain. An intracellular signaling domain is generally responsible for activation of at least one of the normal effector functions of the immune cell in which the CAR has been introduced.

[0674] Examples of intracellular signaling domains for use in the CAR include the cytoplasmic sequences of the T cell receptor (TCR) and co-receptors that act in concert to initiate signal transduction following antigen receptor engagement, as well as any derivative or variant of these sequences and any recombinant sequence that has the same functional capability.

[0675] A primary signaling domain regulates primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary intracellular signaling domains that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs.

[0676] Examples of ITAM containing primary intracellular signaling domains include those of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In one embodiment, a CAR comprises an intracellular signaling domain, e.g., a primary signaling domain of CD3-zeta.

[0677] The intracellular signaling domain of the CAR can comprise the CD3-zeta signaling domain by itself or it can be combined with any other desired intracellular signaling domain(s) useful in the context of a CAR of the invention. For example, the intracellular signaling domain of the CAR can comprise a CD3 zeta chain portion and a costimulatory signaling domain. The costimulatory signaling domain refers to a portion of the CAR comprising the intracellular domain of a costimulatory molecule. A costimulatory molecule is a cell surface molecule other than an antigen receptor or its ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that binds to CD83, and the like. For example, CD27 costimulation has been demonstrated to enhance expansion, effector function, and survival of human CART cells in vitro and augments human T cell persistence and antitumor activity in vivo (Song et al. Blood. 2012; 119(3):696-706). Further examples of such costimulatory molecules include CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96

(Tactile), NKG2D, CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, and CD19a.

Activation and Expansion of Immune Effector Cells (e.g., T Cells)

[0678] Immune effector cells such as T cells may be activated and expanded generally using methods as described, for example, in U.S. Patents 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466; 6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publication No. 2006/0121005, incorporated herein by reference.

[0679] Examples of immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloid-derived phagocytes.

[0680] Methods of making CAR-expressing cells are described, e.g., in US 2016/0185861, incorporated herein by reference.

Exemplary Cancer Vaccines

[0681] Anti-human ENTPD2 antibody molecules can be combined with an immunogenic agent, such as cancerous cells, purified tumor antigens (including recombinant proteins, peptides, and carbohydrate molecules), cells, and cells transfected with genes encoding immune stimulating cytokines (He *et al.* (2004) *J. Immunol.* 173:4919-28). Non-limiting examples of tumor vaccines that can be used include peptides of melanoma antigens, such as peptides of gp100, MAGE antigens, Trp-2, MART1 and/or tyrosinase, tumor cells transfected to express the cytokine GM-CSF, DNA-based vaccines, RNA-based vaccines, and viral transduction-based vaccines. The cancer vaccine may be prophylactic or therapeutic.

[0682] ENTPD2 blockade can be used in conjunction with a collection of recombinant proteins and/or peptides expressed in a tumor in order to generate an immune response to these proteins.

[0683] Other tumor vaccines may include the proteins from viruses implicated in human cancers such a Human Papilloma Viruses (HPV), Hepatitis Viruses (HBV and HCV), Kaposi's Herpes Sarcoma Virus (KHSV), and Epstein–Barr virus (EBV). Another form of tumor specific antigen which may be used in conjunction with ENTPD2 blockade is purified heat shock proteins (HSP) isolated from the tumor tissue itself. These heat shock proteins

contain fragments of proteins from the tumor cells and these HSPs are highly efficient at delivery to antigen presenting cells for eliciting tumor immunity (Suot, R & Srivastava, P (1995) *Science* 269:1585-1588; Tamura, Y. *et al.* (1997) *Science* 278:117-120).

[0684] Dendritic cells (DC) are potent antigen presenting cells that can be used to prime antigen-specific responses. DC's can be produced *ex vivo* and loaded with various protein and peptide antigens as well as tumor cell extracts (Nestle, F. *et al.* (1998) *Nature Medicine* 4: 328-332). DCs may also be transduced by genetic means to express these tumor antigens as well. DCs have also been fused directly to tumor cells for the purposes of immunization (Kugler, A. *et al.* (2000) *Nature Medicine* 6:332-336). As a method of vaccination, DC immunization may be effectively combined with CD73 blockade to activate more potent anti-tumor responses.

Exemplary Oncolytic Viruses

[0685] Anti-human ENTPD2 antibody molecules can be administered in combination with oncolytic viruses. In embodiments, oncolytic viruses are capable of selectively replicating in and triggering the death of or slowing the growth of a cancer cell. In some cases, oncolytic viruses have no effect or a minimal effect on non-cancer cells. In some embodiments, the combination is used to treat a cancer, *e.g.,* a cancer described herein. An oncolytic virus includes, but is not limited to, an oncolytic adenovirus, oncolytic Herpes Simplex Viruses, oncolytic retrovirus, oncolytic parvovirus, oncolytic vaccinia virus, oncolytic Sindbis virus, oncolytic influenza virus, or oncolytic RNA virus (*e.g.,* oncolytic reovirus, oncolytic Newcastle Disease Virus (NDV), oncolytic measles virus, or oncolytic vesicular stomatitis virus (VSV)).

[0686] Exemplary oncolytic viruses include but are not limited to the following:

Group B Oncolytic Adenovirus (ColoAd1) (PsiOxus Therapeutics Ltd.) (*see*, *e.g.,* Clinical Trial Identifier: NCT02053220);

ONCOS-102 (previously called CGTG-102), which is an adenovirus comprising granulocyte-macrophage colony stimulating factor (GM-CSF) (Oncos Therapeutics) (*see*, *e.g.,* Clinical Trial Identifier: NCT01598129);

VCN-01, which is a genetically modified oncolytic human adenovirus encoding human PH20 hyaluronidase (VCN Biosciences, S.L.) (*see*, *e.g.,* Clinical Trial Identifiers: NCT02045602 and NCT02045589);

Conditionally Replicative Adenovirus ICOVIR-5, which is a virus derived from wild-type human adenovirus serotype 5 (Had5) that has been modified to selectively replicate in

cancer cells with a deregulated retinoblastoma/E2F pathway (Institut Català d'Oncologia) (*see*, *e.g.,* Clinical Trial Identifier: NCT01864759);

Celyvir, which comprises bone marrow-derived autologous mesenchymal stem cells (MSCs) infected with ICOVIR5, an oncolytic adenovirus (Hospital Infantil Universitario Niño Jesús, Madrid, Spain/ Ramon Alemany) (*see*, *e.g.,* Clinical Trial Identifier: NCT01844661);

CG0070, which is a conditionally replicating oncolytic serotype 5 adenovirus (Ad5) in which human E2F-1 promoter drives expression of the essential E1a viral genes, thereby restricting viral replication and cytotoxicity to Rb pathway-defective tumor cells (Cold Genesys, Inc.) (*see*, *e.g.,* Clinical Trial Identifier: NCT02143804); or

DNX-2401 (formerly named Delta-24-RGD), which is an adenovirus that has been engineered to replicate selectively in retinoblastoma (Rb)-pathway deficient cells and to infect cells that express certain RGD-binding integrins more efficiently (Clinica Universidad de Navarra, Universidad de Navarra/ DNAtrix, Inc.) (*see*, *e.g.,* Clinical Trial Identifier: NCT01956734).

[0687] In some embodiments, an oncolytic virus described herein is administering by injection, *e.g.,* subcutaneous, intra-arterial, intravenous, intramuscular, intrathecal, or intraperitoneal injection. In embodiments, an oncolytic virus described herein is administered intratumorally, transdermally, transmucosally, orally, intranasally, or via pulmonary administration.

Additional Exemplary Cancer Therapies

[0688] Exemplary combinations of anti-human ENTPD2 antibody molecules (alone or in combination with other stimulatory agents) and standard of care for cancer, include at least the following. In certain embodiments, the anti-human ENTPD2 antibody molecule, *e.g.*, the anti-human ENTPD2 antibody molecule described herein, is used in combination with a standard of cancer care chemotherapeutic agent including, but not limited to, anastrozole (Arimidex®), bicalutamide (Casodex®), bleomycin sulfate (Blenoxane®), busulfan (Myleran®), busulfan injection (Busulfex®), capecitabine (Xeloda®), N4-pentoxycarbonyl-5-deoxy-5-fluorocytidine, carboplatin (Paraplatin®), carmustine (BiCNU®), chlorambucil (Leukeran®), cisplatin (Platinol®), cladribine (Leustatin®), cyclophosphamide (Cytoxan® or Neosar®), cytarabine, cytosine arabinoside (Cytosar-U®), cytarabine liposome injection (DepoCyt®), dacarbazine (DTIC-Dome®), dactinomycin

(Actinomycin D, Cosmegan), daunorubicin hydrochloride (Cerubidine®), daunorubicin citrate liposome injection (DaunoXome®), dexamethasone, docetaxel (Taxotere®), doxorubicin hydrochloride (Adriamycin®, Rubex®), etoposide (Vepesid®), fludarabine phosphate (Fludara®), 5-fluorouracil (Adrucil®, Efudex®), flutamide (Eulexin®), tezacitibine, Gemcitabine (difluorodeoxycitidine), hydroxyurea (Hydrea®), Idarubicin (Idamycin®), ifosfamide (IFEX®), irinotecan (Camptosar®), L-asparaginase (ELSPAR®), leucovorin calcium, melphalan (Alkeran®), 6-mercaptopurine (Purinethol®), methotrexate (Folex®), mitoxantrone (Novantrone®), mylotarg, paclitaxel (Taxol®), phoenix (Yttrium90/MX-DTPA), pentostatin, polifeprosan 20 with carmustine implant (Gliadel®), tamoxifen citrate (Nolvadex®), teniposide (Vumon®), 6-thioguanine, thiotepa, tirapazamine (Tirazone®), topotecan hydrochloride for injection (Hycamptin®), vinblastine (Velban®), vincristine (Oncovin®), vinorelbine (Navelbine®), Ibrutinib, idelalisib, and brentuximab vedotin.

[0689] In certain embodiments, the anti-human ENTPD2 antibody molecule, *e.g.*, the anti-human ENTPD2 antibody molecule described herein, is used in combination with an alkylating agent including, but not limited to, nitrogen mustards, ethylenimine derivatives, alkyl sulfonates, nitrosoureas and triazenes): uracil mustard (Aminouracil Mustard®, Chlorethaminacil®, Demethyldopan®, Desmethyldopan®, Haemanthamine®, Nordopan®, Uracil nitrogen mustard®, Uracillost®, Uracilmostaza®, Uramustin®, Uramustine®), chlormethine (Mustargen®), cyclophosphamide (Cytoxan®, Neosar®, Clafen®, Endoxan®, Procytox®, Revimmune™), ifosfamide (Mitoxana®), melphalan (Alkeran®), Chlorambucil (Leukeran®), pipobroman (Amedel®, Vercyte®), triethylenemelamine (Hemel®, Hexalen®, Hexastat®), triethylenethiophosphoramine, Temozolomide (Temodar®), thiotepa (Thioplex®), busulfan (Busilvex®, Myleran®), carmustine (BiCNU®), lomustine (CeeNU®), streptozocin (Zanosar®), and Dacarbazine (DTIC-Dome®). Additional exemplary alkylating agents include, without limitation, Oxaliplatin (Eloxatin®); Temozolomide (Temodar® and Temodal®); Dactinomycin (also known as actinomycin-D, Cosmegen®); Melphalan (also known as L-PAM, L-sarcolysin, and phenylalanine mustard, Alkeran®); Altretamine (also known as hexamethylmelamine (HMM), Hexalen®); Carmustine (BiCNU®); Bendamustine (Treanda®); Busulfan (Busulfex® and Myleran®); Carboplatin (Paraplatin®); Lomustine (also known as CCNU, CeeNU®); Cisplatin (also known as CDDP, Platinol® and Platinol®-AQ); Chlorambucil (Leukeran®);

Cyclophosphamide (Cytoxan® and Neosar®); Dacarbazine (also known as DTIC, DIC and imidazole carboxamide, DTIC-Dome®); Altretamine (also known as hexamethylmelamine (HMM), Hexalen®); Ifosfamide (Ifex®); Prednumustine; Procarbazine (Matulane®); Mechlorethamine (also known as nitrogen mustard, mustine and mechloroethamine hydrochloride, Mustargen®); Streptozocin (Zanosar®); Thiotepa (also known as thiophosphoamide, TESPA and TSPA, Thioplex®); Cyclophosphamide (Endoxan®, Cytoxan®, Neosar®, Procytox®, Revimmune®); and Bendamustine HCl (Treanda®).

[0690] In certain embodiments, the anti-human ENTPD2 antibody molecule, *e.g.*, the anti-human ENTPD2 antibody molecule described herein, is used in combination with anthracyclines including, but not limited to, *e.g.*, doxorubicin (Adriamycin® and Rubex®); bleomycin (lenoxane®); daunorubicin (dauorubicin hydrochloride, daunomycin, and rubidomycin hydrochloride, Cerubidine®); daunorubicin liposomal (daunorubicin citrate liposome, DaunoXome®); mitoxantrone (DHAD, Novantrone®); epirubicin (Ellence™); idarubicin (Idamycin®, Idamycin PFS®); mitomycin C (Mutamycin®); geldanamycin; herbimycin; ravidomycin; and desacetylravidomycin. Exemplary vinca alkaloids that can be used in combination with the anti-human ENTPD2 antibody molecules, include, but ate not limited to, vinorelbine tartrate (Navelbine®), Vincristine (Oncovin®), and Vindesine (Eldisine®)); vinblastine (also known as vinblastine sulfate, vincaleukoblastine and VLB, Alkaban-AQ® and Velban®); and vinorelbine (Navelbine®).

[0691] Exemplary proteosome inhibitors that can be used in combination with the anti-human ENTPD2 antibody as described herein include, but are not limited to, bortezomib (Velcade®); carfilzomib (PX-171-007, (*S*)-4-Methyl-*N*-((*S*)-1-(((*S*)-4-methyl-1-((*R*)-2-methyloxiran-2-yl)-1-oxopentan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)-2-((*S*)-2-(2-morpholinoacetamido)-4-phenylbutanamido)-pentanamide); marizomib (NPI-0052); ixazomib citrate (MLN-9708); delanzomib (CEP-18770); and *O*-Methyl-*N*-[(2-methyl-5-thiazolyl)carbonyl]-L-seryl-*O*-methyl-*N*-[(1*S*)-2-[(2*R*)-2-methyl-2-oxiranyl]-2-oxo-1-(phenylmethyl)ethyl]- L-serinamide (ONX-0912).

[0692] In certain embodiments, the anti-human ENTPD2 antibody molecule, is administered in combination with radiation therapy. Radiation therapy can be administered through one of several methods, or a combination of methods, including without limitation external-beam therapy, internal radiation therapy, implant radiation, stereotactic radiosurgery, systemic radiation therapy, radiotherapy and permanent or temporary interstitial brachytherapy. The term “brachytherapy,” refers to radiation therapy delivered by a spatially

confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. The term is intended without limitation to include exposure to radioactive isotopes (*e.g.*, At-211, I-131, I-125, Y-90, Re-186, Re-188, Sm-153, Bi-212, P-32, and radioactive isotopes of Lu). Suitable radiation sources for use as a cell conditioner of the present invention include both solids and liquids. By way of non-limiting example, the radiation source can be a radionuclide, such as I-125, I-131, Yb-169, Ir-192 as a solid source, I-125 as a solid source, or other radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material can also be a fluid made from any solution of radionuclide(s), *e.g.,* a solution of I-125 or I-131, or a radioactive fluid can be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90.

[0693] ENTPD2 blockade may also be effectively combined with chemotherapeutic regimes. In these instances, it may be possible to reduce the dose of chemotherapeutic reagent administered.

[0694] Exemplary cytotoxic agents that can be administered in combination with an anti-human ENTPD2 antibody molecule include antimicrotubule agents, topoisomerase inhibitors, anti-metabolites, mitotic inhibitors, alkylating agents, anthracyclines, vinca alkaloids, intercalating agents, agents capable of interfering with a signal transduction pathway, agents that promote apoptosis, proteosome inhibitors, and radiation (*e.g.*, local or whole body irradiation).

Sample Preparation

[0695] Samples used in the methods described herein can be obtained from a subject using any one of the methods known in the art, e.g., by biopsy or surgery. The sample may be flash frozen and stored at -80°C for later use. The sample may also be fixed with a fixative, such as formaldehyde, paraformaldehyde, or acetic acid/ethanol. RNA or protein may be extracted from a fresh, frozen or fixed sample for analysis.

Pharmaceutical Compositions, Dosage, and Methods of Administration

[0696] Also provided herein are compositions, e.g., pharmaceutical compositions, for use in treatment of a ENTPD2-associated disease, e.g., a cancer as described herein. Such compositions include one or more antibodies or antigen binding fragments described herein, nucleic acids encoding such antibodies or antigen binding fragments, or vectors comprising a

nucleic acid encoding such antibodies or antigen binding fragments. Such compositions can further include another agent, e.g., a current standard of care for the disease to be treated.

[0697] Pharmaceutical compositions typically include a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" includes saline, solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Pharmaceutical compositions are typically formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral (e.g., intravenous, intraarterial, intraperitoneal), intracranial, intrathecal, or intranasal (e.g., inhalation), intradermal, subcutaneous, or intratumor administration.

[0698] The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0699] In some embodiments, the pharmaceutical compositions comprise one or more pharmaceutically acceptable carriers, including, e.g., ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol, and wool fat.

[0700] Methods of formulating suitable pharmaceutical compositions are known in the art, see, e.g., Remington: The Science and Practice of Pharmacy. 21st ed., 2005; and the books in the series Drugs and the Pharmaceutical Sciences: a Series of Textbooks and Monographs (Dekker, NY). For example, solutions or suspensions used for parenteral or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerin, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents

for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[0701] Pharmaceutical compositions suitable for injectable use can include sterile aqueous solutions (where water soluble) or dispersions and sterile powders, for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent that delays absorption, for example, aluminum monostearate and gelatin.

[0702] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization.

[0703] Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle, which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying, which yield a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[0704] Parenteral formulations can be a single bolus dose, an infusion or a loading bolus dose followed with a maintenance dose. These compositions can be administered at specific fixed or variable intervals, e.g., once a day, or on an “as needed” basis.

[0705] A suitable pharmaceutical composition for injection can comprise a buffer (e.g., acetate, phosphate or citrate buffer), a surfactant (e.g., polysorbate), optionally a stabilizer agent (e.g., human albumin), etc. Preparations for peripheral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include, e.g., water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. In some embodiments, the pharmaceutical composition comprises 0.01-0.1 M phosphate buffer or 0.8% saline. Other common parenteral vehicles include sodium phosphate solutions, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers, such as those based on Ringer's dextrose, and the like. Preservatives and other additives can also be present such as, for example, antimicrobials, antioxidants, chelating agents, and inert gases and the like.

[0706] In one embodiment, the therapeutic compounds are prepared with carriers that will protect the therapeutic compounds against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems.

[0707] The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

[0708] Dosage, toxicity and therapeutic efficacy of the therapeutic compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds which exhibit high therapeutic indices are preferred. While compounds that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

[0709] The data obtained from cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma

concentration range that includes the IC50 (i.e., the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

Kits

[0710] Also provided herein are kits including one or more of the compositions provided herein and instructions for use. Instructions for use can include instructions for diagnosis or treatment of a ENTPD2-associated disease, e.g., a cancer, as described herein. Kits as provided herein can be used in accordance with any one of the methods described herein. Those skilled in the art will be aware of other suitable uses for kits provided herein, and will be able to employ the kits for such uses. Kits as provided herein can also include a mailer (e.g., a postage paid envelope or mailing pack) that can be used to return the sample for analysis, e.g., to a laboratory. The kit can include one or more containers for the sample, or the sample can be in a standard blood collection vial. The kit can also include one or more of an informed consent form, a test requisition form, and instructions on how to use the kit in a method described herein. Methods for using such kits are also included herein. One or more of the forms (e.g., the test requisition form) and the container holding the sample can be coded, for example, with a bar code for identifying the subject who provided the sample.

[0711] One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. Indeed, the present invention is in no way limited to the methods and materials described.

EXAMPLES

[0712] 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 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. The invention is further described in the following examples, which do not limit the scope of the invention described in the claims.

Example 1: Expression of ENTPD2 in Cancer

[0713] Ectonucleoside triphosphate diphosphohydrolase 2 (also referred to as ENTPD2, NTPDase 2, NTPDase-2, Ecto-ATPase 2, Ecto-ATPDase 2, CD39 Antigen-like 1, CD39L1, ecto-ATP-Diphosphohydrolase 2) belongs to a family of extracellular ATP hydrolases that regulate purinergic signaling, specifically ATP, UTP, as well as ADP and UDP in the extracellular space (for review see Robson et al Purinergic Signaling 2:409-430 (2006)). End product of ATP/ADP hydrolysis 5'AMP is subsequently dephosphorylated to adenosine by the ecto-5'-nucleotidase (also known as Ecto5'Ntase or CD73).

[0714] The functional role of ENTPD2 in cancer has not been well described. Early reports focused on ENTPD2 overexpression in a rat glioma model which led to enhanced *in vivo* tumor growth through ADP-mediated modulation of platelets and the tumor microenvironment, as well as promoted an inflammatory state potentiating tumor spread (Braganhol et al Cancer Sci 100(8): 1434-42 (2009); Braganhol et al Purinergic Signal 8(2):235-43 (2012)). More recently elevated expression of ENTPD2 was reported in hepatocellular carcinoma, where its expression was associated with worse prognosis due to enhanced myeloid-derived suppressor cell accumulation / maintenance (Chiu et al Nature Communications 8(1): 517 (2017)).

[0715] Although the functional characterization of ENTPD2 in cancer is limited in the public domain, the purinergic mediators such as ATP and adenosine, released into the extracellular space, have been shown to play important role in immunity and inflammation. ATP released from stressed, damaged or apoptotic cells triggers rapid inflammation via activation of P2RX and P2RY receptors that enhance recruitment of immune cells, potentiate TCR signaling in T cells and promote dendritic and macrophage cell activation. On the other hand, adenosine signaling results in an immunosuppressive niche through inhibition of effector T cells, as well as deregulation of mononuclear phagocyte cells (for reviews see Cekic et al Nature Reviews Immunology 16: 177-192 (2016), Antonioli et al Nature Reviews Cancer 13: 842-857 (2013)). Pre-clinically blockade of adenosine signaling or restoration of extracellular ATP at the tumor site have demonstrated to induce lymphocyte recruitment and anti-tumor responses (Michaud et al Science 334(6062): 1573-7 (2011); Allard et al Clinical Cancer Research 19(20): 5626-35 (2013)) .

[0716] Elevated expression of ENTPD2 in cancer cells has the potential to dramatically alter the balance of purinergic signaling in the tumor microenvironment, shifting it towards a more immunosuppressive state. Targeted inhibition of ENTPD2 catalytic

function can therefore provide an opportunity to shift the balance towards an ATP-driven pro-inflammatory Th-1 like state, potentiating anti-tumor immune response.

[0717] ENTPD2 expression has not been carefully examined across different tumor subtypes. Anti-human ENTPD2 mAb1 was used to assess ENTPD2 expression across cancer cell lines from different indications. Cells were stained with Anti-human ENTPD2 mAb1 at 5 μg/ml for 45 min on ice, followed by an incubation with goat anti-human IgG, Fcγ specific, Alexa Fluor 647 or APC conjugated secondary Ab (1:400 dilution; Jackson ImmunoResearch Laboratories, West Grove, PA). All incubations and washes were performed in FACS Buffer composed of 1x HyClone Phosphate Buffered Saline (GE Healthcare, Pittsburg, PA), 1% HyClone Fetal Bovine Serum (GE Healthcare, Pittsburg, PA), 2mM EDTA (ThermoFisher, Waltham MA).

[0718] Elevated expression of ENTPD2 was observed in representative cancer cell lines from colorectal, esophageal, gastric, breast and lung cancer indications as shown in FIG. 1A. ENTPD2 receptor density was quantified using the Quantum Simply Cellular anti-Human IgG from Bangs Laboratories (Fishers, IN) according to manufacturer's directions (Table 20, FIG. 1B).

[0719] In order to assess ENTPD2 protein expression in primary tumor tissues, formalin-fixed paraffin-embedded tumor tissue microarrays with matched adjacent normal tissues were obtained from Cureline (Brisbane, CA). IHC staining was performed with the anti-CD39L1/ENTPD2 IHC Ab (NBP1-85752, Novus, Littleton, CO) using an automated Ventana protocol with standard high pH CC1 antigen retrieval at 95°C, and followed by incubations with Ventana DISCOVERY® OmniMap anti-Rb HRP secondary Ab and Ventana DISCOVERY® ChromoMap DAB Kit (Ventana, Tuscon AZ).

[0720] Elevated ENTPD2 expression, localized to the cell membrane, was observed in subsets of colorectal, esophageal and ovarian tumor samples. None or very low background levels of ENTPD2 expression was detected in the matched normal tissue sections (FIG. 2).

Example 2: Generation of humanized monoclonal antibodies that bind to human ENTPD2

Generation of expression constructs for human, rat, mouse and cynomolgus monkey ENTPD2

[0721] Nucleotide sequences encoding full-length ENTPD2 from human, cynomolgus macaque (cyno), rat and mouse as well as ENTPD1 (CD39) from human and mouse were synthesized based on amino acid sequences from the GenBank® or UniProtKB databases (see Table 24). All synthesized DNA fragments were cloned into appropriate expression vectors.

Table 24. Sequences of reagents used for generating anti-ENTPD2 antibody

Human ENTPD2: NP_982293	
SEQ ID NO: 291	MAGKVRSLLPPLLLAAAGLAGLLLLCVPTRDVREPPALKYGIVL DAGSSHTSMFIYKWPADKENDTGIVGQHSSCDVPGGGISSYADN PSGASQSLVGCLEQALQDVPKERHAGTPLYLGATAGMRLLNLTN PEASTSVLMAVTHTLTQYPFDFRGARILSGQEEGVFGWVTANYL LENFIKYGWVGRWFRPRKGTLGAMDLGGASTQITFETTSPAEDR ASEVQLHLYGQHYRVYTHSFLCYGRDQVLQRLLASALQTHGFH PCWPRGFSTQVLLGDVYQSPCTMAQRPQNFNSSARVSLSGSSDP HLCRDLVSGLFSFSSCPFSRCSFNGVFQPPVAGNFVAFSAFFYTVD FLRTSMGLPVATLQQLEAAAVNVCNQTWAQLQARVPGQRARLA DYCAGAMFVQQLLSRGYGFDERAFGGVIFQKKAADTAVGWAL GYMLNLTNLIPADPPGLRKGTDFSSWVVLLLLFASALLAALVLLL RQVHSAKLPSTI
SEQ ID NO: 342	ATGGCCGGGAAGGTGCGGTCACTGCTGCCGCCGCTGCTGCTG GCCGCCGCGGGCCTCGCCGGCCTCCTACTGCTGTGCGTCCCCA CCCGCGACGTCCGGGAGCCGCCCGCCCTCAAGTATGGCATCGT CCTGGACGCTGGTTCTTCACACACGTCCATGTTTATCTACAAG TGGCCGGCAGACAAGGAGAACGACACAGGCATTGTGGGCCAG CACAGCTCCTGTGATGTTCCAGGTGGGGGCATCTCCAGCTATG CAGACAACCCTTCTGGGGCCAGCCAGAGTCTTGTTGGATGCCT CGAACAGGCGCTTCAGGATGTGCCCAAAGAGAGACACGCGGG CACACCCCTCTACCTGGGAGCCACAGCGGGTATGCGCCTGCTC AACCTGACCAATCCAGAGGCCTCGACCAGTGTGCTCATGGCA GTGACTCACACACTGACCCAGTACCCCTTTGACTTCCGGGGTG CACGCATCCTCTCGGGCCAGGAAGAGGGGGTGTTTGGCTGGG TGACTGCCAACTACCTGCTGGAGAACTTCATCAAGTACGGCTG GGTGGGCCGGTGGTTCCGGCCACGGAAGGGGACACTGGGGGC CATGGACCTGGGGGGTGCCTCTACCCAGATCACTTTTGAGACA ACCAGTCCAGCTGAGGACAGAGCCAGCGAGGTCCAGCTGCAT CTCTACGGCCAGCACTACCGAGTCTACACCCACAGCTTCCTCT GCTATGGCCGTGACCAGGTCCTCCAGAGGCTGCTGGCCAGCG CCCTCCAGACCCACGGCTTCCACCCCTGCTGGCCGAGGGGCTT TTCCACCCAAGTGCTGCTCGGGGATGTGTACCAGTCACCATGC ACCATGGCCCAGCGGCCCCAGAACTTCAACAGCAGTGCCAGG GTCAGCCTGTCAGGGAGCAGTGACCCCCACCTCTGCCGAGATC TGGTTTCTGGGCTCTTCAGCTTCTCCTCCTGCCCCTTCTCCCGA TGCTCTTTCAATGGGGTCTTCCAGCCCCCAGTGGCTGGGAACT TTGTGGCCTTCTCTGCCTTCTTCTACACTGTGGACTTTTTGCGG ACTTCGATGGGGCTGCCCGTGGCCACCCTGCAGCAGCTGGAG GCAGCCGCAGTGAATGTCTGCAACCAGACCTGGGCTCAGCTG CAAGCTCGGGTGCCAGGGCAACGGGCCCGCCTGGCCGACTAC TGCGCCGGGGCCATGTTCGTGCAGCAGCTGCTGAGTCGCGGCT ACGGCTTCGACGAGCGCGCCTTCGGCGGCGTGATCTTCCAGAA

	GAAGGCCGCGGACACTGCAGTGGGCTGGGCGCTCGGCTACAT GCTGAACCTGACCAACCTGATCCCCGCCGACCCGCCGGGGCT GCGCAAGGGCACAGACTTCAGCTCCTGGGTCGTCCTCCTGCTG CTCTTCGCCTCCGCGCTCCTGGCTGCGCTTGTCCTGCTGCTGCG TCAGGTGCACTCCGCCAAGCTGCCAAGCACCATT
CynoENTPD2: XP_005580409	
SEQ ID NO: 343	MAGKVRSLLPPLLLAAAGLAGLLLLCVPTRDIREPPALKYGIVLD AGSSHTSMFIYKWPADKENDTGIVGQHSSCDVPGGGISSYADNPS GAGQSLVGCLEQALRDVPKERHAGTPLYLGATAGMRLLNLTNP EASTSVLTAVTHTLTQYPFDFRGARILSGQEEGVFGWVTANYLLE NFIKYGWVGRWFRPRKGTLGAMDLGGASTQITFETTSPAEDRAS EVQLRLYGQHYRVYTHSFLCYGRDQVLQRLLASALQTHSFHPC WPRGFSTHVLLGDVYQSPCTVAQRPQTFNSSARVSLSGSSDPHLC RDLVSGLFSFSSCPFSRCSFNGVFQPPVAGNFIAFSAFFYTVNFLRT SMGLPVATLQQLEAAAVNVCNQTWAQLQARVPGQQAHLADYC AGAMFVQQLLSRGYGFDERAFGGVIFQKKAADTAVGWALGYM LNLTNLIPADPPGLRKGTDFSSWVVLLLLFASALLAALVLLLHQV HSAKLPSTI
SEQ ID NO: 344	ATGGCCGGGAAGGTGCGGTCACTGCTGCCGCCGCTGCTGCTG GCCGCCGCGGGCCTCGCCGGCCTCCTACTGCTGTGCGTGCCCA CCAGGGACATTAGGGAGCCTCCCGCTCTGAAATACGGCATCG TGCTGGACGCCGGAAGCAGCCACACCTCCATGTTCATCTACAA GTGGCCCGCCGACAAGGAGAACGACACAGGCATCGTGGGCCA GCATAGCTCCTGCGACGTGCCTGGAGGCGGCATCTCCAGCTAC GCCGACAATCCTTCCGGCGCTGGACAGTCCCTGGTGGGATGTC TGGAGCAGGCCCTGAGGGACGTGCCTAAGGAGAGACACGCCG GCACCCCTCTGTACCTGGGAGCCACAGCCGGCATGAGACTCCT GAATCTGACCAACCCTGAGGCCTCCACCTCCGTCCTGACAGCC GTGACACATACCCTGACCCAGTACCCCTTCGATTTCAGGGGAG CCAGAATACTGAGCGGCCAGGAAGAAGGCGTGTTCGGATGGG TGACCGCCAACTACCTCCTGGAGAACTTCATCAAGTACGGCTG GGTGGGCAGGTGGTTTAGACCCAGGAAGGGCACCCTGGGAGC TATGGATCTGGGCGGAGCTTCCACACAGATCACCTTCGAGACC ACCTCCCCCGCTGAGGACAGAGCCTCCGAGGTGCAGCTGAGG CTGTACGGCCAGCATTACAGGGTGTATACACACAGCTTCCTGT GCTACGGCAGGGACCAGGTCCTGCAGAGACTGCTCGCTTCCG CCCTGCAGACCCACTCCTTCCACCCTTGCTGGCCTAGGGGCTT TAGCACCCATGTGCTCCTGGGAGATGTGTACCAGAGCCCCTGC ACCGTGGCCCAAAGACCCCAGACCTTTAACTCCTCCGCTAGAG TGAGCCTGAGCGGCAGCTCCGATCCCCACCTGTGTAGGGACCT GGTCAGCGGACTGTTCAGCTTCAGCAGCTGCCCTTTCAGCAGG TGCAGCTTCAATGGCGTGTTCCAGCCTCCCGTGGCCGGCAACT TCATCGCTTTCTCCGCCTTCTTCTACACCGTCaACTTTCTGAGG ACAAGCATGGGACTGCCCGTGGCTACCCTCCAACAACTGGAG GCCGCCGCCGTGAACGTGTGCAACCAGACATGGGCCCAACTG CAGGCTAGGGTGCCCGGCCAACAGGCCCATCTGGCTGACTAC TGTGCCGGCGCCATGTTCGTGCAGCAGCTGCTGAGCAGGGGCT ATGGATTCGACGAGAGGGCCTTCGGCGGCGTCATCTTCCAAA AGAAGGCCGCCGATACAGCCGTGGGCTGGGCTCTGGGCTACA TGCTGAACCTGACAAACCTGATCCCCGCTGACCCCCCCGGACT GAGGAAGGGAACCGATTTCAGCAGCTGGGTCGTGCTCCTGCT

	GCTGTTTGCTAGCGCCCTGCTCGCCGCTCTGGTGCTGCTGCTG CACCAGGTGCACTCCGCCAAGCTGCCCAGCACCATT
Mouse ENTPD2: NP_033979	
SEQ ID NO: 345	MAGKLVSLVPPLLLAAVGLAGLLLLCVPTQDVREPPALKYGIVL DAGSSHTSMFVYKWPADKENDTGIVGQHSSCDVRGGGISSYAN DPSRAGQSLVECLEQALRDVPKDRYASTPLYLGATAGMRLLNLT SPEATAKVLEAVTQTLTRYPFDFRGARILSGQDEGVFGWVTANY LLENFIKYGWVGRWIRPRKGTLGAMDLGGASTQITFETTSPSEDP DNEVHLRLYGQHYRVYTHSFLCYGRDQVLQRLLASALQIHRFHP CWPKGYSTQVLLREVYQSPCTMGQRPQTFNSSATVSLSGTSNAA LCRDLVSGLFNISSCPFSQCSFNGVFQPPVAGNFIAFSAFYYTVDF LKTVMGLPVGTLKQLEDATETTCNQTWAELQARVPGQQTRLPD YCAVAMFIHQLLSRGYRFDERSFRGVVFEKKAADTAVGWALGY MLNLTNLIPADLPGLRKGTHFSSWVALLLLFTVLILAALVLLLRQ VRSAKSPGAL
SEQ ID NO: 346	ATGGCTGGAAAGTTGGTGTCACTGGTGCCACCCCTGCTGCTGG CTGCCGTGGGCCTCGCCGGCCTCCTGCTACTGTGCGTCCCTAC CCAAGACGTCCGGGAGCCGCCCGCCCTCAAGTATGGCATCGTT CTGGATGCTGGCTCTTCACACACATCCATGTTTGTCTACAAGT GGCCAGCGGACAAGGAAAATGACACAGGTATCGTGGGCCAGC ACAGCTCTTGCGATGTTCGAGGTGGTGGCATCTCCAGCTACGC AAATGACCCTTCTAGGGCAGGCCAGAGTCTGGTTGAATGTCTT GAACAGGCACTTCGGGATGTGCCCAAAGACAGATATGCCAGC ACTCCACTCTACCTGGGAGCTACAGCAGGCATGCGCCTACTCA ACCTGACCAGCCCAGAGGCCACAGCCAAGGTGCTGGAGGCAG TGACACAGACGCTCACACGGTACCCCTTTGACTTCCGTGGTGC CCGCATCCTCTCGGGACAGGATGAAGGGGTGTTTGGCTGGGT GACTGCCAACTACCTGCTGGAGAACTTCATCAAGTATGGCTGG GTAGGCCGGTGGATACGGCCAAGGAAGGGAACTCTGGGGGCC ATGGACCTTGGGGGTGCCTCAACACAGATCACCTTTGAGACA ACCAGTCCATCTGAAGATCCAGATAATGAGGTCCATTTGCGGC TCTATGGCCAGCATTACCGTGTCTACACCCATAGCTTCCTCTG CTATGGCCGGGACCAGGTTCTCCAGAGGCTTCTGGCCAGTGCC CTCCAGATCCATCGCTTCCACCCCTGCTGGCCAAAGGGCTACT CCACCCAAGTGCTGCTCCGGGAAGTCTACCAGTCTCCATGCAC TATGGGTCAGCGTCCCCAGACCTTCAACAGCAGTGCCACTGTC AGCCTGTCAGGGACCAGCAACGCTGCCCTCTGTCGTGACCTCG TCTCTGGGCTCTTCAATATCTCCTCCTGTCCCTTTTCCCAATGC TCCTTCAATGGGGTTTTCCAGCCTCCCGTGGCTGGGAACTTCA TAGCCTTTTCTGCTTTCTACTATACTGTAGACTTCCTGAAGACA GTGATGGGGCTGCCTGTGGGAACCCTGAAGCAGCTGGAGGAT GCCACAGAGACCACCTGCAACCAGACCTGGGCTGAGCTTCAG GCCCGAGTACCCGGACAGCAGACCCGCCTGCCTGACTACTGC GCTGTAGCCATGTTCATACATCAGCTATTGAGCCGCGGTTATC GCTTCGACGAGCGCTCTTTCCGTGGAGTGGTCTTCGAAAAGAA GGCGGCAGACACGGCTGTCGGCTGGGCGCTGGGCTACATGCT GAATTTGACCAACCTGATTCCCgctgacctcccgggactacgtaagggcacccac TTCAGCTCCTGGGTTGCTCTCCTGCTGCTCTTCACAGTCCTGAT CTTGGCGGCTTTGGTCCTGCTCTTGCGCCAGGTGCGCTCTGCC AAGTCCCCAGGCGCCCTC
RatENTPD2: NP_742027	

SEQ ID NO: 347	MAGKLVSLVPPLLLAAAGLAGLLLLCVPTQDVREPPALKYGIVL DAGSSHTSMFVYKWPADKENDTGIVGQHSSCDVQGGGISSYAN DPSKAGQSLVRCLEQALRDVPRDRHASTPLYLGATAGMRLLNLT SPEATARVLEAVTQTLTQYPFDFRGARILSGQDEGVFGWVTANY LLENFIKYGWVGRWIRPRKGTLGAMDLGGASTQITFETTSPSEDP GNEVHLRLYGQHYRVYTHSFLCYGRDQILLRLLASALQIHRFHPC WPKGYSTQVLLQEVYQSPCTMGQRPRAFNGSAIVSLSGTSNATL CRDLVSRLFNISSCPFSQCSFNGVFQPPVTGNFIAFSAFYYTVDFLT TVMGLPVGTLKQLEEATEITCNQTWTELQARVPGQKTRLADYC AVAMFIHQLLSRGYHFDERSFREVVFQKKAADTAVGWALGYML NFTNLIPADLPGLRKGTHFSSWVALLLLFTVLILAALVLLLRQVRS AKSPGAL
SEQ ID NO: 348	ATGGCTGGAAAGTTGGTGTCACTGGTGCCACCCCTGCTGCTGG CTGCCGcGGGCCTCGCCGGCCTCCTGCTACTGTGCGTCCCTACC CAAGACGTCCGGGAGCCGCCCGCCCTCAAGTATGGCATCGTTC TGGATGCTGGCTCTTCACACACATCCATGTTTGTCTACAAGTG GCCAGCGGACAAGGAAAATGACACAGGTATCGTGGGCCAGCA CAGCTCCTGCGATGTGCAGGGCGGCGGCATTTCCAGCTATGCC AACGACCCCTCCAAAGCCGGACAGTCCCTGGTCAGGTGCCTG GAGCAGGCCCTGAGAGACGTCCCCAGAGACAGACACGCGAGC ACCCCTCTGTATCTCGGCGCCACAGCCGGCATGAGGCTGCTGA ACCTGACCTCCCCTGAGGCCACAGCCAGAGTCCTGGAGGCTGT CACCCAGACCCTGACACAGTACCCCTTCGACTTTAGGGGCGCC AGAATACTGTCCGGCCAGGATGAAGGCGTGTTCGGCTGGGTG ACAGCCAACTACCTGCTGGAGAACTTTATTAAGTACGGCTGGG TGGGCAGATGGATCAGGCCCAGGAAGGGCACCCTGGGAGCCA TGGATCTCGGCGGAGCCTCCACCCAGATCACCTTTGAGACCAC CAGCCCCTCCGAAGACCCGGGCAATGAGGTCCACCTGAGGCT GTACGGCCAGCACTATAGAGTCTACACCCACAGCTTCCTGTGC TACGGCAGAGATCAAATCCTGCTGAGACTGCTCGCTTCCGCCC TGCAGATTCATAGGTTTCACCCCTGCTGGCCCAAAGGCTACAG CACCCAGGTGCTGCTCCAAGAGGTGTACCAGAGCCCTTGCACC ATGGGACAGAGACCCAGGGCTTTCAACGGAAGCGCCATCGTG TCCCTCAGCGGCACCAGCAACGCCACCCTGTGTAGGGACCTCG TGAGCAGACTGTTCAACATCTCCTCCTGCCCTTTCAGCCAGTG TTCCTTCAATGGCGTGTTTCAGCCCCCTGTGACAGGCAACTTC ATCGCCTTCAGCGCTTTCTACTACACCGTGGACTTTCTCACAA CCGTCATGGGCCTGCCCGTGGGAACCCTGAAGCAACTGGAGG AAGCCACCGAGATCACCTGCAACCAGACCTGGACCGAACTGC AAGCCAGGGTGCCCGGCCAGAAGACCAGACTGGCCGACTACT GTGCTGTCGCCATGTTCATTCACCAACTGCTGAGCAGGGGCTA CCACTTCGATGAAAGGAGCTTCAGGGAGGTGGTGTTCCAGAA GAAGGCCGCCGATACCGCTGTGGGCTGGGCTCTGGGCTACAT GCTCAACTTCACCAACCTGATCCCCgccgatctccccggactgaggaagggaa cccacTTCAGCTCCTGGGTTGCTCTCCTGCTGCTCTTCACAGTCCT GATCTTGGCGGCTTTGGTCCTGCTCTTGCGCCAGGTGCGCTCT GCCAAGTCCCCAGGCGCCCTC
HumanENTPD1: NP_001767	
SEQ ID NO: 349	MEDTKESNVKTFCSKNILAILGFSSIIAVIALLAVGLTQNKALPEN VKYGIVLDAGSSHTSLYIYKWPAEKENDTGVVHQVEECRVKGPG ISKFVQKVNEIGIYLTDCMERAREVIPRSQHQETPVYLGATAGMR LLRMESEELADRVLDVVERSLSNYPFDFQGARIITGQEEGAYGWI

	TINYLLGKFSQKTRWFSIVPYETNNQETFGALDLGGASTQVTFVP QNQTIESPDNALQFRLYGKDYNVYTHSFLCYGKDQALWQKLAK DIQVASNEILRDPCFHPGYKKVVNVSDLYKTPCTKRFEMTLPFQQ FEIQGIGNYQQCHQSILELFNTSYCPYSQCAFNGIFLPPLQGDFGA FSAFYFVMKFLNLTSEKVSQEKVTEMMKKFCAQPWEEIKTSYAG VKEKYLSEYCFSGTYILSLLLQGYHFTADSWEHIHFIGKIQGSDAG WTLGYMLNLTNMIPAEQPLSTPLSHSTYVFLMVLFSLVLFTVAII GLLIFHKPSYFWKDMV
SEQ ID NO: 350	ATGGAAGATACAAAGGAGTCTAACGTGAAGACATTTTGCTCC AAGAATATCCTAGCCATCCTTGGCTTCTCCTCTATCATAGCTGT GATAGCTTTGCTTGCTGTGGGGTTGACCCAGAACAAAGCATTG CCAGAAAACGTTAAGTATGGGATTGTGCTGGATGCGGGTTCTT CTCACACAAGTTTATACATCTATAAGTGGCCAGCAGAAAAGG AGAATGACACAGGCGTGGTGCATCAAGTAGAAGAATGCAGGG TTAAAGGTCCTGGAATCTCAAAATTTGTTCAGAAAGTAAATGA AATAGGCATTTACCTGACTGATTGCATGGAAAGAGCTAGGGA AGTGATTCCAAGGTCCCAGCACCAAGAGACACCCGTTTACCTG GGAGCCACGGCAGGCATGCGGTTGCTCAGGATGGAAAGTGAA GAGTTGGCAGACAGGGTTCTGGATGTGGTGGAGAGGAGCCTC AGCAACTACCCCTTTGACTTCCAGGGTGCCAGGATCATTACTG GCCAAGAGGAAGGTGCCTATGGCTGGATTACTATCAACTATCT GCTGGGCAAATTCAGTCAGAAAACAAGGTGGTTCAGCATAGT CCCATATGAAACCAATAATCAGGAAACCTTTGGAGCTTTGGAC CTTGGGGGAGCCTCTACACAAGTCACTTTTGTACCCCAAAACC AGACTATCGAGTCCCCAGATAATGCTCTGCAATTTCGCCTCTA TGGCAAGGACTACAATGTCTACACACATAGCTTCTTGTGCTAT GGGAAGGATCAGGCACTCTGGCAGAAACTGGCCAAGGACATT CAGGTTGCAAGTAATGAAATTCTCAGGGACCCATGCTTTCATC CTGGATATAAGAAGGTAGTGAACGTAAGTGACCTTTACAAGA CCCCCTGCACCAAGAGATTTGAGATGACTCTTCCATTCCAGCA GTTTGAAATCCAGGGTATTGGAAACTATCAACAATGCCATCAA AGCATCCTGGAGCTCTTCAACACCAGTTACTGCCCTTACTCCC AGTGTGCCTTCAATGGGATTTTCTTGCCACCACTCCAGGGGGA TTTTGGGGCATTTTCAGCTTTTTACTTTGTGATGAAGTTTTTAA ACTTGACATCAGAGAAAGTCTCTCAGGAAAAGGTGACTGAGA TGATGAAAAAGTTCTGTGCTCAGCCTTGGGAGGAGATAAAAA CATCTTACGCTGGAGTAAAGGAGAAGTACCTGAGTGAATACT GCTTTTCTGGTACCTACATTCTCTCCCTCCTTCTGCAAGGCTAT CATTTCACAGCTGATTCCTGGGAGCACATCCATTTCATTGGCA AGATCCAGGGCAGCGACGCCGGCTGGACTTTGGGCTACATGC TGAACCTGACCAACATGATCCCAGCTGAGCAACCATTGTCCAC ACCTCTCTCCCACTCCACCTATGTCTTCCTCATGGTTCTATTCT CCCTGGTCCTTTTCACAGTGGCCATCATAGGCTTGCTTATCTTT CACAAGCCTTCATATTTCTGGAAAGATATGGTA
MouseENTPD1: NP_033978	
SEQ ID NO: 351	MEDIKDSKVKRFCSKNILIILGFTSILAVIALIAVGLTQNKPLPENV KYGIVLDAGSSHTNLYIYKWPAEKENDTGVVQQLEECQVKGPGI SKYAQKTDEIGAYLAECMELSTELIPTSKHHQTPVYLGATAGMR LLRMESEQSADEVLAAVSTSLKSYPFDFQGAKIITGQEEGAYGWI TINYLLGRFTQEQSWLSLISDSQKQETFGALDLGGASTQITFVPQN STIESPENSLQFRLYGEDYTVYTHSFLCYGKDQALWQKLAKDIQ VSSGGVLKDPCFNPGYEKVVNVSELYGTPCTKRFEKKLPFDQFRI

	QGTGDYEQCHQSILELFNNSHCPYSQCAFNGVFLPPLHGSFGAFS AFYFVMDFFKKVAKNSVISQEKMTEITKNFCSKSWEETKTSYPSV KEKYLSEYCFSGAYILSLLQGYNFTDSSWEQIHFMGKIKDSNAG WTLGYMLNLTNMIPAEQPLSPPLPHSTYIGLMVLFSLLLVAVAIT GLFIYSKPSYFWKEAV
SEQ ID NO: 352	ATGGAAGATATAAAGGATTCTAAGGTGAAGAGATTTTGCTCC AAAAATATTCTGATCATCCTTGGTTTCACCTCTATCTTGGCTGT GATAGCTTTGATTGCTGTGGGACTGACCCAGAACAAACCTTTG CCAGAAAATGTTAAGTATGGGATTGTGTTGGATGCGGGGTCAT CTCACACCAACCTGTACATCTACAAGTGGCCGGCCGAGAAGG AGAATGACACAGGGGTGGTGCAGCAGTTAGAGGAATGCCAAG TGAAAGGTCCTGGAATCTCAAAATATGCTCAGAAAACAGATG AAATCGGTGCGTACCTGGCCGAATGCATGGAACTGTCCACCG AACTGATACCAACATCCAAGCATCACCAGACTCCTGTCTACCT GGGAGCCACAGCAGGCATGCGCTTGCTTAGAATGGAAAGCGA ACAATCGGCAGACGAGGTCCTGGCTGCAGTGTCAACAAGCCT TAAGAGCTACCCCTTTGACTTCCAGGGTGCCAAGATCATCACT GGACAAGAGGAAGGTGCCTATGGGTGGATTACTATTAACTAT CTGCTGGGCAGATTCACTCAGGAACAGAGTTGGCTAAGCCTC ATCTCAGACAGTCAGAAACAGGAAACCTTTGGCGCTTTGGATC TCGGCGGAGCCTCCACACAGATCACCTTCGTGCCCCAAAACA GCACTATAGAGTCCCCAGAAAACTCTCTGCAATTCCGTCTCTA TGGCGAGGACTATACTGTGTACACACACAGCTTCCTGTGCTAT GGGAAGGATCAGGCTCTCTGGCAGAAACTGGCCAAGGACATT CAGGTTTCAAGTGGTGGCGTCCTTAAGGACCCATGCTTTAACC CAGGATACGAGAAGGTTGTGAATGTAAGTGAGCTCTATGGCA CTCCCTGCACCAAAAGATTCGAAAAGAAGCTACCATTTGATCA GTTTCGAATCCAGGGCACTGGAGACTACGAACAGTGCCACCA GAGCATCCTTGAGCTCTTCAACAACAGCCACTGCCCTTACTCC CAGTGTGCCTTCAATGGCGTCTTCCTGCCACCTCTCCATGGGA GTTTTGGGGCGTTTTCTGCTTTCTACTTTGTGATGGATTTTTTT AAGAAGGTAGCGAAAAACAGTGTCATCTCTCAGGAGAAAATG ACCGAGATAACAAAAAATTTTTGCTCAAAATCTTGGGAAGAG ACAAAGACATCTTATCCTTCAGTAAAGGAGAAGTACCTGAGT GAGTACTGCTTCTCGGGCGCCTACATCCTCTCTCTCCTGCAAG GCTATAACTTCACAGACAGCTCCTGGGAACAGATTCATTTTAT GGGCAAGATCAAAGACAGCAACGCGGGGTGGACTTTGGGCTA CATGCTGAACTTGACCAACATGATCCCAGCTGAACAGCCGTTG TCCCCGCCTCTCCCTCACTCCACCTACATCGGCCTCATGGTTCT CTTCTCCCTGCTCTTGGTTGCTGTGGCCATCACAGGCCTGTTCA TCTATAGCAAGCCTTCATATTTCTGGAAAGAGGCAGTA

Expression and purification of recombinant mouse ENTPD1 and mouse and rat ENTPD2 from HEK cultures

[0722] Recombinant monomeric mouse or rat ENTPD2, as well as mouse ENTPD1 were generated as follows: FreeStyle™ 293-F cells (Thermo Fisher Scientific) were cultivated in Gibco™ FreeStyle™ 293 Expression medium and transiently transfected with a plasmid containing a CMV promoter, a mouse IgK signal peptide, residues 29-462 of mouse

or rat ENTPD2 (the extracellular domain) or residues 38-478 of mouse ENTPD1, and a polyhistidine (His_6) tag (SEQ ID NO: 1010). Four days post-transfection, cells from a 1 L culture were pelleted at 2600×*g* for 10 minutes and supernatant was clarified by filtration through a 0.22 μm filter. The supernatant was supplemented with 20 mM Tris-HCl pH 8.0 and 20 mM Imidazole and loaded onto a column pre-packed with 6 mL Ni-NTA agarose (Qiagen). The column was washed with 10 column volumes of Wash Buffer [20 mM Tris (pH 8.0),150 mM NaCl, 20 mM Imidazole], and eluted with 5 column volumes of Elution Buffer [20 mM Tris (pH 8.0), 150 mM NaCl, 250 mM Imidazole]. Protein was buffer exchanged into TBS pH 7.4 using a PD-10 desalting column (GE Healthcare) and frozen for storage.

Expression and purification of human ENTPD1 and human and cyno ENTPD2 from insect cells

[0723] The Bac-to-Bac® Baculovirus expression system (Thermo Fisher Scientific) was used to express recombinant human ENTPD1 and human and cyno ENTPD2 proteins. Residues 38-478 of human ENTPD1 or residues 29-462 of human or cyno ENTPD2 were cloned into expression vector pFastBac™1 (Thermo Fisher Scientific) with a GP67 signal peptide and a C-terminal Avi-His_6 tag (SEQ ID NO: 1010). The cloned vectors were transformed into DH10Bac™ *Escherichia coli* (Thermo Fisher Scientific) competent cells to make recombinant bacmids. The recombinant bacmids were then extracted using the PureLink® HiPure Plasmid Miniprep kit (Thermo Fisher Scientific) and transfected into Sf9 (*Spodoptera frugiperda*) cells using FuGene® HD (Promega) to generate recombinant baculovirus (BV). After one round of amplification, the resulting BV was used to infect High Five™ (*Trichoplusia ni*) cells (Thermo Fisher Scientific) in a 1 L suspension culture at a density of 2×10^6 cells/ml and at a multiplicity of infection (MOI) of 10. At 72 h post-infection, cells were pelleted by centrifugation at 2600×*g* for 10 min and the media containing the secreted, glycosylated, recombinant protein was collected. The supernatant was then supplemented with 50 mM Tris pH 8.0, 1 mM $NiCl_2$, 5 mM $CaCl_2$ and then centrifuged at 2600×*g* for 30min. The supernatant was subjected to filtration through a 0.22 μm filter and loaded onto a column packed with 6 mL Ni-NTA agarose (Qiagen). The column was washed with 10 column volumes of Wash Buffer described above, and eluted with Elution Buffer (also described above). Protein was buffer exchanged into TBS (20 mM Tris pH 7.4, 150 mM NaCl) using a PD-10 column (GE Healthcare) and frozen for storage.

Generation of cell lines stably expressing ENTPD1 or ENTPD2

[0724] Stable ENTPD1- or ENTPD2-expressing cell lines were generated using retroviral transduction. To generate retrovirus, 293T cells were co-transfected with a retroviral expression vector expressing ENTPD1 or ENTPD2 and a pCL-Eco or pCL-10A1packaging vector (Novus Biologicals, cat#NBP2-29540 or NBP2-2952) using FuGene® 6 transfection reagent (Promega, cat# E2692) according to the manufacturer's recommendation. Cells were maintained in a humidified incubator at 37°C and 5% CO_2, and virus-containing cell supernatants were collected 48 hours post-transfection. NIH/3T3 and 300.19 cells (ATCC®) were grown to near confluence in 6-well plate. Growth media was removed from the cells and viral supernatant was added in the presence of 8 ug Polybrene/ml (EMD Millipore, cat#TR-1003-G). Following incubation for 3-6 hours at 37°C, fresh media was added. Cells were then cultured under appropriate selection conditions to produce stable ENTPD1 or ENTPD2-expressing cell lines.

Generation, expression and purification of virus-like particles (VLPs)

[0725] 300.19 cells were maintained in DMEM with 10% FBS. To make VLPs, cells were exchanged into DMEM with 4% FBS, then co-transfected with a human ENTPD2 expression plasmid and a retroviral Gag expression plasmid at a µg ratio of 3:2. Forty-eight hours post-transfection, cell supernatant was collected and clarified by centrifugation at 2500 × *g* for 5 min in a benchtop centrifuge and kept on ice. VLPs were purified by ultracentrifugation at 100,000 × *g* through a 20% sucrose cushion in Ultra-Clear™ 38.5 ml centrifugation tubes (Beckman Coulter®, catalog # 344058) in a Beckman Coulter® SW 32 Ti rotor in a Sorvall™ RC 6 Plus ultracentrifuge. Resulting pellets were resuspended in 300 µl of cold sterile PBS and quantitated using a Pierce BCA Assay (Thermo Fisher Scientific catalog # 23225).

Hybridoma generation

[0726] *Bcl-2* transgenic mice [C57BL/6-Tgn (bcl-2) 22 WEHI strain] were immunized with antigen using a procedure that calls for Repetitive Immunization at Multiple Sites (RIMMS) (K.E. Kilpatrick et al. Hybridoma 1997). Briefly, mice were injected with 22.5 µg of His_6-tagged human ENTPD2 29-462 ECD protein ("His6" disclosed as SEQ ID NO: 1010) at 8 specific sites proximal to peripheral lymph nodes (PLNs). This procedure was repeated 8 times over a 20 day period. On Day 18, a test bleed was collected and the serum antibody titer was analyzed by FACS and ELISA. In some instances, BALB/c mice were immunized with 50 µg of His_6-tagged human ENTPD2 29-462 ECD ("His6" disclosed

as SEQ ID NO: 1010) protein in Freund's Complete, Sigma Adjuvant System®, or Freund's Incomplete adjuvant, 50 μg of human ENTPD2-expressing VLPs in PBS, or 5x10e6 300.19 cells stably over-expressing human ENTPD2 (SEQ ID NO: 291) in PBS. Animals were injected subcutaneously or intraperitoneally twice two weeks apart, followed by an intravenous boost approximately two weeks later with either 50 μg of human ENTPD2-expressing VLPs or His_6-tagged human ENTPD2 29-462 ECD protein in PBS ("His6" disclosed as SEQ ID NO: 1010). Ten days after the second immunization, a test bleed was collected and serum antibody titer was analyzed by FACS and ELISA. Spleens and pooled peripheral lymph nodes (PLNs) were removed from high-titer mice. To harvest lymphocytes, spleens and PLNs were washed once in PBS, and then dissociated by passage through a 70 micron screen (Falcon #352350). The resulting lymphocytes were washed 2 additional times prior to fusion in Cytofusion® medium (BTXpress Cytofusion® Electroporation Medium cat# 47001).

[0727] For the fusion, F0 myeloma cells were mixed with lymphocytes at a 1:4 ratio. The cell mixture was centrifuged, suspended in Cytofusion® medium and subsequently added to an electrofusion chamber (Harvard Apparatus Coaxial chamber 9ML Part #470020). Electrofusion was carried out per manufacturer's instructions using the CEEF-50B Hybrimune/Hybridoma system (Cyto Pulse Sciences, Inc). Fused cells were allowed to recover for 5 minutes in the chamber, diluted 1:10 in media without hypoxanthine-aminopterin-thymidine (HAT) [DMEM + 20% FBS, 1% Penicillin-Streptomycin-Glutamine (PSG), 1X Non-Essential Amino Acids (NEAA), 0.5X Hybridoma Fusion and Cloning Supplement (Roche; HFCS)) and placed at 37°C and 5% CO_2 for one hour. Next, 4X HAT medium (DMEM + 20% FBS, 1% PSG, 1X NEAA, 4X HAT, 0.5X HFCS) was added to bring the concentration of HAT to 1X, and the density was adjusted to 66,000 cells/ml. The cells were plated in 384-well plates at 60 ul/well.

FACS screening

[0728] Ten days after fusion, hybridoma plates were screened for the presence of ENTPD2-specific antibodies using flow cytometry to confirm specific binding of candidate antibodies to cell surface-expressed human ENTPD2 using three cell lines: parental NIH/3T3 cells, NIH/3T3 cells stably overexpressing human ENTPD2, and RKO cells (ATCC®), which expresses endogenous human ENTPD2. Cells were rinsed thoroughly with PBS, treated with Accutase (Millipore #SCR005) to lift them from the growth plates, and resuspended in cold PBS. Cells were biotinylated and labeled with a fluorescent dye according to manufacturer's

instructions (FluoReporter™ Cell-Surface Biotinylation Kit, Thermo Fisher Scientific Cat# F-20650; PE-Cy7 Steptavidin, ThermoFisher Scientific Cat# SA1012). Cells were resuspended at approximately $1X10^6$ cells/ml in FACS buffer (PBS with 2% FBS + 0.1% NaN_3). In a 384-well plate, 20 µL of hybridoma supernatant was pre-seeded and 20 µL of cell suspension was added. Cells were incubated for 1 hour at 4°C, washed twice with cold FACS buffer, and resuspended in 20 µL of FACS buffer containing secondary antibody at a 1:400 dilution (Allophycocyanin-conjugated F(ab')2 goat anti-mouse IgG, Fcγ specific; Jackson Immunoresearch, cat# 115-136-071). After additional incubation for 45 min at 4°C, cells were washed twice with FACS buffer and resuspended in 20 µL of FACS buffer with 2 µg/ml propidium iodide (Sigma Aldrich Cat# P4864). Geometric mean fluorescence intensity was calculated on live single cells using FlowJo™ software.

[0729] Hits from this primary cell-based flow cytometry screen were confirmed in a secondary flow cytometry screen. Hybridomas expressing antibodies that bound to both NIH/3T3-hENTPD2 and RKO cells were expanded into 45 mL protein production cultures in hybridoma serum-free medium with HT Media Supplement (50×) Hybri-Max™ (Sigma, cat# H0137) in CellStar® Autoflasks™ (Greiner Bio-One). Cultures were maintained in a shaking incubator at 37°C and 5% CO2 for approximately 8 days and then cells were pelleted and supernatants were taken through purification over Protein G resin. Proteins were subsequently buffer exchanged into PBS using NAP-10™ columns (GE Healthcare).

Recombinant Antibody Production

[0730] Hybridoma-derived mAbs were screened in a cell-based assay for inhibition of ATP hydrolysis by ENTPD2. Two lead inhibitory mAbs were identified in this assay: mAb17 and mAb16.

[0731] Chimeric antibodies comprised of murine variable regions and human constant regions were prepared. Variable region (VH and VL) DNA sequences of hybridomas were obtained for cloning and antibody optimization (humanization, removal of potential post-translational modifications, etc.). Variable region DNA from murine monoclonal antibodies was amplified by 5' RACE from RNA obtained from each selected hybridoma cell line using standard methods. Polypeptide sequences for each of the murine variable heavy/light chains are shown in Table 1 for mAb17 and mAb16, respectively. Corresponding variable heavy/light nucleotide sequences for each of the hybridomas are shown in SEQ ID NO: 234/SEQ ID NO: 238, and SEQ ID NO: 226/SEQ ID NO: 230. For preparation of chimeric

antibodies, DNA sequences coding for the hybridoma VL and VH amplified by 5' RACE-PCR were cloned into expression vectors containing the respective human wild type heavy chain and human light chain constant region sequences (IgG1, kappa). These vectors were miniprepped using the QIAprep Spin Miniprep Kit (QIAGEN, cat # 27106) and nucleofected into a proprietary CHO cell line using an Amaxa™ 4D-Nucleofector™ (Lonza). Transfected cells were placed in selective media for stable pool generation, and resulting pools were subjected to a 14-day fed-batch protein production process. Protein-containing cell supernatants were clarified by centrifugation at 3000 ×*g* for 15 minutes and filtration through a 0.22 μm filter. Proteins were purified using MabSelect SuRe™ resin (GE Healthcare) on an ÄKTA™ Pure or an ÄKTA™ Purifier and eluted using Pierce™ IgG Elution Buffer (Thermo Fisher Scientific # 21004), then buffer exchanged into PBS either by dialysis or using a HiPrep Desalting column (GE Healthcare). In cases where the resulting protein was <95% dimer by analytical size exclusion chromatography (AnSEC) using a Superdex® 200 Increase, the protein was subjected to preparative SEC using a HiLoad® Superdex® 200 column (GE Healthcare) using PBS as the mobile phase.

Humanization

[0732] Variable region constructs were also designed for humanization and optimization of sequences (*e.g.*, removal of potential post-translational modification sites) using an internal software program. One or more human frameworks were chosen for each mouse VH and VL with back mutations in the Vernier Zones (Foote and Winter 1992, Journal of Molecular Biology; 224 (2):487-499) to maintain affinity and desired functional activity. Both mAb17 and mAb16 were also humanized using three-dimensional crystal structure-based design. Briefly, the crystal structure was loaded into Molecular Operating Environment (MOE™) (Chemical Computing Group ULC) and prepared using the standard structure preparation methodology with the Amber10EHT force field. The Fab was then compared structurally with an in-house library of humanized Fabs using a custom script called "cdr_grafter SVL". The script structurally compares the input murine Fab structure with human Fab structures in an internal database and lists detailed parameters regarding structural similarities between the murine (donor) and human (acceptor) Fabs. These parameters include framework and stem region RMSDs and CDR length comparisons. Based on these parameters, four candidate acceptor Fabs were selected for grafting donor CDRs from mAb17 and three candidate acceptor Fabs were selected for grafting donor CDRs from

mAb16. Humanization of mAb17 led to the generation of mAb1, mAb2, mAb3, and mAb7. Humanization and optimization of mAb16 led to the generation of mAb4, mAb5, and mAb6.

[0733] DNA sequences coding for the designed humanized VL and VH domains from both humanization strategies were ordered from GeneArt (Life Technologies Inc. Regensburg, Germany) with codon optimization for *Cricetulus griseus*. These variable regions were subcloned into expression vectors containing the respective human wild-type heavy chain and human light chain constant region sequences (IgG1, kappa) using standard methods.

[0734] Recombinant antibodies were produced by co-transfection of vectors encoding heavy and light chains into FreeStyle™ 293-F cells (Thermo Fisher Scientific). Transfected cells were maintained in Gibco® FreeStyle™ 293 Expression Medium (Thermo Fisher Scientific #12338018) in CellStar® Autoflasks™ (Greiner Bio-One) housed in a shaking incubator at 37°C and 5% CO_2 for approximately 5 days and then cells were pelleted and protein-containing supernatants were taken through purification over MabSelect SuRe™ resin (GE Healthcare). Proteins were subsequently buffer exchanged into PBS using NAP-10™ columns (GE Healthcare).

Example 3. Generation of human anti-human ENTPD2 antibodies and Fab fragments thereof using phage display

[0735] Fabs that specifically bind to human ENTPD2 (SEQ ID NO: 291) were generated using the MorphoSys HuCAL PLATINUM® phage display technology. The phagemid library is based on the HuCAL® concept (Knappik et al., 2000, J Mol Biol *296*, 57-86) and employs the CysDisplayTM technology for displaying the Fab on the phage surface (Lohning, WO 2001/05950).

[0736] Four types of panning were performed: solid-phase panning against directly coated recombinant human ENTPD2 (hENTPD2), solution panning against ENTPD2, whole-cell panning, and affinity maturation panning.

Bead-Based Panning

[0737] Prior to a bead-based panning, the antigen was immobilized on magnetic carboxylic acid-coated beads (Dynabeads™ M-270 Carboxylic Acid, Thermo Fisher Scientific Cat# 14306D). Per phage pool, $1x10^7$ antigen-coated beads were blocked 1x ChemiBlocker (EMD Millipore). In parallel, an appropriate amount of phage-antibodies was blocked with 50% human serum/0.33x chemiblocker/0.05 % Tween20. For prevention of

selecting bead-binding phage, blocked phage particles were pre-incubated using beads with immobilized irrelevant protein. Blocked antigen-coated beads were added to the pre-adsorbed and blocked phage particles and the phage-antibodies were allowed to bind to the antigen coated beads. Phage particles bound to the antigen-coated beads were collected by magnetic separation. Several washing steps removed non-specifically bound phage. Finally, specifically bound phage were eluted from antigen-coated beads. The eluate was transferred into 14 ml of *E. coli* TG1 culture and incubated for phage infection.

[0738] Upon centrifugation, the infected bacteria were pelleted and resuspended in 2xYT medium, plated on LB/chloramphenicol agar plates and incubated overnight. Colonies were scraped off the plates and were used for phage rescue, polyclonal amplification of selected clones, and phage production. With purified phage the next panning round was started. The second and third round of solid phase panning was performed using the same protocol as the first round except that less antigen and more stringent washing conditions were used.

Solution Panning

[0739] An appropriate amount of Streptavidin beads (Dynabeads™ M-280 Streptavidin, Thermo Fisher Scientific Cat# 11206D) were blocked. In parallel, an appropriate amount of phage-antibodies were blocked. For removal of Streptavidin- or bead-binding phage, pre-adsorption of blocked phage particles was performed using blocked Streptavidin beads coated with biotinylated irrelevant protein. Then, biotinylated ENTPD2 was added to the pre-adsorbed and blocked phage particles and the phage-antibodies were allowed to bind to the antigen in solution. The phage-antigen complexes were captured using blocked Streptavidin beads and phage particles bound to the Streptavidin beads were collected with a magnetic separator. Unspecifically-bound phage were washed off by several washing steps. Specifically-bound phage were eluted from Streptavidin beads. The eluate was transferred into 14 ml of *E. coli* TG1 culture and incubated for phage infection. Subsequent phage infection and phage production were performed according to the Bead-based Panning protocol and the next panning round was started. The second and third round of bead-based solution panning were performed using the same protocol the first panning round except that washing conditions with increased stringency were applied.

Whole Cell Panning

[0740] For each panning, an appropriate amount of phage-antibodies was blocked. In parallel, an appropriate amount of target cells expressing ENTPD2 and an appropriate amount of adsorption cells without expression of antigen ENTPD2 were blocked for each phage pool. The blocked target cells were spun down, re-suspended in the pre-blocked phage particles and the phage-antibodies were allowed to bind to the antigen presented on the cell. The phage-cell complexes were washed several times. Specifically-bound phage were eluted from target cells. After centrifugation, the supernatant (eluate) was applied to antigen-negative adsorption cells for removal of phage binding to cell surface molecules other than the target antigen (post-adsorption). The final supernatant was transferred to an *E. coli* TG1 culture for phage infection. The second and third round of the whole-cell panning were performed using the same protocol as the first panning round.

Affinity Maturation Panning

[0741] Generation of HuCAL PLATINUM® Maturation Libraries

[0742] Four Fab candidates were selected for affinity maturation. To increase affinity and biological activity of selected antibodies, CDR-L3 and CDR-H2 regions were optimized by cassette mutagenesis using trinucleotide-directed mutagenesis, while the framework regions were kept constant (Virnekäs et al. 1994, *Nucleic Acids Research* 22 (25), pp. 5600–5607). For CDR-L3 optimization, a ~400bp DNA fragment encoding for the CDR-L3, framework 4 as well as the constant region of the light chain was removed from the sequence encoding the parental antibodies by restriction digest and replaced by a repertoire of DNA fragments encoding for diversified CDR-L3 regions together with framework 4 and the constant domain. In a second library set the CDR-H2 -encoding sequence was diversified, while the connecting framework regions were kept constant. In order to reduce the background of the parental undiversified sequence a ~ 150 bp DNA fragment containing the parental CDR-H2 and the framework 3 sequences was replaced by a ~ 590 bp dummy sequence via restriction digest and ligation, before the diversified CDR-H2 cassette (incl. framework 3) was inserted also via restriction digest and ligation. Electroporation of ligation mixtures were in MC1061F′ cells yielded approximately 10^8 to 10^9 in > $5x10^6$ independent colonies. Amplification of the library was performed as described previously (Rauchenberger et al. 2003, *J biol chem* 278 (40), pp. 38194–38205). For quality control, approx. 10 - 20 single clones per library were randomly picked and sequenced.

[0743] For the selection of candidates that are affinity improved, phage derived from maturation libraries were subjected to two to three rounds of maturation panning. Panning stringency was increased by lowering the antigen concentration in each panning round (Low et al. 1996, *J.Mol.Biol.* 260, pp. 359–368). In addition to antigen reduction, off-rate selection was performed (Hawkins et al. 1992, *J.Mol.Biol.* 226 (3), pp. 889–896). These strategies were combined with prolonged washing steps.

Expression

Subcloning from Display Vector into Fab-expression Vector for E. coli

[0744] To facilitate rapid expression of soluble Fab, the Fab-encoding inserts of the selected HuCAL PLATINUM® phage were subcloned from pMORPH®30 display vector into pMORPH®x11 expression vector pMORPH®x11_FH. After transformation of *E. coli* TG1 F- single clone expression and preparation of periplasmic extracts containing HuCAL®-Fab fragments were performed as described previously (Rauchenberger et al., 2003, J Biol Chem 278: 38194-38205).

Micro Scale Production of His-tagged Fab Fragments

[0745] Expression of Fab fragments encoded by bacterial expression vector in E. coli TG1 F- cells was carried out in 50 mL Falcon tubes using 25 mL of 2xYT medium supplemented with 0.1% glucose, 34 µg/mL chloramphenicol and 1 mM IPTG (isopropyl-ß-D-thiogalactopyranoside). Cultures were shaken at 30°C for 18 h. Cells were harvested and disrupted using a combination of lysozyme and Bug Buster® Protein Extraction Reagent (Merck, Germany). His6-tagged Fab fragments ("His6" disclosed as SEQ ID NO: 1010) were isolated via IMAC (GE Healthcare, Germany) and eluted using imidazole. Buffer exchange to 1X Dulbecco´s PBS (pH 7.2) was performed using 'PD MultiTrap™ G-25' plates (GE Healthcare, Germany). Protein concentrations were determined by UV-spectrophotometry. The purity of *representatively* selected samples was analyzed in denaturing, non-reducing 15% SDS-PAGE.

Subcloning Into IgG & FabCys Expression Vector and Expression in HKB11 Cells

[0746] For full-length IgG expression in HKB11 cells, selected candidates or candidate pools were cloned into the pMORPH®4_IgG1f vector. Subcloning was performed as a two-step method for a convenient and efficient conversion of a large number of sequence-unique Fab clones into the IgG format.

[0747] Eukaryotic HKB11 cells were transfected with mammalian expression vector DNA encoding both heavy and light chains of IgG. Cell culture supernatants were harvested on day 3 or 6 post- transfection and subjected to standard Protein A affinity chromatography (MabSelect™ SuRe™, GE Healthcare). Unless stated otherwise, buffer exchange was performed to 1x Dulbcecco´s PBS (pH 7.2, Invitrogen) and samples were sterile filtered (0.2 μm pore size).

[0748] Protein concentrations were determined by UV-spectrophotometry and purities of IgG were analyzed under denaturing, reducing and non-reducing conditions using CE-SDS (LabChip GXII, Perkin Elmer, USA). HP-SEC was performed to analyze IgG preparations in native state.

Summary of Antibodies

[0749] Table 1 sets forth sequence information for anti- human ENTPD2 antibodies derived from murine hybridomas and phage display.

Example 4. Biochemical characterization of anti-human ENTPD2 antibodies

[0750] Anti-human ENTPD2 antibodies were evaluated in the following assays.

[0751] FACS screening: Specific binding of candidate antibodies to endogenously expressed ENTPD2 was assessed by flow cytometry. Cells were rinsed thoroughly with 1xPBS and treated with Accutase (Millipore #SCR005) to lift from growth plates and resuspended at approximately $1x10^5$ cells/90 μL in 1x FACS buffer (2% FBS + 0.1% NaN3 in PBS). In a 96-well U-bottom plate, 10 μL of 10x antibody solution in FACS buffer was pre-seeded and 90 μL of cell suspension was added. Cell were incubated for 30 minutes at 4°C, washed 1x with cold PBS and resuspended in 100 μL of 1:500 secondary antibody 1x FACS buffer (Allophycocyanin conjugated F(ab')2 goat anti-human IgG, Fcγ specific; Jackson Immunoresearch, Cat# 109-136-098). After additional incubation for 15 min at 4°C, cells were washed twice with PBS and resuspended in 100 μL of 1xFACS buffer with 4 μg/mL propidium iodide (Life Technologies, Cat# P3566). Geometric mean fluorescence intensity was calculated on live single cells using FlowJo software.

[0752] ELISA screening on directly coated antigen: Maxisorp™ 384-well plates (Thermo Nunc) were coated with 2 μg/ml of recombinant ENTPD2 diluted in PBS. After blocking with 2% BSA (bovine serum albumin) in PBS for 1 hr at room temperature, washing plates 3x with TBST (0.05% Tween 20 in TBS, Sigma Cat# T9039), primary

antibodies in TBST and 2% BSA were added in a serial dilution and incubated for 1 hr at room temperature. Plates were washed again and bound antibodies were detected by incubation with anti-hFc gamma conjugated to horseradish peroxidase (HRP; Jackson ImmunoResearch, Cat#115-035-098, diluted 1:5000 in 1xTBST +2% BSA) for 1hr at room temperature followed by washing with TBST and afterwards addition of SureBlue Peroxidase substrate (KPL, #52-00-03) substrate. After 15 min, absorbance at 650nM was recorded and analyzed in GraphPad Prism6.

[0753] Biacore Screening: Affinity was measured by determining the kinetic rate constants using surface plasmon resonance (SPR) on a Biacore T200 or T100 with the T200 sensitivity upgrade instrument (Biacore, GE Healthcare). Antibodies were captured on CM5 sensor chips (Biacore, GE Healthcare) prepared with a mouse anti-human IgG Fc antibody (ThermoFisher catalogue # 05-4200) amine coupled to the surface. Binding of human and cynomologus (cyno) ENTPD2 ECDs at 25°C were detected at concentrations ranging from 0.78 nM to 500 nM depending on the affinity of the antibody. ENTPD2 analytes were allowed to associate for 180 s and dissociate for up to 1800 s depending on the off-rate of the antibody at a flow rate of 30 µL/min. The running buffer was PBS pH 7.2 (prepared from a Corning 10X stock, cat# 46-013-CM) + 0.05% Tween 20. Regeneration was accomplished with 30 s injections of 3 or 4 M MgCl2 to remove all the captured antibody and remaining complex from the surface, after which fresh antibody was captured. The raw data were analyzed using Biacore T200 Evaluation Software version 1.0 and fit to a 1:1 binding model, with all parameters set to fit globally except for RI, which was set to fit locally.

[0754] Antibody specificity for mAb1-mAb10 was confirmed. All clones showed significant nM to sub-nM binding to human ENTPD2. Antibodies mAb8, mAb9, and mAb10 show weak affinity to mouse ENTPD2. None of the selected antibodies bind to rat ENTPD2. See Table 21 and Table 22.

Table 21: Dissociation constant (K_D) for select anti-human ENTPD2 antibodies

	Human ENTPD2			Cyno ENTPD2			Mouse ENTPD2
	BIACore K_D (nM)	k_a (1/Ms)	k_d (1/s)	BIACore K_D (nM)	k_a (1/Ms)	k_d (1/s)	BIACore K_D (nM)
MAB1	1.7	1.1E+05	1.9E-04	3.4	3.6E+05	1.2E-03	No binding
MAB2	1.7	1.1E+05	1.8E-04	2.8	4.3E+05	1.2E-03	No binding
MAB3	1.3	1.3E+05	1.6E-04	2.2	4.5E+05	9.8E-04	No binding

MAB4	0.7	3.0E+05	2.2E-04	42.1	1.4E+05	5.7E-03	No binding
MAB5	0.6	2.7E+05	1.6E-04	10.7	2.9E+05	3.0E-03	No binding
MAB6	0.7	3.5E+05	2.6E-04	35.6	2.9E+05	1.0E-02	No binding
MAB7	0.9	2.1E+05	1.9E-04	1.1	1.2E+06	1.2E-03	No binding
MAB8	3.3	2.9E+05	9.4E-04	81.1	3.0E+05	2.4E-02	Weak binding
MAB9	0.9	3.8E+05	3.0E-04	20.9	9.9E+05	2.1E-02	750
MAB10	0.8	3.4E+05	2.4E-04	15.2	1.2E+06	1.8E-02	Weak binding

Table 22: Binding of select anti-human ENTPD2 antibodies to ENTPD2 Expressing Cells

	Apparent FACS Affinity; EC50 (nM)		
Antibody	NIH3T3 humanENTPD2	NIH3T3 cynoENTPD2	RKO
ANTI-HUMAN ENTPD2 MAB1	1.5	3.3	0.9
ANTI-HUMAN ENTPD2 MAB2	2.1	4.2	1.3
ANTI-HUMAN ENTPD2 MAB3	2.8	5.4	2.1
ANTI-HUMAN ENTPD2 MAB4	0.9	6.1	0.5
ANTI-HUMAN ENTPD2 MAB5	0.9	5.2	0.4
ANTI-HUMAN ENTPD2 MAB6	0.9	7.0	0.4
ANTI-HUMAN ENTPD2 MAB7	0.5	0.8	0.4
ANTI-HUMAN ENTPD2 MAB8	0.6	2.1	0.3
ANTI-HUMAN ENTPD2 MAB9	0.6	1.3	0.5
ANTI-HUMAN ENTPD2 MAB10	0.8	1.7	0.6

[0755] Cross reactivity Human ENTPD1 (NP_001767) expressing NIH/3T3 cells were generated using a retroviral transduction approach. 72hrs post transduction, engineered cells were stained with the anti-Human CD39/ENTPD1 APC-conjugated Antibody (R&D systems, Minneapolis, MN) and live cells that expressed human ENTPD1 were separated from the rest of the population via fluorescence activated cell sorting. Stable expression of

ENTPD1 was periodically re-confirmed by FACS with the above described anti-Human CD39/ENTPD1 APC-conjugated Antibody (1:100).

[0756] H520 cells were identified as a cancer cell line with ENTPD3 (Ct 25) and ENTPD8 (Ct 26) expression by Taqman and were used for selectivity screening.

[0757] No significant binding to any of the control cell lines was observed with any of the Anti-human ENTPD2 Abs tested (Table 25).

Table 25. Cross Reactivity of Anti-human ENTPD2 mAbs.

	Apparent FACS binding at 50 nM		
Antibody	NIH/3T3 cells	NIH/3T3 – ENTPD1	H520 Cells
ANTI-HUMAN ENTPD2 MAB1	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB2	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB3	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB4	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB5	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB6	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB7	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB8	No binding	>100 nM	No binding
ANTI-HUMAN ENTPD2 MAB9	No binding	No binding	No binding
ANTI-HUMAN ENTPD2 MAB10	No binding	No binding	No binding

Epitope binning using Octet Red96 system

[0758] Epitope binning of anti-human ENTPD2 antibodies was performed using the Octet Red96 system (ForteBio, USA) that measures biolayer interferometry (BLI). Human ENTPD2-Avi-His_6 protein ("His6" disclosed as SEQ ID NO: 1010) was biotinylated via an AviTag™ utilizing BirA biotin ligase according to manufacturer's recommendations (Avidity, LLC, USA cat# BirA500). The biotinylated immunogen scaffold was loaded at 0.5 μg/mL onto pre-equilibrated streptavidin sensors (ForteBio, USA). The sensors were then transferred to a solution containing 100 nM antibody A in 1X kinetics buffer (ForteBio, USA). Sensors were briefly washed in 1X kinetics buffer and transferred to a second solution

containing 100 nM of competitor antibody. Binding kinetics was determined from raw data using the Octet Red96 system analysis software (Version 9.0, ForteBio, USA). Antibodies were tested in all pairwise combinations, as both the first (blocking) antibody bound to hENTPD2 and as the second (competitor) antibody. All of the antibodies demonstrated significant cross-blocking in this assay, indicating that mAb1-10 may have similar epitope.

Example 5. Crystallography and Epitope mapping of anti-human ENTPD2 FAb22

[0759] In this Example, anti-human ENTPD2 FAb22 was crystallized in complex with human ENTPD2 (Y350A mutant) ectodomain and the corresponding structure was determined. Analysis of anti-human ENTPD2 FAb22 binding to human ENTPD2 based on the X-ray data provided molecular details of antigen engagement and insights to the Fab paratopes and antigen epitopes revealed.

Materials and Methods

Expression and purification of Fab fragments

[0760] DNA sequences coding for the identified VH and VL domains were subcloned into mammalian expression vectors containing the respective human wild-type CH1 and human kappa light chain constant region sequences. Recombinant human Fabs were produced by transient co-transfection of vectors into cells using transfection reagent. Following transfection, cells were cultured for 5 to 6 days, and purification of antibodies was carried out. Cells were pelleted by centrifugation (2600x*g* for 10 minutes), and antibody-containing cell supernatants were clarified by filtration through a 0.22 □m filter. Fabs were purified over Protein G (GE Healthcare Life Sciences) columns and eluted using acidic eluate buffer conditions.

Preparation of human ENTPD2 and anti-human ENTPD2 FAb22 complex

[0761] To prepare the ENTPD2- FAb22 complex, a 1.3-fold molar excess of FAb22 was combined with hENTPD2 Y350A in 20mM Tris pH 7.5 with 150mM NaCl to give a final concentration of 5.65 mg/mL. The complex sample was incubated on ice for 2 hours and submitted for crystallization screen set ups.

Crystallization and X-ray data collection

[0762] Crystals were grown in 96-well plates (Greiner Bio-One Crystalquick Plus plates) by sitting drop vapor diffusion. In detail, 0.2µl of protein stock was mixed with 0.2µl of reservoir solution, and the drop was equilibrated against 50µl of the same reservoir

solution at 20°C. The experiments were set up with a Phoenix robotic system (Art Robbins Instruments), and stored in in-house custom engineered crystal imager and gantry (Novartis GNF internal systems).

[0763] For X-ray data collection, a single crystal was directly mounted in a cryo-loop and flash cooled into liquid nitrogen. X-ray data were collected at the Advanced Light Source, BL5.03, with Quantum Q315 CCD detector, using 0.9765Å X-ray radiation. 180 images of 1.0° oscillation each were recorded at a crystal-to-detector distance of 350mm and processed with HKL2000 (Z. Otwinowski and W. Minor, "Processing of X-ray Diffraction Data Collected in Oscillation Mode", Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A, p.307-326, 1997,C.W. Carter, Jr. & R. M. Sweet, Eds., Academic Press (New York).

Structure determination and analysis

[0764] The structure of the FAb22-ENTPD2 complex was determined by molecular replacement with the program Phaser (McCoy et al., 2007, J Appl Crystallogr 40:658-674), using the refined structures of human ENTPD2 previously determined in house and coordinates for anti-RSV Fab B21m (PDB code 3QRG) as independent search models. The structure was refined using iterative cycles of model building followed by automated crystallographic refinement with the programs Coot 0.8.0 (Crystallographic Object-Oriented Toolkit; Emsley et al., 2010, Acta Crystallogr Sect D: Biol Crystallogr; 66:486-501) and Autobuster 2.11.5 (Bricogne et al., 2011, BUSTER version 2.11.2. Cambridge, United Kingdom: Global Phasing Ltd.).

[0765] Visual inspection of the crystal structures was carried out using the programs Coot (Emsley et al., 2010, Acta Crystallogr Sect D: Biol Crystallogr; 66:486-501) and PyMOL (Molecular Graphics System; DeLano Scientific: Palo Alto, CA). The quality of the final refined models was assessed with the programs Coot and PROCHECK v3.3 (Laskowski et al., 1992, J Appl Crystallogr; 26:283-291). Residues of human ENTPD2 that become less accessible to solvent upon binding of the anti-human ENTPD2 FAb22 were identified by the program AREAIMOL of the CCP4 program suite (Collaborative Computational Project, Number 4, 1994). Intermolecular contacts were defined using a cut-off distance of 4.0Å and were identified with the CCP4 program NCONT.

Results

Crystal Structure of the anti-hENTPD2 FAb22 in complex with human ENTPD2

[0766] The anti-hENTPD2 FAb22 complexed with human ENTPD2 Y350A mutant was crystallized in 96-well plates by the method of vapor diffusion in sitting drops, at 20°C. Crystals grew in 0.1M HEPES pH 7.5, 20% polyethylene glycol 3350, 0.2M magnesium chloride. Crystals appeared after approximately 6 weeks and grew to full size within a few days.

[0767] The crystal of the FAb22-ENTPD2 complex was in monoclinic space group C2, with one complex per asymmetric unit. A complete diffraction data set was collected for the complex to 2.75 Angstrom resolution.

[0768] Structure determination by molecular replacement was performed using the previously determined human ENTPD2 coordinates and Fab coordinates from PDB code 3QRG. Refinement with AutoBuster led to good refinement statistics and overall geometry. Two FAb22 residues, Ala55L and Tyr33H, and four ENTPD2 residues, Gly120, Thr122, Tyr229, and Ala430, were Ramachandran outliers in the structure of the FAb22-ENTPD2 complex. ENTPD2 residues Gly120 and Thr122, in addition to Fab residues Ala55L and Tyr33H are well-defined in the electron-density and are likely genuine geometry outliers. Worthy of note, Tyr33H is a CDR residue involved in ENTPD2 binding as described below. ENTPD2 residues Tyr229 and Ala430 were loosely modeled in the electron density.

[0769] The amino-acid sequences of the anti-human ENTPD2 FAb22 heavy chain and light chain are provided in FIG. 3A, with the CDRs underlined (as defined by Kabat, 1991, Sequences of proteins of immunological interest, NIH Publication No. 91-3242) and residues located at the Fab-antigen interface labeled with *. An overall view of the three dimensional structure of the anti-human ENTPD2 FAb22/ENTPD2 Y350A complex is depicted in FIG. 6.

[0770] The amino-acid sequence of recombinant human ENTPD2 used in this example (SEQ ID NO: 291) is provided in FIG. 4A. Soluble extracellular domain of human ENTPD2 spans residues 29-462. An engineered mutation of Y350A was present in the construct and highlighted in gray italics. The construct used here utilized an N-terminal GP67 secretion signal peptide (first 38 residues) and a C-terminal 6xHistidine tag (SEQ ID NO: 1010). Asn64, Asn129, Asn294, Asn378, and Asn443 are predicted N-linked glycosylation sites for which only those where glycosylation was observed in the crystal structure highlighted in gray italics . The secondary structure elements are shown below the amino acid sequence with bars representing α-helices, arrows representing □-strands.

Residues for which no secondary structure elements are labeled represent unstructured loop and turn segments.

[0771] The human ENTPD2 amino acid sequence bears high sequence homology with rodent species and other mammals and the structure possesses a nearly identical overall fold to that described for the rat ENTPD2 (i.e. PDB code 3CJA, Zebisch, M., Strater, N. (2008) Proc.Natl.Acad.Sci.Usa 105: 6882-6887). Invariant and conserved disulfide pairings are observed for Cys75/Cys99, Cys242/Cys284, Cys265/Cys310, Cys323/Cys328 and Cys377/Cys399. The RMSD (root mean squared deviation) across 388 C-α carbons between the human and rat ENTPD2 structures is approximately 0.365Å.

[0772] The final model for the FAb22/ENTPD2 complex contained residues 37-448 of ENTPD2. The active site for ATP hydrolysis resides between the two subdomains (subdomain 1: Pro36-Ser161 and Lys427-Phe461; subdomain 2: Gly162-Gln426). ENTPD2 residues omitted from final model include residues 29-36 of the N-terminus and 60-65 corresponding to loop residues connecting strands β2 and β3, residues 179-193 corresponding to the membrane interacting loop (MIL), and C-terminal residues beyond Ile448. All heavy and light chain Fab residues were included in the final refined model except the terminal cysteines (Cys228 heavy chain/Cys218 light chain).

[0773] The FAb22 binds ENTPD2 antigen primarily through engagement of the predicted membrane distal lobe through interactions involving all 6 CDRs of heavy and light chain variable domains. No FAb22 CDR residues appear to penetrate appreciably into the ENTPD2 active site cleft to affect ATP substrate binding. Heavy chain CDR3 and CDR2 residues sequester residues including and flanking the antiparallel 2 stranded β-sheet comprised of strands β10/β11. Terminal heavy chain CDR3 residues make additional binding contacts to residues of the N-terminal end of helix α14, as well as α8 and α13 helices. Light chain variable domain binding interactions with ENTPD2 largely involve CDR1 and CDR3 residues which bind predominantly the N-terminal end of helix α14. Formation of the FAb22/ENTPD2 complex buries approximately 16700 Å2 of the total combined solvent-accessible surface with nearly equal contributions from heavy and light Fab chains. Epitope and paratope residues involved in direct intermolecular contacts calculated within a 4.0Å distance cut-off are listed in Table 17, and labeled in FIG. 3A and 4A. A total of 25 Fab residues and 26 ENTPD2 residues are involved in direct intermolecular contacts, with heavy chain CDRs contributing more binding residues than

light chain CDRs. Of these Fab paratope residues, CDR tyrosines contribute a large number of ENTPD2 contacts with 10 of 14 CDR Tyr residues involved. Heavy chain CDR residues in intermolecular contacts include CDR1 residues Ser31, Gly32, Tyr33, and Tyr34; CDR2 residues Tyr54, Asp55, Asp57; and CDR3 residues Tyr100, Tyr101, Arg102, Tyr103, Ser106, Tyr107, Asp112, Tyr113. Tyr27 of heavy chain FR1 also makes contact to the ENTPD2 antigen. Light chain CDR1 residues involved in ENTPD2 binding include Tyr31, Asp32, Gly33, and Tyr36 as well as CDR2 light chain residues Glu59, Ser60, and CDR3 residues Ser95, Asn96, and Asp 98. Glu1 whose side chain is disordered and not modeled in complex structure in addition to Gly61 of FR3 are within contact distance of N-linked glycosylation observed for Asn294 of ENTPD2 antigen and highlighted in FIG. 3A.

Table 17. Epitope and paratope residues FAb22/hENTPD2

Human ENTPD2 epitope		**Anti-human ENTPD2 FAb22 paratope**	
Structural element	Contact residues	Contact residues	Structural element
β3–α1 loop	Gly79	Asp32L, Gly33L	L-CDR1
α8	Gln250	Tyr103H	H-CDR3
	Leu253	Tyr103H	H-CDR3
α8 -β10 loop	Trp266	Tyr107H	H-CDR3
	Arg268	Tyr54H, Asp55H, Asp57H	H-CDR2
	Gly269	Tyr34H Tyr54H, Asp55H	H-CDR1 H-CDR2
	Phe270	Tyr34H, Tyr54H Tyr101H, Tyr107H	H-CDR1, H-CDR2 H-CDR3
β10	Ser271	Gly32H, Tyr33H, Tyr34H Tyr54H, Tyr101H	H-CDR1 H-CDR2, H-CDR3
	Thr272	Tyr101H	H-CDR3
	Gln273	Tyr33H, Tyr103H Tyr100H, Tyr101H, Tyr113H	H-CDR1, H-CDR3 H-CDR3

	Val274	Tyr103H	H-CDR3
β10–α9 loop	Leu275	Arg102H	H-CDR3
α9	Asp278	Tyr103H	H-CDR3
β11	Arg298	Asp112H, Tyr113H Glu59L, Ser60L	H-CDR3 L-CDR2
	Ser300	Tyr27H, Tyr33H	H-FR1, H-CDR1
	Ser302	Ser31H, Gly32H Tyr54H	H-CDR1 H-CDR2
β11–α10 loop	Gly303	Tyr54H	H-CDR2
α12–α13 loop	Thr380	Asp57H	H-CDR2
α13	Trp381	Tyr34H, Tyr101H	H-CDR1, H-CDR3
	Ala382	Asp57H	H-CDR2
α13–α14 loop	Gly390	Tyr31L	L-CDR1
	Gln391	Tyr31L	L-CDR1
α14	Arg392	Tyr101H Ser95L, Asn96L, Asp98L	H-CDR3 L-CDR3
	Ala393	Ser106H Tyr31L, Tyr36L	H-CDR3 L-CDR1
	Arg394	Tyr31L, Asp32L	L-CDR1
	Asp397	Tyr107H	H-CDR3
The lists of epitope and paratope residues in direct contact were derived from the final refined coordinates with the CCP4 program NCONT, using a 4.0Å distance cut-off.			

Example 6. Crystallography and Epitope mapping of anti-human ENTPD2 FAb23

[0774] In this Example, anti-human ENTPD2 FAb23 was crystallized in complex with human ENTPD2 (Y350A mutant) ectodomain and the corresponding structure was determined. Analysis of anti-human ENTPD2 FAb23 binding to human ENTPD2 based on the X-ray data provided molecular details of antigen engagement and insights to the Fab paratopes and antigen epitopes revealed.

Materials and Methods

Preparation of human ENTPD2 and anti-human ENTPD2 FAb23 complex

[0775] To prepare the ENTPD2-FAb23 complex, a 1.6-fold molar excess of ENTPD2 was combined with the FAb23 in 20mM Tris pH 7.5 with 100mM NaCl and concentrated to 9.08 mg/mL by ultrafiltration, incubated on ice for 10 minutes, and submitted for crystallization trial set ups.

Crystallization and X-ray data collection

[0776] The anti-hENTPD2 FAb23 complexed with human ENTPD2 Y350A mutant was crystallized in 96-well plates (Greiner Bio-One) by the method of vapor diffusion in sitting drops, at 20°C. In detail, 0.2µl of protein stock was mixed with 0.2µl of reservoir solution, and the drop was equilibrated against 50µl of the same reservoir solution at 20°C. The experiments were set up with a Phoenix robotic system (Art Robbins Instruments), and stored in in-house custom engineered crystal imager and gantry (Novartis GNF internal systems).

[0777] For X-ray data collection, one crystal was directly mounted in a cryo-loop and flash cooled into liquid nitrogen. X-ray data sets were collected at the Advanced Light Source, BL5.03, with Quantum Q315r CCD detector, using 0.9765Å X-ray radiation. 140 images of 1.0° oscillation each were recorded at a crystal-to-detector distance of 300mm and processed with HKL2000 (Z. Otwinowski and W. Minor, " Processing of X-ray Diffraction Data Collected in Oscillation Mode ", Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A, p.307-326, 1997,C.W. Carter, Jr. & R. M. Sweet, Eds., Academic Press (New York).

Structure Determination and Analysis

[0778] The structure of the FAb23-ENTPD2 complex was determined by molecular replacement with the program Phaser (McCoy et al., 2007, J Appl Crystallogr 40:658-674), using the refined coordinates of human ENTPD2 previously determined in house and a homology model of the FAb23 generated with the antibody modeler tool in MOE software (Molecular Operating Environment (MOE), 2013.08; Chemical Computing Group ULC, 1010 Sherbooke St. West, Suite #910, Montreal, QC, Canada, H3A 2R7, 2018) which showed high sequence similarity to the Fab fragment of ICSM 18 - anti-PRP (PDB code 4W9D) as independent search models. The structure was refined using iterative cycles of model building followed by automated crystallographic refinement with the programs Coot

0.8.0 (Crystallographic Object-Oriented Toolkit; Emsley et al., 2010, Acta Crystallogr Sect D: Biol Crystallogr; 66:486-501) and Autobuster 2.11.5 (Bricogne et al., 2011, BUSTER version 2.11.2. Cambridge, United Kingdom: Global Phasing Ltd.).

[0779] Visual inspection of the crystal structure was carried out using the programs Coot (Emsley et al., 2010, Acta Crystallogr Sect D: Biol Crystallogr; 66:486-501) and PyMOL (Molecular Graphics System; DeLano Scientific: Palo Alto, CA). The quality of the final refined models was assessed with the programs Coot and PROCHECK v3.3 (Laskowski et al., 1992, J Appl Crystallogr; 26:283-291). Residues of human ENTPD2 that become less accessible to solvent upon binding of the anti-human ENTPD2 MAB17 Fab were identified by the program AREAIMOL of the CCP4 program suite (Collaborative Computational Project, Number 4, 1994). Intermolecular contacts were defined using a cut-off distance of 4.0Å and were identified with the CCP4 program NCONT.

Results

Crystal Structure of the anti-hENTPD2 FAb23 /ENTPD2 complex

[0780] The anti-hENTPD2 FAb23 complexed with human ENTPD2 Y350A mutant was crystallized in 96-well plates by the method of vapor diffusion in sitting drops, at 20°C. Crystals grew in 0.08M Bis-Tris propane pH 8.8, 0.02M citric acid, 16% PEG3350. Crystals appeared after approximately 6 weeks and grew to full size within a few days.

[0781] The crystal of the FAb23-ENTPD2 complex was in monoclinic space group P21, with one complex per asymmetric unit. A complete diffraction data set was collected for the complex to 2.0 Angstrom resolution. The final model for the FAb23 complexed with ENTPD2 was refined with AutoBuster with good refinement statistics and overall geometry. A total of four Ramachandran outliers were present in the final model with two residues from the FAb23 light chain (Ser39 and Thr50) and two from ENTPD2 (Thr122 and Ala430). Electron density was poor for Ser39 of the Fab light chain and tentatively modeled. All other residues were adequately defined in the electron density and likely genuine Ramachandran outliers. ENTPD2 residues omitted from final model include residues 29-34 of the N-terminus and residues beyond 448 of the C-terminus. Residues 139-144 of the FAb23 chain constant region and the terminal cysteine (Cys227) were also omitted from the final model. The last two residues of the FAb23 light chain (Glu212 and Cys213) were also absent from final model due to disorder.

[0782] The amino-acid sequences of the anti-human ENTPD2 FAb23 heavy chain and light chains are provided in FIG. 3B, with the CDRs underlined (as defined by Kabat, 1991, Sequences of proteins of immunological interest, NIH Publication No. 91-3242) and residues located at the Fab-antigen interface labeled with *. An overall view of the three dimensional structure of the FAb23/ENTPD2 Y350A complex is depicted in FIG. 7.

[0783] In contrast to FAb22, binding of the FAb23 to ENTPD2 involves significant engagement of both membrane proximal and distal lobes by both heavy and light chain variable domains. Heavy chain variable region loops CDR2 and CDR3 participate in ENTPD2 binding, with no contribution from CDR1. Residues from all 3 CDRs from the light chain variable region are involved in ENTPD2 binding. Contacts with the ENTPD2 membrane distal lobe are largely conferred by residues from heavy chain CDR3, light chain CDR2, and light chain FR3 residues binding to residues of the ENTPD2 loop region residues between α13 and α14, as well as FR3 interactions with antiparallel strands β10/β11 and helix α9. CDR3 light chain and CDR2 heavy chain residues confer extensive binding to α2 helix and loop residues connecting β3 and α1 of the membrane proximal lobe of ENTPD2. Heavy chain CDR3 projects terminal residues Tyr104, Tyr105, and Gly106 into the ENTPD2 active site cleft between N-terminal ends of helices α8, α11, and α14 of the membrane distal lobe. Superposition of the ATP analog AMP-PNP from bound rat ENTPD2 crystal structure PDB 3CJA suggest Tyr105 is positioned where the adenine ring of ATP would be predicted to bind, potentially sterically obstructing substrate binding. Tyr105 and Tyr104 of the heavy chain CDR3 terminus may also perturb ENTPD2 active site residues including Tyr350 and Arg394 necessary for π-π and cation-π stacking interactions with the adenine ring of substrate ATP. Binding of the FAb23 to ENTPD2 buries approximately 17500 Å2 of combined solvent-accessible surface. Epitope and paratope residues involved in direct intermolecular contacts calculated within a 4.0Å distance cut-off are listed in Table 18, and labeled in FIGs. 3B and 4A. 25 Fab residues and 29 ENTPD2 residues were involved in direct intermolecular contacts. Heavy chain residues Tyr55, Ile57, Thr59, Gln62 of CDR2, as well as Phe102, Tyr105, Ile107, Tyr110 of CDR3 contribute to ENTPD2 binding with no contribution from CDR1 residues. Light chain residues contributing to ENTPD2 binding include Ser27 and Tyr31 from CDR1, Ser49 and Asn52 from CDR2, and Trp90, Ser91, Ser92, Tyr93, and Trp95 of CDR3. Non-CDR light chain residues contributing to ENTPD2 binding include Glu1, which is observed and modeled as pyroglutamate in the crystal structure, Thr22 of FR1, and Ser64, Gly65, Ser66, Gly67, Thr68, and Phe69 of FR3.

TABLE 18. Epitope and paratope residues FAb23 /human ENTPD2

Human ENTPD2 epitope		**Anti-human ENTPD2 FAb23 paratope**	
Structural element	Contact residues	Contact residues	Structural element
β1–β2 loop	His50	Ile107H	H-CDR3
β3	Asp76	Ile107H	H-CDR3
β3–α1 loop	Pro78	Tyr110H, Trp95L	H-CDR3, L-CDR3
	Gly79	Trp90L, Ser91L	L-CDR3
	Gly80	Ser91L	L-CDR3
α1	Tyr85	Ser91L, Ser92L, Tyr93L	L-CDR3
α1–α2 loop	Asp87	Ser27L	L-CDR1
	Asn88	Glu1L, Tyr93L	L-FR1, L-CDR3
α2	Gly91	Tyr93L	L-CDR3
	Gln94	Gln62H, Tyr93L	H-CDR2, L-CDR3
	Ser95	Tyr93L	L-CDR3
	Gly98	Ile57H, Thr59H	H-CDR2
	Glu101	Ile57H	H-CDR2
	Gln102	Tyr55H, Ile57H	H-CDR2
	Gln105	Tyr55H, Ile57H	H-CDR2
	Asp106	Tyr55H	H-CDR2
α8	Arg245	Tyr104H, Tyr105H	H-CDR3
β10	Thr272	Ser64L, Gly65L	L-FR3
	Gln273	Phe69L	L-FR3
	Leu275	Thr68L, Phe69L	L-FR3
α9	Asp278	Ser66L, Gly67L, Thr68L, Phe69L	L-FR3
β11	Arg298	Thr22L, Phe69L	L-FR1, L-FR3

β12–α11 loop	Ala347	Tyr105H	H-CDR3
α11	Ala350	Tyr105H	H-CDR3
	Thr351	Tyr105H	H-CDR3
α13–α14 loop	Arg392	Asn52L	L-CDR2
	Ala393	Phe102H, Tyr104H, Ser49L	H-CDR3, L-CDR2
	Arg394	Tyr104H, Tyr31L	H-CDR3, L-CDR1
α14	Tyr398	Tyr104H, Tyr105H	H-CDR3
The lists of epitope and paratope residues in direct contact were derived from the final refined coordinates with the CCP4 program NCONT, using a 4.0Å distance cut-off.			

Example 7. Crystallography and Epitope mapping of anti-mouse ENTPD2 FAb24

[0784] In this Example, anti-murine ENTPD2 Fab MAB13 was crystallized in complex with murine ENTPD2 ectodomain and the corresponding structure was determined. Analysis of anti-mouse ENTPD2 FAb24 binding to murine ENTPD2 based on the X-ray data provided molecular details of antigen engagement and insights to the Fab paratopes and antigen epitopes revealed.

Materials and Methods

Preparation of murine ENTPD2 and anti-mouse ENTPD2 FAb24 complex

[0785] To prepare the murine ENTPD2 FAb24 complex, purified murine ENTPD2 and FAb24 in 20mM Tris pH 7.5 with 100mM NaCl were combined in 1:1 molar ratio, incubated on ice at 4 degrees Celcius overnight. The following morning, sample was concentrated to 9.88 mg/mL by ultrafiltration, and submitted for crystallization trial set ups.

Crystallization and X-ray data collection

[0786] The anti-mouse ENTPD2 FAb24 complexed with ENTPD2 Y350A mutant was crystallized in 96-well plates (Greiner Bio-One) by the method of vapor diffusion in sitting drops, at 20°C. In detail, 0.2µl of protein stock was mixed with 0.2µl of reservoir solution, and the drop was equilibrated against 50µl of the same reservoir solution at 20°C. The experiments were set up with a Phoenix robotic system (Art Robbins Instruments), and stored in in-house custom engineered crystal imager and gantry (Novartis GNF internal systems).

[0787] For X-ray data collection, one crystal was directly mounted in a cryo-loop and flash cooled into liquid nitrogen. X-ray data sets were collected at the SSRL, beamline 7-1, using 1.1808Å X-ray radiation, equipped with an ADSC Quantum 315r CCD detector. 340 images of 0.5° oscillation each were recorded at a crystal-to-detector distance of 400mm and processed with HKL2000 (Z. Otwinowski and W. Minor, " Processing of X-ray Diffraction Data Collected in Oscillation Mode ", Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A, p.307-326, 1997,C.W. Carter, Jr. & R. M. Sweet, Eds., Academic Press (New York).

Structure Determination and Analysis

[0788] The FAb24-mouse ENTPD2 complex structure was determined by molecular replacement with the program Phaser (McCoy et al., 2007, J Appl Crystallogr 40:658-674), using the refined structures of murine ENTPD2 and FAb24 previously determined in house as independent search models. The structure was refined using iterative cycles of model building followed by automated crystallographic refinement with the programs Coot 0.8.0 (Crystallographic Object-Oriented Toolkit; Emsley et al., 2010, Acta Crystallogr Sect D: Biol Crystallogr; 66:486-501) and Autobuster 2.11.5 (Bricogne et al., 2011, BUSTER version 2.11.2. Cambridge, United Kingdom: Global Phasing Ltd.).

[0789] Visual inspection of the crystal structure was carried out using the programs Coot (Emsley et al., 2010, Acta Crystallogr Sect D: Biol Crystallogr; 66:486-501) and PyMOL (Molecular Graphics System; DeLano Scientific: Palo Alto, CA). The quality of the final refined models was assessed with the programs Coot and PROCHECK v3.3 (Laskowski et al., 1992, J Appl Crystallogr; 26:283-291). Residues of murine ENTPD2 that become less accessible to solvent upon binding of the anti-mouse ENTPD2 FAb24 were identified by the program AREAIMOL of the CCP4 program suite (Collaborative Computational Project, Number 4, 1994). Intermolecular contacts were defined using a cut-off distance of 4.0Å and were identified with the CCP4 program NCONT.

[0790] The FAb24-mouse ENTPD2 complex structure was determined by molecular replacement with the program Phaser (McCoy et al., 2007, J Appl Crystallogr 40:658-674), using the refined structures of murine ENTPD2 and FAb24 previously determined in house as independent search models. The structure was refined using iterative cycles of model building followed by automated crystallographic refinement with the programs Coot 0.8.0 (Crystallographic Object-Oriented Toolkit; Emsley et al., 2010, Acta Crystallogr Sect D: Biol

Crystallogr; 66:486-501) and Autobuster 2.11.5 (Bricogne et al., 2011, BUSTER version 2.11.2. Cambridge, United Kingdom: Global Phasing Ltd.).

Results

Crystal Structure of the anti-mouse ENTPD2 FAb24/mouse ENTPD2 complex

[0791] The anti-mouse ENTPD2 FAb24 complexed with murine ENTPD2 was crystallized in 96-well plates by the method of vapor diffusion in sitting drops, at 20°C. Crystals grew in 0.2M tri-ammonium citrate pH 7.0, 20% PEG3350. Crystals appeared after approximately 1 month and grew to full size within a few days.

[0792] The FAb24-mouse ENTPD2 complex crystal was in monoclinic space group P21, with one complex per asymmetric unit. A complete diffraction data set was collected for the complex to 3.0 Angstrom resolution. The final model for the FAb24 complexed with mouse ENTPD2 was refined with AutoBuster with good refinement statistics and overall geometry. Two Ramachandran outliers Thr122 of mouse ENTPD2 and Ala57 of the FAb24 were present in final model, both of which were well-defined in electron density. Asn129 and Asn378 were only residues where N-linked glycosylation was observed. Glu1 of the FAb24 heavy chain was observed and modeled as pyroglutamate. Mouse ENTPD2 residues omitted from final model include residues 29-35 of the N-terminus, 61-66 corresponding to loop residues connecting strands β2 and β3, residues 182-194 corresponding to the membrane interacting loop (MIL), loop residues 290-293 between α9 and β11, and C-terminal residues beyond Ala450. All heavy and light chain residues of the FAb24 were included in the final refined model except the terminal cysteine of the heavy chain Cys225.

[0793] The amino-acid sequences of the anti-mouse ENTPD2 FAb24 heavy and light chains are provided in FIG. 3C, with the CDRs underlined (as defined by Kabat, 1991, Sequences of proteins of immunological interest, NIH Publication No. 91-3242) and residues located at the Fab-antigen interface labeled with *. An overall view of the three dimensional structure of the FAb24/mENTPD2 complex is depicted in FIG. 8.

[0794] Anti-mouse ENTPD2 FAb24 engages predominantly the presumed membrane distal lobe (residues G162-E426) of the ENTPD2 antigen. An equal contribution to ENTPD2 binding is observed for CDR residues of the heavy chain and light chain variable domains.

[0795] Compared to FAb22 and FAb23 binding to human ENTPD2, the FAb24 engages the murine ENTPD2 from an entirely different direction orthogonal to what is

observed in FAb22 and FAb23 complexes with hENTPD2. The FAb24 binds predominantly the murine ENTPD2 membrane distal lobe through extensive heavy chain CDR interactions and relatively few light chain CDR interactions. Heavy chain CDR1 and CDR3 residues in conjunction with light chain CDR1 and CDR2 residues bind to helices α11 and α13 of mENTPD2. Residues of heavy chain CDR2 make interactions with the interconnecting loop residues between α13 and α14. The CDR3 heavy chain CDR3 is observed in a conformation where it is bent nearly 90 degrees and adopts a short β-turn motif at its terminal end. Two residues of the FR3 heavy chain make sole contacts to the mouse ENTPD2 proximal lobe through interactions with β3 of the 5-stranded antiparallel sheet. No MAB13 CDRs are observed to extend far enough into the mouse ENTPD2 site to affect ATP hydrolysis activity through direct obstruction of the substrate binding site. Binding of FAb24 to murine ENTPD2 buries approximately 16300 Å2 total combined solvent-accessible surface. Epitope and paratope residues involved in direct intermolecular contacts calculated within a 4.0Å distance cut-off are listed in Table 19 and labeled in FIGs. 3C and 4B. 22 Fab residues and 18 murine ENTPD2 residues were involved in direct intermolecular contacts and comprise the observed paratope and epitope in Fab/ENTPD2 engagement. Heavy chain CDR residues include CDR1 Thr28, Thr30, His31, Tyr32, and Gly33; CDR2 Trp50, Asn52, Thr53, and Asp54, Thr55; CDR3 Tyr99, Gly100, Thr101, Leu102, Tyr103, and Phe110. Two FR3 residues Thr74 and Ser75 from the heavy chain also contribute to binding. Light chain CDR residues contributing to binding include Thr34 and Lys36 from CDR1, Tyr56 from CDR2, and Trp97 from CDR3.

TABLE 19. Epitope and paratope residues FAB24/mouse ENTPD2

Mouse ENTPD2 epitope		**Anti-mouse ENTPD2 FAb24 paratope**	
Structural element	Contact residues	Contact residues	Structural element
β3	Ser74	Ser75H	H-FR3
	Cys75	Ser75H	H-FR3
	Asp76	Thr74H, Ser75H	H-FR3
α11	Tyr349	Thr28H	H-CDR1
	Tyr350	Thr28H, His31H	H-CDR1

	Asp353	Thr28H, His31H	H-CDR1
	Phe354	His31H	H-CDR1
	Thr357	Tyr32H Thr101H, Leu102H, Tyr103H	H-CDR1 H-CDR3
	Val358	Tyr32H Thr101H, Tyr103H	H-CDR1 H-CDR3
α11–α12 loop	Gly360	Tyr103H	H-CDR3
α13	Gln385	Thr34L	L-CDR1
	Ala386	Phe110H Lys36L Tyr56L	H-CDR3 L-CDR1 L-CDR2
	Arg387	Gly100H, Thr101H	H-CDR3
α13–α14 loop	Val388	His31H	H-CDR1
	Pro389	Tyr99H, Gly100H, Phe110H Trp97L	H-CDR3 L-CDR3
	Gly390	Trp50H	H-CDR2
	Gln391	Thr30H, Tyr32H, Gly33H Trp50H, Asn52H, Thr53H, Asp54H	H-CDR1 H-CDR2
	Thr393	Asp54H, Thr55H	H-CDR2
	Arg394	Asp54H	H-CDR2
α14	Tyr398	His31H	H-CDR1
The lists of epitope and paratope residues in direct contact were derived from the final refined coordinates with the CCP4 program NCONT, using a 4.0Å distance cut-off.			

Example 8. Inhibition of tumor growth by anti-ENTPD2 MAB13 in combination with anti-PD-1 Ab in the syngeneic B16LM3 tumor model

[0796] B16LM3 model was established in female C57BL/6 mice by subcutaneous injection of $0.5x10^6$ cells into the right flank of each mouse. The day after implant mice were randomized into treatment groups (n=10 per group). Mice received treatments of either anti-mouse ENTPD2 mAb13 or a non-specific mIgG2a isotype control (clone MOPC-173, BioLegend, San Diego, CA) at a final dose 15 mg/kg on Day 1, 5, 8, 12, 15.

[0797] Anti-PD-1 Ab (clone RMP1-14 Bio X Cell, West Lebanon, NH) or non-specific rIgG2a isotype control (clone RTK2758, BioLegend, San Diego, CA) were delivered i.p. at a final dose of 10 mg/kg on days 1, 5, 8, 12, 15. All doses were adjusted to individual mouse body weights.

[0798] All test agents were tolerated on study and no overt clinical symptoms of toxicities or body weight loss were observed in any of the treatment groups. Combination of anti-mouse ENTPD2 mAb13 with anti-PD-1 Ab treatment significantly extended mouse survival relative to No Treatment ($p<0.005$), Isotype Control ($p<0.05$) or anti-PD-1 Ab ($p<0.01$) (Log-rank (Mantel-Cox) test was used to determine if survival curves were significantly different)) (FIG. 9).

Example 9. Combination treatment of anti-ENTPD2 mAb13 with anti-PD-1 Ab in the syngeneic B16F10 tumor model induces tumor influx of activated T cells

[0799] B16F10 model was established in female C57BL/6 mice by subcutaneous injection of $0.5x10^6$ cells into the right flank of each mouse. On day 7 once tumors reached approximately 30 mm^3, mice were randomized according to tumor volume into treatment groups (n=10 per group). Mice received treatment of either anti-mouse ENTPD2 mAb13 at a final dose 15 mg/kg, anti-PD-1 Ab (clone RMP1-14 Bio X Cell, West Lebanon, NH) i.p. at a final dose of 10 mg/kg or the combination of both treatments on days 1, 5, and 8. All doses were adjusted to individual mouse body weights.

[0800] No significant anti-tumor efficacy was observed after treatment with anti-mouse ENTPD2 mAb13 or anti-PD-1 Ab alone, however a significant reduction in tumor growth relative to No Treatment control was observed in the combination arm of anti-mouse ENTPD2 mAb13 and anti-PD-1 Ab ($p<0.05$ One-Way ANOVA / Tukey's Multiple Comparisons Test) (FIGs. 10A-10B).

[0801] In order to understand the impact of treatments on the tumor microenvironment, mice were euthanized on day 8 and tumors were dissociated in HyClone RPMI1640 media (GE Healthcare, Pittsburg, PA) using gentleMacs C-tubes (Miltenyi Biotec, Auburn, CA) on the gentleMacs Octo Dissociator (Miltenyi Biotec, Auburn, CA). Approximately $2x10^6$ dissociated tumor cells were blocked with rat anti-mouse CD16/CD32 Ab (Biolegend, San Diego , CA) to reduce non-specific FcyRIII/II binding and subsequently stained with the following cocktail of Abs: rat anti-mouse CD45-BUV395 (clone 30-F11)

(BD Biosciences, San Jose, CA), rat anti-mouse CD8a-BUV737 (clone 53-6.7) (BD Biosciences, San Jose, CA), rat anti-mouse CD4-BV510 (clone RM4-5) (BD Bioscience, San Jose CA), anti-mouse CD69-PercPCy5.5 (clone H1-2F3) (Biolegend, San Diego, CA) and rat anti-mouse CD25-eFluor450 (clone eBio3C7) (eBioscience, San Diego, CA) at the manufacturers' recommended dilutions. All incubations and washes were performed in FACS Buffer composed of 1x HyClone Phosphate Buffered Saline (GE Healthcare, Pittsburg, PA), 1% HyClone Fetal Bovine Serum (GE Healthcare, Pittsburg, PA), 2mM EDTA (ThermoFisher, Waltham MA). After staining with the cell surface antigen antibody cocktail, dissociated tumor cells were washed in FACS buffer, fixed and permeabilized using the eBioscience Foxp3 / Transcription Factor Staining Buffer Kit (ThermoFisher, Waltham MA) to allow for intracellular staining with the mouse anti-mouse FOXP3-eFluor660 (clone 150D/E4) (eBioscience, San Diego, CA).

[0802] A significant influx of activated CD4 T-helper cells (defined as CD45+ CD8- CD4+ FOXP3- CD69+ CD25+) (7.0-fold increase vs No Treatment, $p<0.0001$ One-Way ANOVA / Tukey's Multiple Comparisons Test) and CD8 T cells (defined as CD45+ CD4- CD8+ CD69+ CD25+) (5.8-fold change vs No Treatment, $p<0.05$ One-Way ANOVA / Tukey's Multiple Comparisons Test) was observed with the Anti-mouse ENTPD2 mAb13 and Anti-PD-1 Ab combination treatment relative to all other treatment groups (FIG. 10C).

Example 10. Dose dependent in vivo efficacy of anti-human ENTPD2 mAb1 and mAb6 in combination with anti-PD-1 Ab in the human ENTPD2 engineered B16LM3 xenograft model in C57BL/6 mice

[0803] To demonstrate targeted anti-tumor activity of anti-human ENTPD2 Abs *in vivo*, a human ENTPD2-engineered model was developed, B16LM3 clone 5. This model was derived from the B16LM3 melanoma model, where endogenous mouse ENTPD2 expression was knocked out via a transient electroporation of CAS9 protein with CRISPR guide RNA sequences against mouse ENTPD2, and human ENTPD2 was overexpressed using a retroviral transduction approach. Human ENTPD2 expression in the model was confirmed *in vitro* by FACS with the human ENTPD2 selective anti-human ENTPD2 mAb17. Mouse ENTPD2 selective anti-mouse ENTPD2 mAb13 was used to demonstrate complete knockout of endogenous mouse ENTPD2 (FIG. 11A). B16LM3 clone B5 demonstrated comparable growth kinetics to the parental line and sustained human ENTPD2 expression in the syngeneic host (FIG. 11B).

[0804] Human ENTPD2 engineered B16LM3 clone B5 model was established in female C57BL/6 mice by subcutaneous injection of $0.5x10^6$ cells into the right flank of each mouse. Once tumors reached approximately 35-50 mm^3, mice were randomized according to tumor volume into treatment groups (n=8 per group). Mice received an i.v. treatment of either anti-human ENTPD2 mAb1 or mAb6 at a final dose of 0.1, 1 or 10 mg/kg or a non-specific human IgG1 isotype control 10 mg/kg on day 1 of study. Anti-PD-1 Ab (clone RMP1-14 Bio X Cell, West Lebanon, NH) was dosed i.p. at a final dose of 10 mg/kg on D1 and D5. All doses were adjusted to individual mouse body weights. All test agents were tolerated on study and no overt clinical symptoms of toxicities or body weight loss were observed in any of the treatment groups (Table 23).

[0805] No significant anti-tumor efficacy was observed after treatment with anti-human ENTPD2 mAb1 or mAb6 as single agents or the combination of the non-specific isotype control and anti-PD-1 Ab. Combination regimen of anti-human ENTPD2 mAb1 with anti-PD-1 Ab (fixed dose of 10 mg/kg) demonstrated a dose dependent anti-tumor effect with $\Delta T/\Delta C$ value of 18.4% (10 mg/kg), 35.7% (1mg/kg) and 33.4% (0.1 mg/kg). Similarly combination regimen of anti-human ENTPD2 mAb6 with anti-PD-1 Ab (fixed dose of 10 mg/kg) also demonstrated a dose dependent anti-tumor effect with $\Delta T/\Delta C$ value of 29.2% (10 mg/kg), 27.3% (1mg/kg) and 41.0% (0.1 mg/kg) (Table 23 and FIGs. 12A-12B).

Table 23. Anti-human ENTPD2 Ab dose response efficacy in human ENTPD2 engineered B16LM3 clone B5 xenograft model on Day 7 of treatment.

	Anti-human ENTPD2 mAb	Anti-PD-1 Ab	Tumor Response	Host Response	
Treatment	Dose, schedule	Dose, schedule	$\Delta T/\Delta C$ (%)	Δ body weight (%)	Survival (alive/total)
No Treatment	None	None		0.1	8/8
Isotype + anti-PD-1 Ab	10 mg/kg dosed D1	10 mg/kg dosed D1 and D5	61.2	0.0	8/8
Anti-human ENTPD2 mAb1 + anti-PD-1 Ab	10 mg/kg dosed D1	10 mg/kg dosed D1 and D5	18.4**	-1.2	8/8
Anti-human ENTPD2 mAb1 + anti-PD-1 Ab	1 mg/kg dosed D1	10 mg/kg dosed D1 and D5	35.7*	-2.9	8/8

Anti-human ENTPD2 mAb1 + anti-PD-1 Ab	0.1 mg/kg dosed D1	10 mg/kg dosed D1 and D5	33.4*	-0.3	8/8
Anti-human ENTPD2 mAb6 + anti-PD-1 Ab	10 mg/kg dosed D1	10 mg/kg dosed D1 and D5	29.2*	-1.9	8/8
Anti-human ENTPD2 mAb6 + anti-PD-1 Ab	1 mg/kg dosed D1	10 mg/kg dosed D1 and D5	27.3*	-1.6	8/8
Anti-human ENTPD2 mAb6 + anti-PD-1 Ab	0.1 mg/kg dosed D1	10 mg/kg dosed D1 and D5	41.0	0.2	8/8
Anti-human ENTPD2 mAb1	10 mg/kg dosed D1	None	71.7	-0.2	8/8
Anti-human ENTPD2 mAb6	10 mg/kg dosed D1	None	60.0	-0.1	8/8
The experiment was evaluated on treatment Day 7, * $p<0.05$ ** $p<0.005$ versus control No Treatment group (One-Way ANOVA / Tukey's Multiple Comparisons Test). % $\Delta T/\Delta C = 100$ $\Delta T/\Delta C$ where: ΔT = mean tumor volume of the drug treated group on D7 of study – mean tumor volume of the drug treated group on initial day of dosing; ΔC = mean tumor volume of the control group on D7 of study – mean tumor volume of the control group on initial day of dosing D1. Δ body weight (%) = (Mean body weight D28-mean body weight D1) *100 / Mean body weight D1 of treatment.					

Example 11. Anti-human ENTPD2 mAb activity in the human ENTPD2 engineered B16LM3 clone B5 xenograft model in C57BL/6 mice

[0806] In order to understand immediate impact of ENTPD2 blockade from immune pathway engagement perspective, plasma and B16LM3 clone B5 tumors (mean tumor volume ~170mm^3) were collected from C57BL/6 mice 24hr after treatment with anti-human ENTPD2 mAb1 or Isotype Control at 10 mg/kg. Anti-human ENTPD2 mAb1 is not mouse ENTPD2 cross-reactive, so any cytokine modulation in the periphery would be reflective of changes in tumor microenvironment.

[0807] Briefly, plasma was isolated via collection of blood into Microvette MV-H-300 Capillary Plasma Lithium Heparin Blood Collection tube (Sai Infusion technologies, Lake Villa, IL), that were spun down at 1000-2000Xg for 10min. Plasma samples were stored at -80°C until use. Tumor samples were surgically excised and immediately frozen in liquid nitrogen. Tumor tissue was then homogenized in T-PER Tissue Protein Extraction Reagent (ThermoFisher, Waltham, MA) using the TissueLyser (Qiagen, Germany) instrument. Tumor lysate samples were spun down at 11,000 rpm for 15min and supernatants were collected for protein concentration analysis using Pierce BCA Protein Assay Kit (ThermoFisher, Waltham, MA). 200µg of protein or 25 µl of undiluted plasma was used for cytokine analysis using the

V-PLEX Mouse Cytokine 29-Plex Kit (MSD, Rockville, MD) according to manufacturer's recommendations.

[0808] A significant decrease in plasma MCP1 ($p<0.05$ Unpaired T-Test), accompanied by an approximately 2-fold increase in MCP1 at the tumor site was observed with anti-human ENTPD2 mAb1 treatment (FIGs. 13B and 13D), potentially reflecting myeloid cell engagement and recruitment to the tumor site. In addition, an approximately 2-fold decrease of IL-1β was observed in plasma from anti-human ENTPD2 mAb1 treated animals ($p=0.05$ Unpaired T-Test) and a trend suggesting a parallel reduction at the tumor site (FIGs. 13A and 13C).

Example 12. Anti-human ENTPD2 mAb activity in combination with A2AR antagonist in the human ENTPD2 engineered B16LM3 clone B5 xenograft model in C57BL/6 mice

[0809] Human ENTPD2-engineered B16LM3 clone B5 was established in female C57BL/6 mice by subcutaneous injection of 0.5×10^6 cells into the right flank of each mouse. Once tumors reached approximately 50 mm^3, mice were randomized according to tumor volume into treatment groups (n=8 per group). Mice received an intravenous (i.v.) treatment of either anti-ENTPD2 mAb1 at a final dose of 10/mg/kg or a non-specific human IgG1 isotype control 10mg/kg on day 1 of study. NIR178 was administered per os (p.o.) for 4 days on and 3 days off, starting at the beginning of study at either 50mg/kg or 200mg/kg. All doses were adjusted to individual mouse body weights. The study was carried out for thirteen days post treatment initiation and tumor volumes were assessed every other day to assess efficacy. All test agents were tolerated on study and no overt clinical symptoms of toxicities or body weight loss were observed in any of the treatment groups (Table 27).

Table 27. In vivo efficacy of anti-human ENTPD2 Ab and A2AR antagonist in human ENTPD2 engineered B16LM3 clone B5 xenograft model on Day 13 of treatment.

	Anti-human ENTPD2 or isotype mAb	NIR178 or Vehicle	Tumor Response	Host Response	
Treatment	Dose, schedule	Dose, schedule	ΔT/ΔC (%)	ΔBody weight (%)	Survival (alive/total)
No Treatment	None	None		-2.2	6/8
Vehicle + hIgG1 Isotype	10 mg/kg, dosed D1	4d ON/3d OFF	96.9	-2.0	6/8

NIR178 + hIgG1 Isotype	10 mg/kg, dosed D1	50mg/kg, 4d ON/3d OFF	123.6	-1.4	7/8
NIR178 + hIgG1 Isotype	10 mg/kg, dosed D1	200 mg/kg, 4d ON/3d OFF	93.3	-2.5	6/8
NIR178 + Anti-human ENTPD2 mAb1	10 mg/kg, dosed D1	50mg/kg, 4d ON/3d OFF	61.6	1.3	8/8
The experiment was evaluated on treatment Day 13. % $\Delta T/\Delta C$ = 100 $\Delta T/\Delta C$ where: ΔT = mean tumor volume of the drug treated group on D13 of study – mean tumor volume of the drug treated group on initial day of dosing; ΔC = mean tumor volume of the control group on D13 of study – mean tumor volume of the control group on initial day of dosing D1. Δ Body weight (%) = (Mean body weight D28-mean body weight D1) *100 / Mean body weight D1 of treatment.					

[0810] No significant anti-tumor efficacy was observed after treatment with the combination of the non-specific isotype control and the A2AR antagonist, NIR178, at either 50 or 200mg/kg. The combination regimen of anti-ENTPD2 mAb1 (10mg/kg) with NIR178 (50mg/kg) demonstrated an anti-tumor effect with T/ΔC value of 61.6% (Table 27 and FIG. 14). These data suggest that there is enhanced anti-tumor efficacy when blocking multiple nodes in the adenosine pathway.

Example 13. Assessment of Anti-ENTPD2 Abs in the biochemical and cell-based functional assays

[0811] Biochemical and cell-based functional assays were developed in-house to understand functional impact of anti-ENTPD2 Abs against purified extracellular domain of ENTPD2 (residues 29-462), as well as against the fully intact protein in the context of the native cell-based conformation. ENTPD2 hydrolyzes ATP to ADP, which can subsequently be detected using the HTRF Transcreener ADP2 TR-FRET Red Assay (BellBrook Labs, Madison, WI) where ENTPD2-produced ADP would compete with the ADP Tracer for binding to the anti-ADP-Tb antibody. The resulting signal is inversely proportional to the concentration of ADP in the sample.

[0812] To evaluate activity of anti-ENTPD2 Abs in the ENTPD2 biochemical assay, anti-ENTPD2 Abs and recombinant ENTPD2 (residues 29-462) were diluted in reaction buffer (50 mM HEPES, pH 7.1, 10 mM $MgCl_2$, 0.01% BSA) to the desired concentration. 4 µL per well of the ENTPD2 solution and 2 µL per well of the Anti-ENTPD2 Ab solution were transferred into a ProxiPlate (PerkinElmer, Waltham, MA) and incubated for 30 min at room temperature. Reaction was then initiated via addition of 2 µl of ATP (final assay concentration of 1 µM), and the sample was incubated for 25 min at room temperature.

Reaction was quenched with 200 mM EDTA/200 mM EGTA (5 µL per well) and detection reagents were added to wells (5 µL per well), with a final concentration of 4 nM ADP2 antibody and 4 nM ADP Tracer in well (BellBrooks Labs, Madison, WI). Plate was then incubated at room temperature for 60 min before measuring the HTRF signal.

[0813] To establish cell-based functional assays, human/cyno/mouse ENTPD2-engineered NIH/3T3 cells or RKO (ATCC, Manassa VA) colorectal cancer cells with endogenous ENTPD2 expression were plated overnight at 150, 200 and 250 cells per well for NIH/3T3 mouse, cyno and human ENTPD2 lines, respectively, or 1000 cells per well for RKO in 384-well tissue culture plate, in 30 µl per well (Perkin Elmer, Waltham, MA). The following day cells were pre-incubated with Anti-ENTPD2 Abs in dose response for 60 min at 37ºC, 5% CO_2 (10 µl of 5X antibody dose per well), and subsequently stimulated with a final concentration of 10 µM ATP (Teknova, Hollister, CA) for 20 minutes at room temperature (10 µl of 5X (50 µM) ATP per well). Reactions were quenched with 40 mM EDTA/40 mM EGTA, 25 µl per well, and 15 µl of quenched media was transferred to low volume Proxiplates (PerkinElmer, Waltham, MA) for ADP detection. ADP production was detected with the Transcreener ADP2 TR-FRET Red Assay (BellBrook Labs, Madison, WI) with a final concentration of 4 nM ADP2 antibody and 13.4 nM of ADP Tracer in wells (4X solution was prepared and 5 µL of "Detection Reagent Mix" was added to the quenched conditioned media). Plates were incubated with detection reagents for 1 hour at room temperature prior to reading plates in HTRF mode.

[0814] HTRF signal (Emission at 620 nm and 665 nm) was assessed in both assays using the Envision plate reader in HTRF mode (Perkin Elmer, Waltham, MA). HTRF ratio was determined using the following formula: HTRF ratio = R = Emission at 665 nm/Emission at 620 nm x 10,000. Subsequently % Residual Activity and % Inhibition were determined as follows: $\%\ Residual\ Activity = \frac{(R-R_{0\%})}{(R_{100\%}-R_{0\%})} * 100;\ \%\ Inhibition = 100 - \left[\frac{(R-R_{0\%})}{(R_{100\%}-R_{0\%})} * 100\right]$.

[0815] Where $R_{0\%}$ is the HTRF ratio of the negative control (0% enzyme activity), and $R_{100\%}$ is the HTRF ratio of the positive control (100% enzyme activity). Data were analyzed in Microsoft Excel and graphed using GraphPad's Prism 7.0 software and IC_{50} values were obtained using non-linear regression, log (agonist) vs. response-variable slope (four parameters) analysis.

Representative activity of anti-ENTPD2 Abs in the biochemical human ENTPD2 functional assay

[0816] Anti-ENTPD2 Abs from the hybridoma and phage display campaigns were triaged for functional activity in the biochemical human ENTPD2 assay. Representative activity of Anti-ENTPD2 Abs and their IC_{50}s are shown in FIG. 15 and Table 28. A range of activities was observed for a number of Abs with some displaying very potent activity in the assay with sub-nanomolar IC_{50} and complete target inhibition or others demonstrating much weaker activity and only partial enzyme inhibition (data not shown).

Table 28: In vitro activity profiles of Anti-ENTPD2 Abs in the human ENTPD2 biochemical functional assay

Antibody	ENTPD2 Biochemical Assay at 1uM ATP IC_{50} (nM)
Anti-ENTPD2 mAb1	0.52
Anti-ENTPD2 mAb16	77.33
Anti-ENTPD2 mAb17	0.27
Anti-ENTPD2 mAb19	4.09
Anti-ENTPD2 mAb20	17.49
Anti-ENTPD2 mAb21	0.87

Activity of anti-ENTPD2 Abs in the cell-based human and cyno ENTPD2 functional assays

[0817] Initial profiling of Abs in the biochemical ENPTD2 assay identified a number of potent hits with strong inhibitory activity against the recombinant extracellular domain of ENTPD2, however differential behavior profiles were observed for a subset of Abs between the biochemical and cell-based functional assays, suggesting that conformational differences may exist between the purified recombinant protein and the native cell-based conformation (data not shown). In order to confirm potent activity of Abs against native ENTPD2, anti-ENTPD2 Abs were profiled for inhibitory activity using human- or cyno-ENTPD2 engineered NIH/3T3 cells or the RKO cell line with endogenous ENTPD2 expression. Summary of anti-ENTPD2 Abs activity profiles across the human or cyno ENTPD2 NIH/3T3 or RKO cell-based assays is captured in Table 29. Representative graphs depicting potent activity across all three functional assays for a subset of anti-ENTPD2 Abs are shown in FIG. 16.

Table 29: In vitro activity profiles of ENTPD2 selective Abs in the human or cyno ENTPD2 NIH/3T3 or RKO cell-based assays

	Human ENTPD2 NIH/3T3 Assay		RKO Assay		Cyno ENTPD2 NIH/3T3 Assay	
Antibody	IC_{50} (nM)	% inhibition	IC_{50} (nM)	% inhibition	IC_{50} (nM)	% inhibition
Anti-ENTPD2 mAb1	1.1	92	0.8	97	4.1	91
Anti-ENTPD2 mAb2	1.4	98	0.8	86	2.7	84
Anti-ENTPD2 mAb3	1.8	91	1.6	95	5.8	84
Anti-ENTPD2 mAb4	0.2	87	0.2	74	2.2	75
Anti-ENTPD2 mAb5	0.3	95	0.2	80	1.5	80
Anti-ENTPD2 mAb6	0.3	95	0.2	90	3.3	73
Anti-ENTPD2 mAb7	0.8	95	0.6	92	2.7	82
Anti-ENTPD2 mAb8	0.1	97	0.2	95	0.9	96
Anti-ENTPD2 mAb9	0.3	92	0.1	70	0.3	71
Anti-ENTPD2 mAb10	0.4	88	0.2	77	0.5	86
Anti-ENTPD2 mAb11	1.5	55				
Anti-ENTPD2 mAb12	26.6	68				
Anti-ENTPD2 mAb16	>133	30			>133	5
Anti-ENTPD2 mAb17	0.6	98	0.5	96	1.0	91
Anti-ENTPD2 mAb18	0.4	88			20	68

Example 14. Structure guided engineering identified more potent surrogate anti-mouse ENTPD2 Abs

[0818] Anti-ENTPD2 mAb13 was identified as a mouse ENTPD2 selective Ab (FACS EC_{50} 3-4 nM) with no binding to human or cyno ENTPD2. Activity of Anti-ENTPD2 mAb13 was assessed using the NIH3T3-mouse ENTPD2 engineered cell line, where Anti-ENTPD2 mAb13 displayed activity as a partial enzymatic inhibitor with a 2.8nM IC_{50} and maximum 44% target inhibition. Examination of the Anti-ENTPD2 mAb13 Fab/mENTPD2 complex crystal structure and superposition of ATP-substrate analog from PDB code 3CJA rENTPD2 within the mENTPD2 active site, revealed T30 in CDR1 of the Anti-ENTPD2 mAb13 HC as an optimal site where substitution of larger amino acid would be predicted to sterically block ATP binding. A subset of constructs with substitutions at the T30 position of Anti-ENTPD2 mAb13 CDR1 were engineered, including Anti-ENTPD2 mAb14 and mAb15. Evaluation of engineered variants of Anti-ENTPD2 mAb14 and mAb15 in the mouse

ENTPD2 NIH/3T3 cell-based functional assay, demonstrated significantly improved target inhibition as compared to the parental Anti-ENTPD2 mAb13, reaching approximately 76-79% mouse ENTPD2 inhibition with a 5-6 nM IC50 (Table 30, FIG. 17).

Table 30: In vitro activity profiles of mouse ENTPD2 selective Abs in the mouse ENTPD2 cell-based functional assay

Antibody	ENTPD2 Functional Assay IC_{50} (nM)	% Inhibition at 100nM (± Std Err)
Anti-ENTPD2 mAb13	2.8	44 ± 7.3
Anti-ENTPD2 mAb14	4.6	79 ± 2.2
Anti-ENTPD2 mAb15	5.9	76 ± 3.4

[0819] Unless defined otherwise, the technical and scientific terms used herein have the same meaning as they usually understood by a specialist familiar with the field to which the disclosure belongs.

[0820] Unless indicated otherwise, all methods, steps, techniques and manipulations that are not specifically described in detail can be performed and have been performed in a manner known per se, as will be clear to the skilled person. Reference is for example again made to the standard handbooks and the general background art mentioned herein and to the further references cited therein. Unless indicated otherwise, each of the references cited herein is incorporated in its entirety by reference.

[0821] Claims to the invention are non-limiting and are provided below.

[0822] Although particular aspects and claims have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, or the scope of subject matter of claims of any corresponding future application. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the disclosure without departing from the spirit and scope of the disclosure as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the aspects described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims. Those skilled in the art will recognize or be able to

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ascertain, using no more than routine experimentation, many equivalents of the specific aspects of the invention described herein. Such equivalents are intended to be encompassed by the following claims. Redrafting of claim scope in later filed corresponding applications may be due to limitations by the patent laws of various countries and should not be interpreted as giving up subject matter of the claims.

[0823] Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

[0824] The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

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CLAIMS

1. An antibody or antigen binding fragment thereof that specifically binds to human ENTPD2 protein, wherein the antibody or antigen binding fragment thereof comprises a heavy chain complementary determining region 1 (HCDR1), a heavy chain complementary determining region 2 (HCDR2), a heavy chain complementary determining region 3 (HCDR3), a light chain complementary determining region 1 (LCDR1), a light chain complementary determining region 2 (LCDR2), and a light chain complementary determining region 3 (LCDR3) of any antibody or antigen binding fragment selected from any one of the following:

1) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 2,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 14,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 16;

2) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 5,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;

3) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 8,
an HCDR3 sequence comprising SEQ ID NO: 9,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and

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an LCDR3 sequence comprising SEQ ID NO: 16;

2. The antibody or antigen binding fragment thereof of claim 1, wherein the antibody or antigen binding fragment thereof is selected from any one of the following:

1) an antibody or antigen binding fragment thereof comprising a heavy chain variable region (VH) comprising SEQ ID NO: 10 or a sequence at least about 95% or more identical thereto, and a light chain variable region (VL) comprising SEQ ID NO: 21 or a sequence at least about 95% or more identical thereto;

2) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

3) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 33 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

4) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 78 or a sequence at least about 95% or more identical thereto;

5) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 233 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 237 or a sequence at least about 95% or more identical thereto;

3. The antibody or antigen binding fragment thereof of claim 1 or claim 2, wherein the antibody or antigen binding fragment thereof is selected from any one of the following:

1) an antibody comprising a heavy chain comprising SEQ ID NO: 12 or a sequence at least about 95% or more identical thereto, and a light chain

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comprising SEQ ID NO: 23 or a sequence at least about 95% or more identical thereto;

2) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;

3) an antibody comprising a heavy chain comprising SEQ ID NO: 35 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;

4) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 80 or a sequence at least about 95% or more identical thereto;

5) an antibody comprising a heavy chain comprising SEQ ID NO: 235 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 239 or a sequence at least about 95% or more identical thereto; or,

6) an antibody comprising a heavy chain comprising SEQ ID NO: 243 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto.

4. The antibody or antigen binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region (VH) comprising SEQ ID NO: 10 or a sequence at least about 95% or more identical thereto, and a light chain variable region (VL) comprising SEQ ID NO: 21 or a sequence at least about 95% or more identical thereto.

5. The antibody or antigen binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen binding fragment thereof comprises SEQ ID NO: 12 or

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a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 23 or a sequence at least about 95% or more identical thereto.

6. The antibody or antigen binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen binding fragment thereof comprises a modified Fc region that has reduced antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) activity compared to the parent antibody.

7. A nucleic acid or set of nucleic acids encoding the antibody or antigen binding fragment thereof of any one of claims 1-6.

8. A vector comprising the nucleic acid or set of nucleic acids of claim 7.

9. A cell comprising the nucleic acid or set of nucleic acids of claim 7 or the vector of claim 8.

10. A method of producing an antibody or antigen binding fragment thereof, the method comprising culturing the cell of claim 9 and collecting the antibody or antigen-binding fragment thereof from the culture medium.

11. A pharmaceutical composition comprising the antibody or antigen binding fragment thereof of any one of claims 1-6, the nucleic acid or set of nucleic acids of claim 7, the vector of claim 8, or the cell of claim 9, and a pharmaceutically acceptable carrier.

12. Use of the antibody or antigen binding fragment thereof of any one of claims 1-6, the nucleic acid of claim 7, the vector of claim 8, the cell of claim 9, or the pharmaceutical composition of claim 11, in the treatment of an ENTPD2+ cancer.

13. Use of the antibody or antigen binding fragment thereof of any one of claims 1-6, the nucleic acid of claim 7, the vector of claim 8, the cell of claim 9, or the pharmaceutical composition of claim 11, in the manufacture of a medicament for treatment of an ENTPD2+ cancer.

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14. Use according to claim 12 or 13, wherein the ENTPD2+ cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

15. Use according to claim 12 or 13, wherein the antibody molecule is administered in combination with at least one additional therapeutic agent or procedure.

16. A method of treating an ENTPD2+ cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the antibody or antigen binding fragment of any one of claims 1-6, the nucleic acid of claim 17, the vector of claim 8, the cell of claim 9, or the pharmaceutical composition of claim 11.

17. The method of claim 16, wherein the ENPTD2+ cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

18. A method of stimulating an immune response in a subject, the method comprising administering to the subject the antibody or antigen binding fragment of any one of claims 1-6, the nucleic acid or set of nucleic acids of claim 7, the vector of claim 8, the cell of claim 9, or the pharmaceutical composition of claim 11, in an amount effective to stimulate the immune response.

19. The method of any one of claims 16-18, further comprising administering to the subject at least one additional therapeutic agent or procedure.

20. The method of claim 19, wherein the antibody or antigen binding fragment of any one of claims 1-6, the nucleic acid or set of nucleic acids of claim 7, the vector of

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claim 8, the cell of claim 9, or the pharmaceutical composition of claim 11 is administered concurrently with, prior to, or subsequent to, the at least one additional therapeutic agent.

FIG. 1A

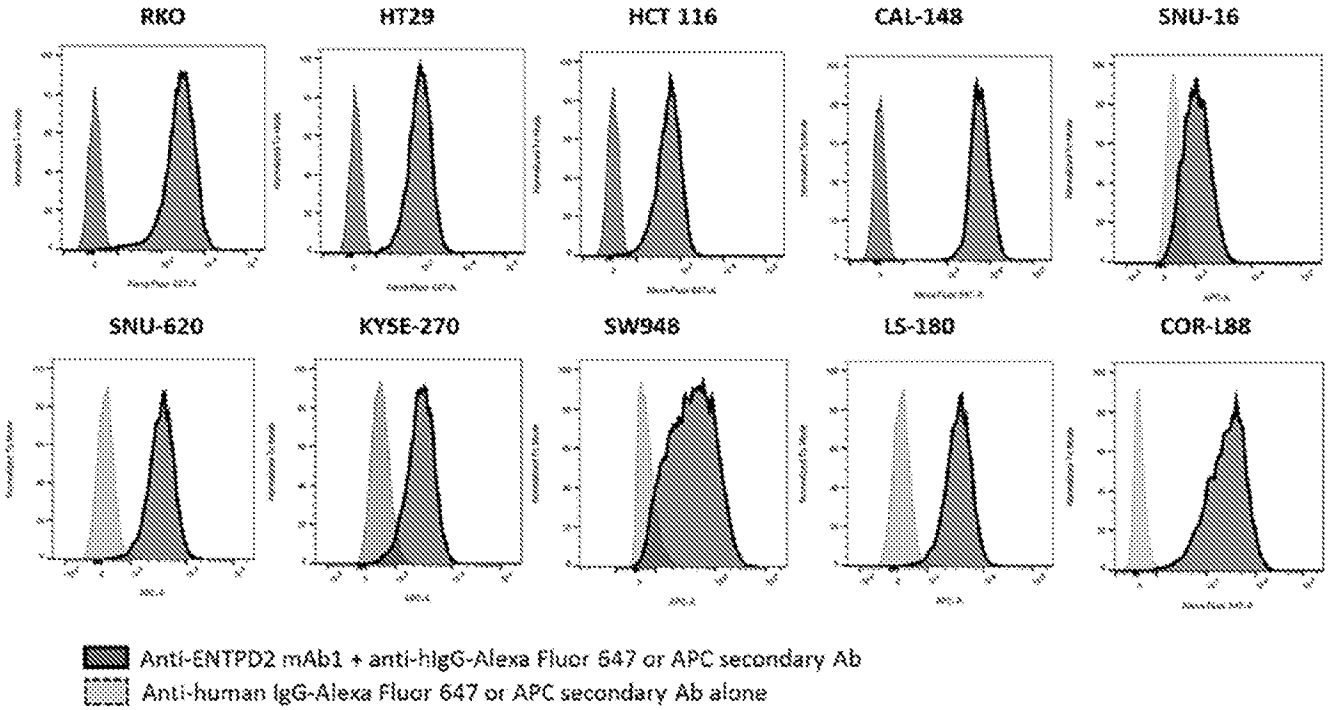

RKO
HT29
HCT 116
CAL-148
SNU-16
SNU-620
KYSE-270
SW948
LS-180
COR-L88
Anti-ENTPD2 mAb1 + anti-hIgG-Alexa Fluor 647 or APC secondary Ab
Anti-human IgG-Alexa Fluor 647 or APC secondary Ab alone

FIG. 1B

Table 20: ENTPD2 expression density across representative cancer cell lines

Cell Line	Source	Indication	Receptor Density
CAL-148	**DSMZ (Germany)**	Breast Adenocarcinoma	111,726
COR-L88	**ECACC (UK)**	Small Cell Lung Cancer	90,000
RKO	**ATCC (Manassas, VA)**	Colorectal Cancer	51,203
LS-180	**ATCC (Manassas, VA)**	Colorectal Cancer	44,708
SW948	**ATCC (Manassas, VA)**	Colorectal Cancer	41,576
HT29	**ATCC (Manassas, VA)**	Colorectal Cancer	28,337
KYSE-270	**DSMZ (Germany)**	Esophageal Cancer	28,273
SNU-620	**KCLB (South Korea)**	Stomach Adenocarcinoma	19,646
HCT 116	**ATCC (Manassas, VA)**	Colorectal Cancer	18,697
SNU-16	**ATCC (Manassas, VA)**	Gastic Carcinoma	12,763

FIG. 2

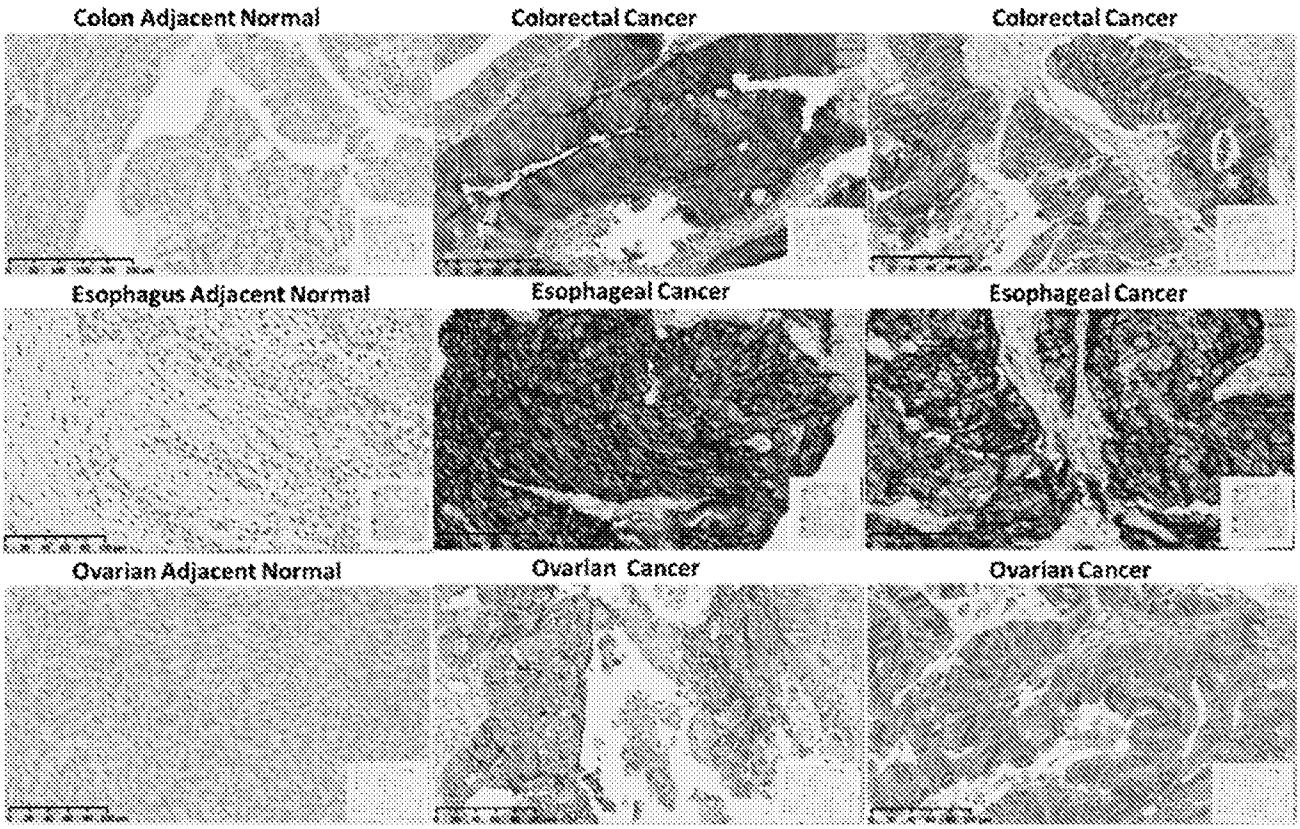

Colon Adjacent Normal
Colorectal Cancer
Colorectal Cancer
Esophagus Adjacent Normal
Esophageal Cancer
Esophageal Cancer
Ovarian Adjacent Normal
Ovarian Cancer
Ovarian Cancer

FIG. 3A

Heavy chain amino acid sequence of anti-human ENTPD2 FAb22 (SEQ ID NO: 330)

EVKLEQSGPGLVKPSQSLSLTCSVTGYSITSGYYWNWIRQFPGNKLEWMSYISYDGDNNYNPSLKNRISITRDTSKNQFF
LKLSSVTTEDTATYYCAGGYYRYGLSYYYVMDYWGQGTSVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC

Light chain amino acid sequence of anti-human ENTPD2 FAb22 (SEQ ID NO: 334)

DIKMTQSPASLAVSLGQRATISCKASQSVDYDGNSYMNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIH
PVEEEDAATYYCQQSNEDPPTFGGGTKLELKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 3B

Heavy chain amino acid sequence of anti-human ENTPD2 FAb23 (SEQ ID NO: 336)

EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMDWVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLTVDKSSSTAY
MELRSLTSEDTAVYYCARRGFFLYYGINYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC

Light chain amino acid sequence of anti-human ENTPD2 FAb23 (SEQ ID NO: 239)

QIVLTQSPAIMSASLGEEITLTCSASSSVSYIHWYQQKSGTSPTLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSVEAE
DAADYYCHQWSSYPWTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 3C

Heavy chain amino acid sequence of anti-murine ENTPD2 FAb24 (SEQ ID NO: 338)

QVQLVQSGAELKQPGQSVKISCKASGYTFT**HYGMN**WVKQAPGQGLKWMG**WINTDTGNPTYADDFKG**RFVFSLDTSVSTAY

LQISNLKNEDTATYYCVR**YGTLYSGYGFFFDS**WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV

TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC

Light chain amino acid sequence of anti-murine ENTPD FAb24 (SEQ ID NO: 340)

DIMMTQSPSSLSVSAGEKATITC**KSSQSLFNSNTNKNYLN**WYLQKPGQSPKLLFY**YASTRHT**GVPDRFIGSGSGTDFTLT

ITSVQDEDLADYYC**QQWYSYPWT**FGPGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL

QSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 4A

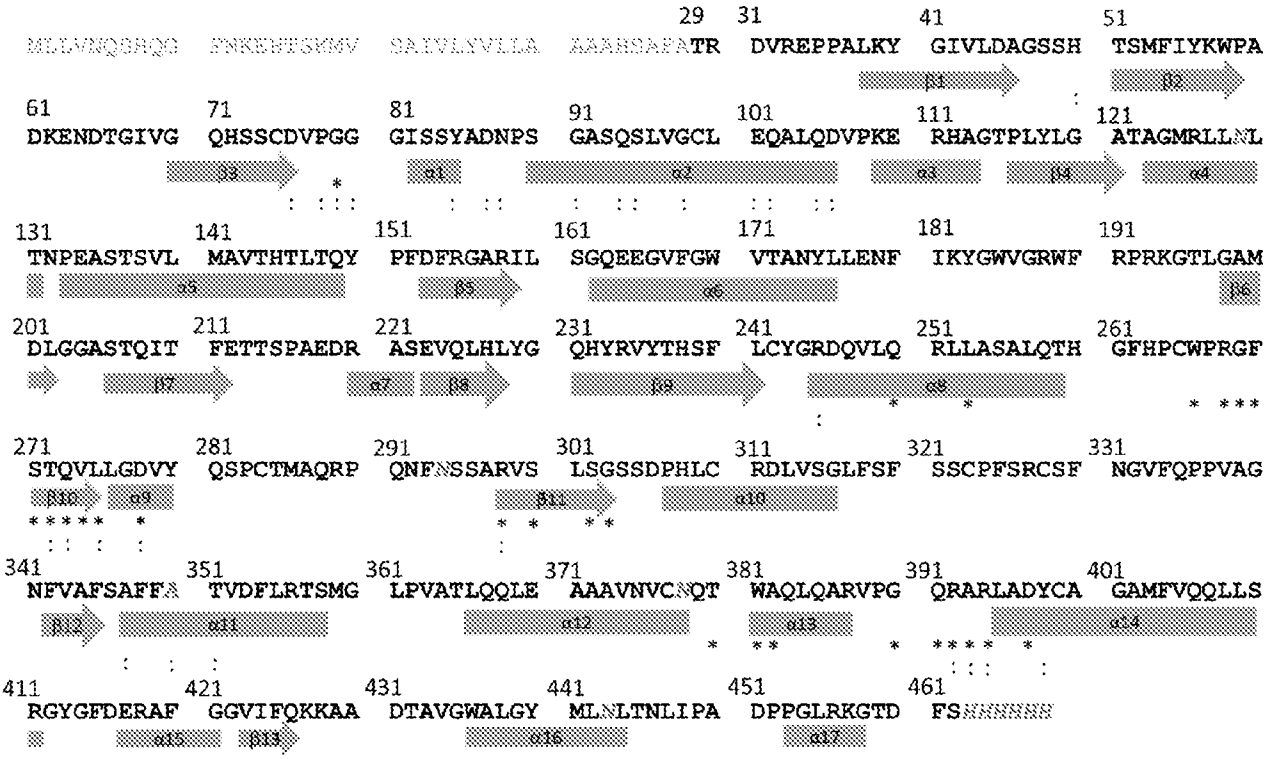


FIG. 4B

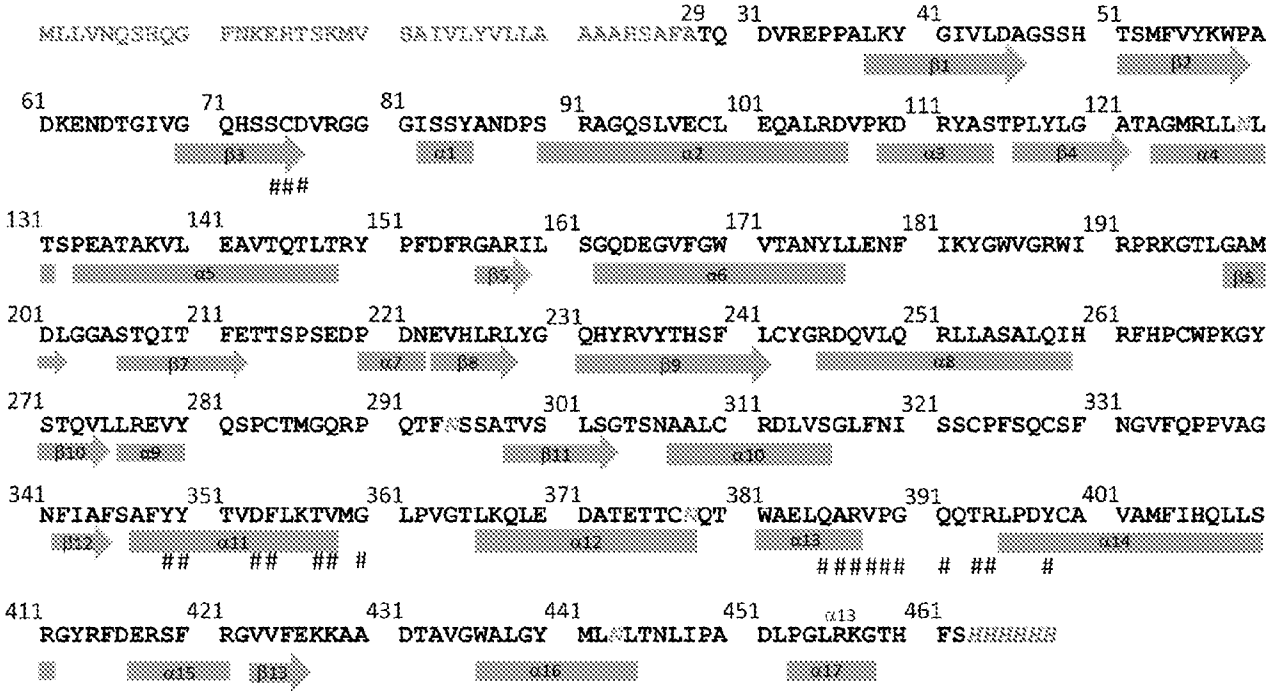

29 31 41 51
DVREPPALKY GIVLDAGSSH TSMFVYKWPA
β1 β2
61 71 81 91 101 111 121
DKENDTGIVG QHSSCDVRGG GISSYANDPS RAGQSLVECL EQALRDVPKD RYASTPLYLG ATAGMRLL
β3 α1 α2 α3 β4 α4
###
131 141 151 161 171 181 191
TSPEATAKVL EAVTQTLTRY PFDFRGARIL SGQDEGVFGW VTANYLLENF IKYGWVGRWI RPRKGTLGAM
α5 β5 α6 β6
201 211 221 231 241 251 261
DLGGASTQIT FETTSPSEDP DNEVHLRLYG QHYRVYTHSF LCYGRDQVLQ RLLASALQIH RFHPCWPKGY
β7 α7 β8 β9 α8
271 281 291 301 311 321 331
STQVLLREVY QSPCTMGQRP QTF SSATVS LSGTSNAALC RDLVSGLFNI SSCPFSQCSF NGVFQPPVAG
β10 α9 β11 α10
341 351 361 371 381 391 401
NFIAFSAFYY TVDFLKTVMG LPVGTLKQLE DATETTC QT WAELQARVPG QQTRLPDYCA VAMFIHQLLS
β12 α11 α12 α13 α14
#
411 421 431 441 451 α13 461
RGYRFDERSF RGVVFEKKAA DTAVGWALGY ML LTNLIPA DLPGLRKGTH FS
α15 β13 α16 α17

FIG. 5A

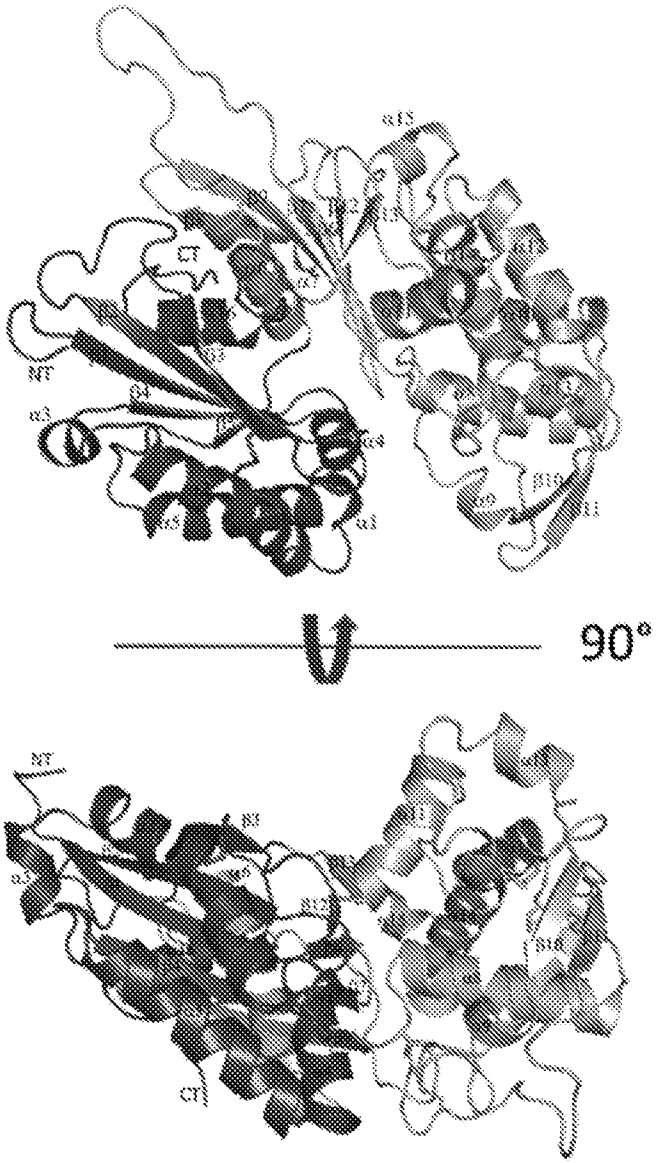


FIG. 5B

FIG. 6

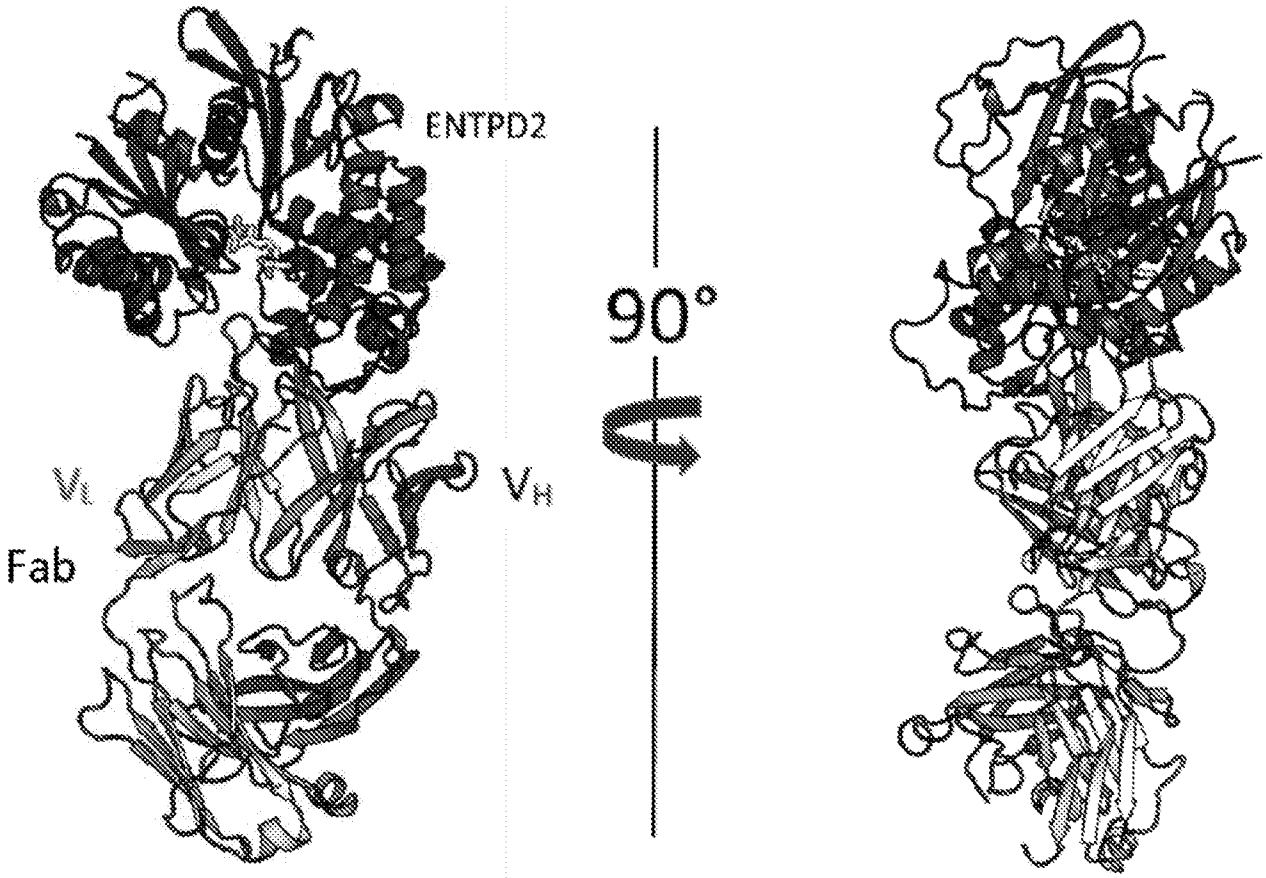


FIG. 7

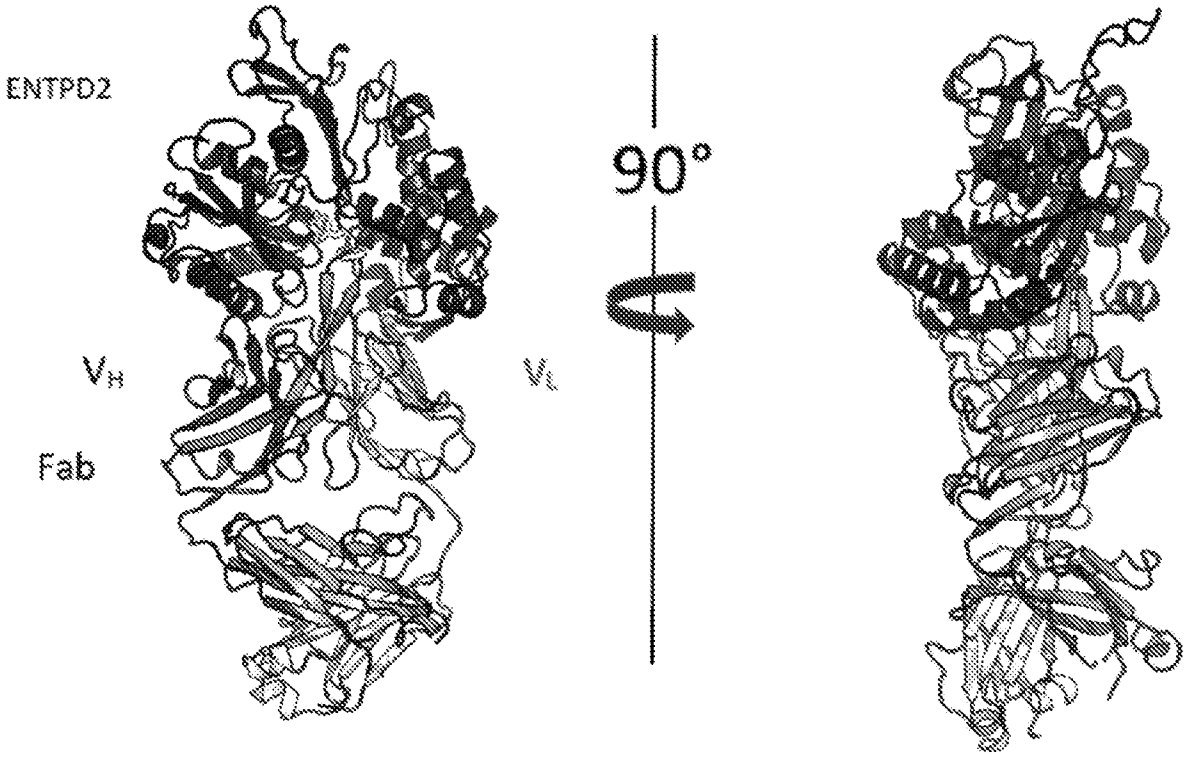


FIG. 8

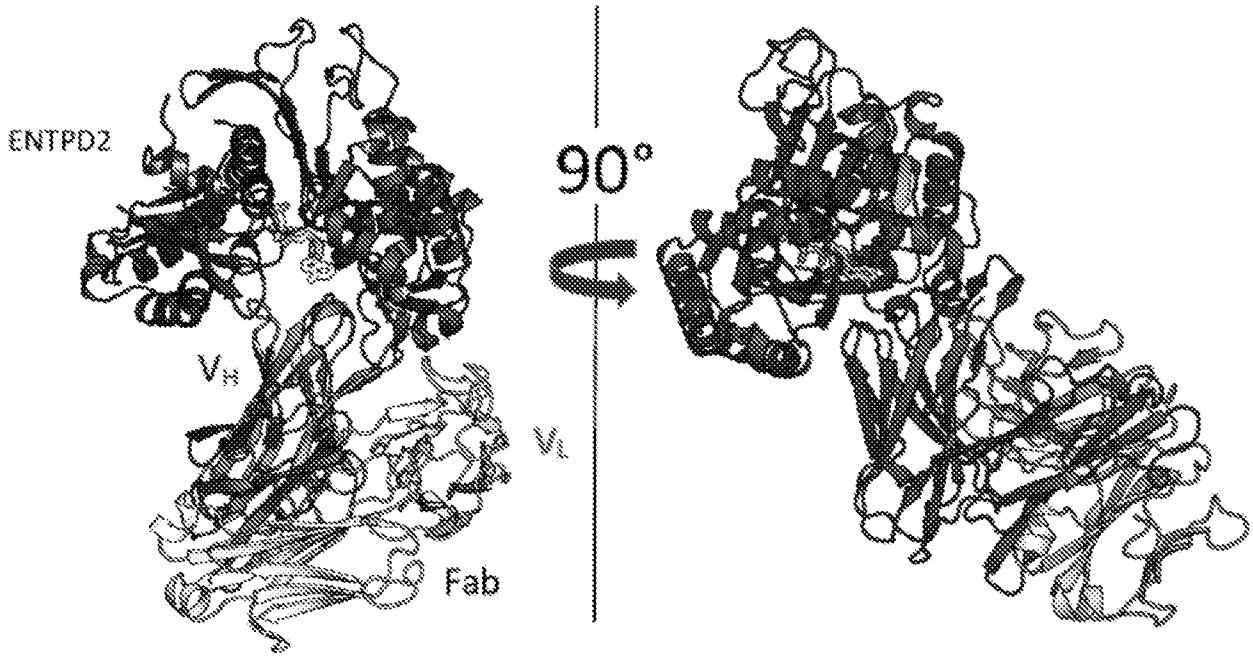


FIG. 9

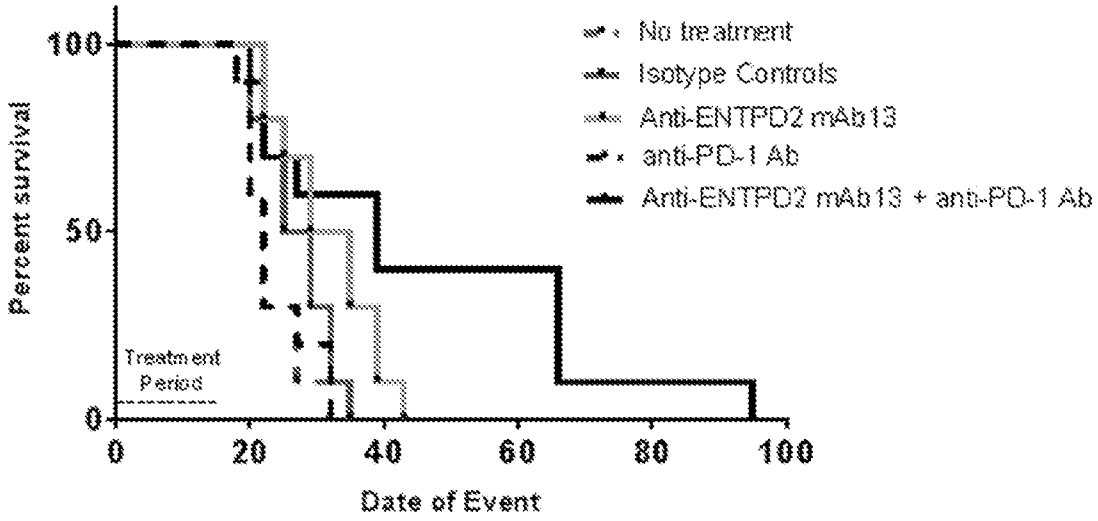

No treatment
Isotype Controls
Anti-ENTPD2 mAb13
anti-PD-1 Ab
Anti-ENTPD2 mAb13 + anti-PD-1 Ab
Percent survival
100
50
0
Treatment Period
0
20
40
60
80
100
Date of Event

FIG. 10A

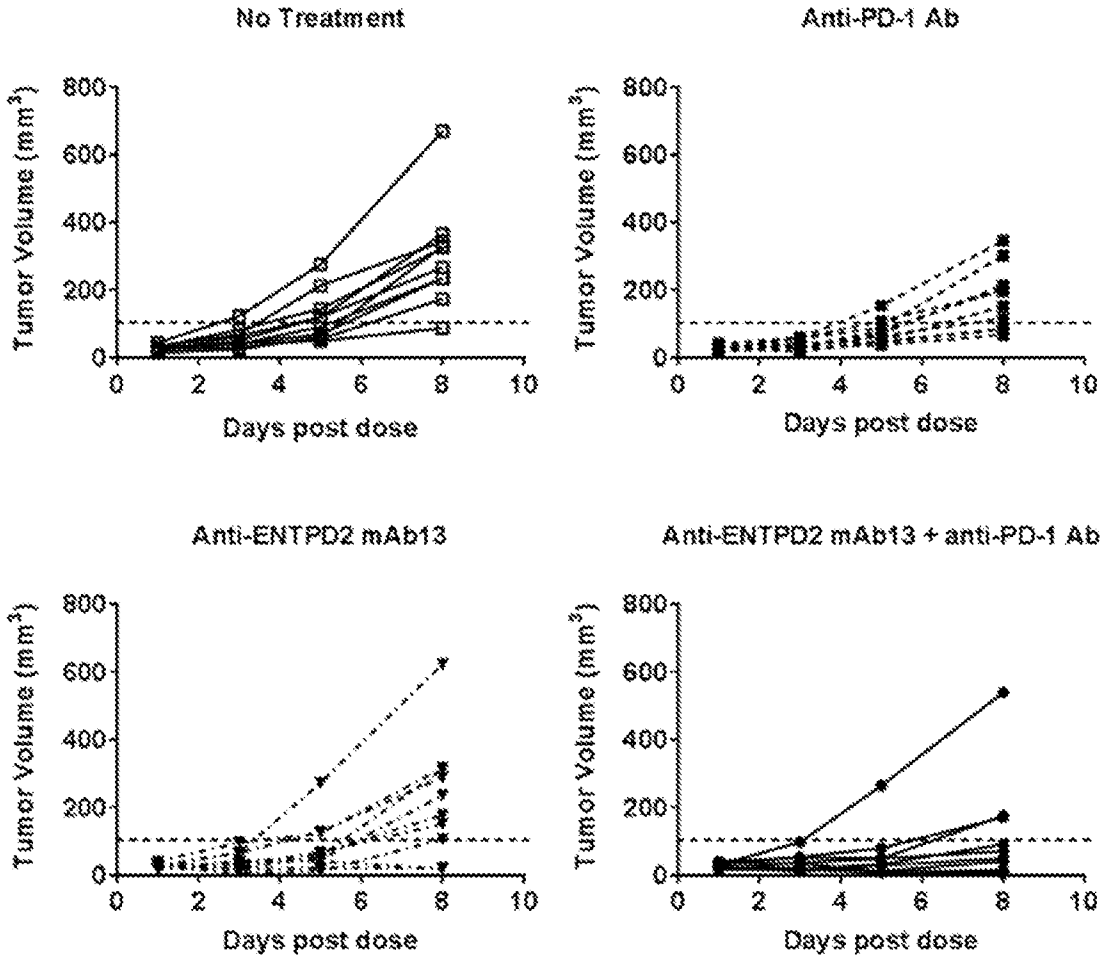

No Treatment
Anti-PD-1 Ab
Anti-ENTPD2 mAb13
Anti-ENTPD2 mAb13 + anti-PD-1 Ab
Tumor Volume (mm3)
Days post dose
0
200
400
600
800
0
2
4
6
8
10

FIG. 10B

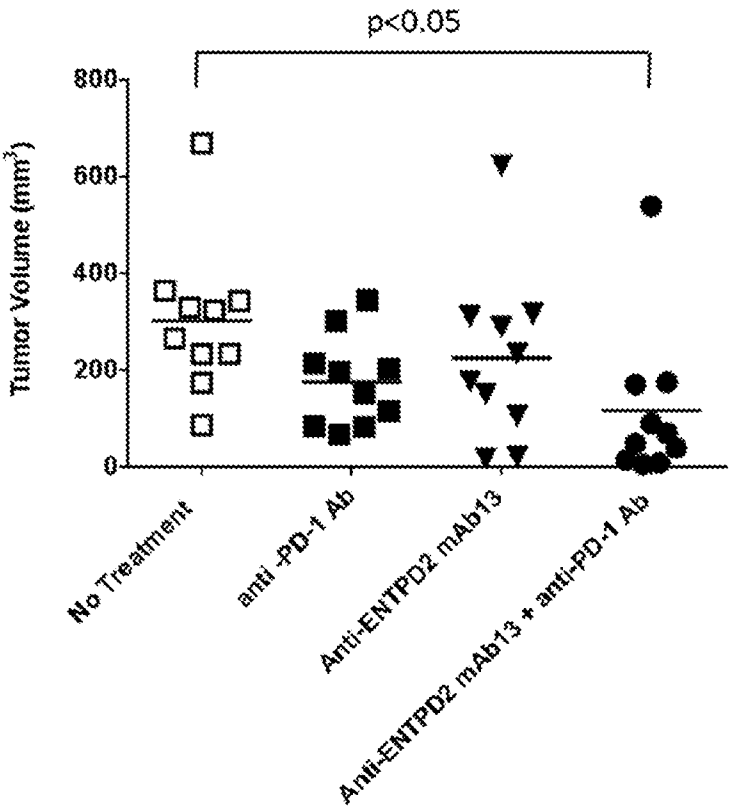

p<0.05
800
600
400
200
0
Tumor Volume (mm3)
No Treatment
anti -PD-1 Ab
Anti-ENTPD2 mAb13
Anti-ENTPD2 mAb13 + anti-PD-1 Ab

FIG. 10C

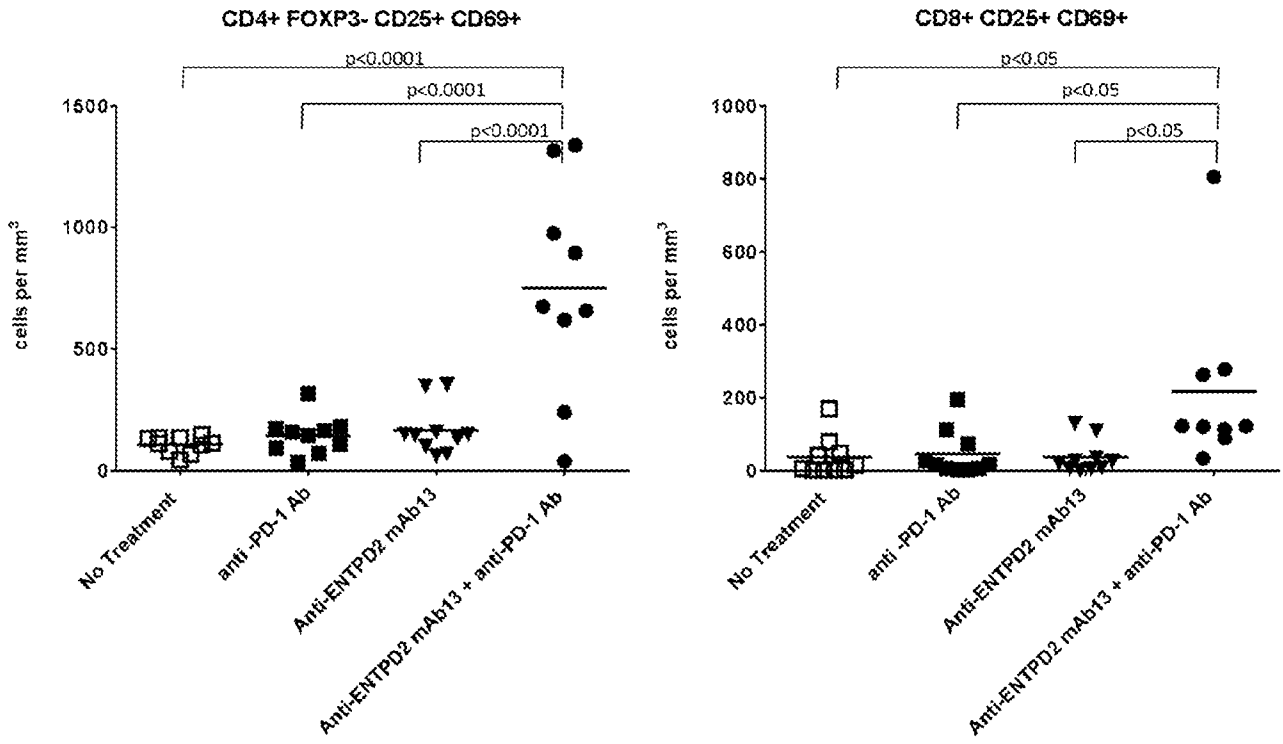

CD4+ FOXP3- CD25+ CD69+
p<0.0001
p<0.0001
p<0.0001
cells per mm3
1500
1000
500
0
No Treatment
anti -PD-1 Ab
Anti-ENTPD2 mAb13
Anti-ENTPD2 mAb13 + anti-PD-1 Ab
CD8+ CD25+ CD69+
p<0.05
p<0.05
p<0.05
cells per mm3
1000
800
600
400
200
0
No Treatment
anti -PD-1 Ab
Anti-ENTPD2 mAb13
Anti-ENTPD2 mAb13 + anti-PD-1 Ab

FIG. 11A

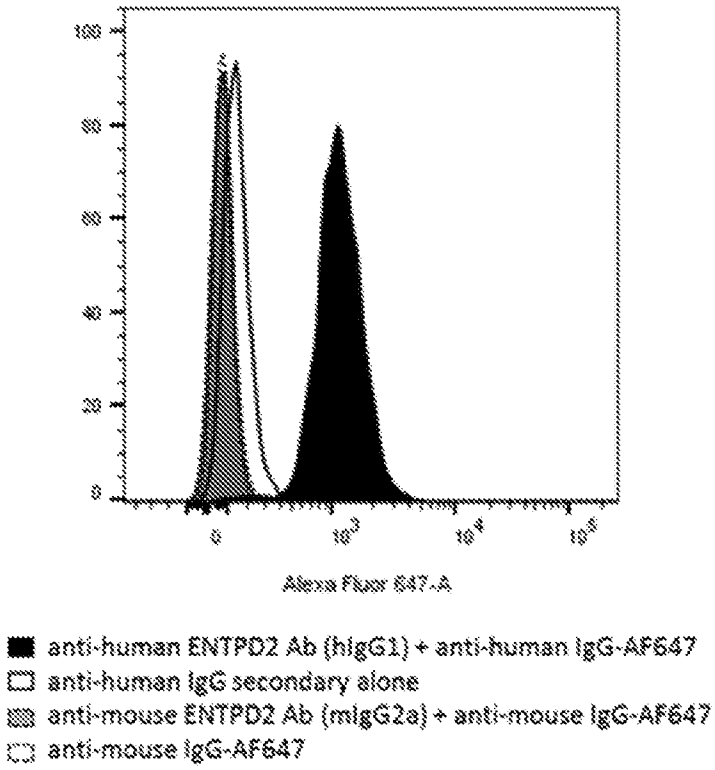

100
80
60
40
20
0
0
10^3
10^4
10^5
Alexa Fluor 647-A
anti-human ENTPD2 Ab (hIgG1) + anti-human IgG-AF647
anti-human IgG secondary alone
anti-mouse ENTPD2 Ab (mIgG2a) + anti-mouse IgG-AF647
anti-mouse IgG-AF647

FIG. 11B

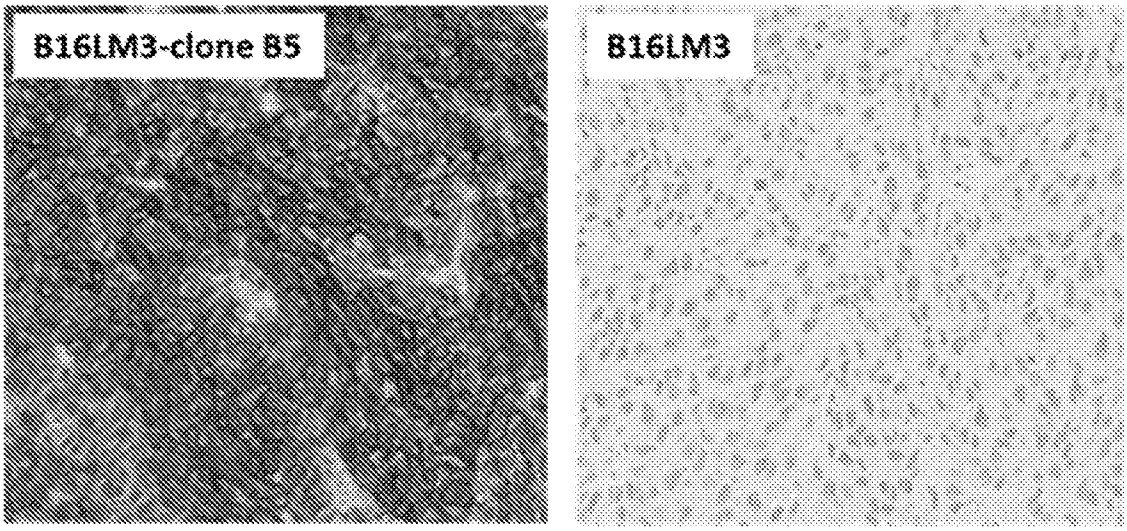


FIG. 12A

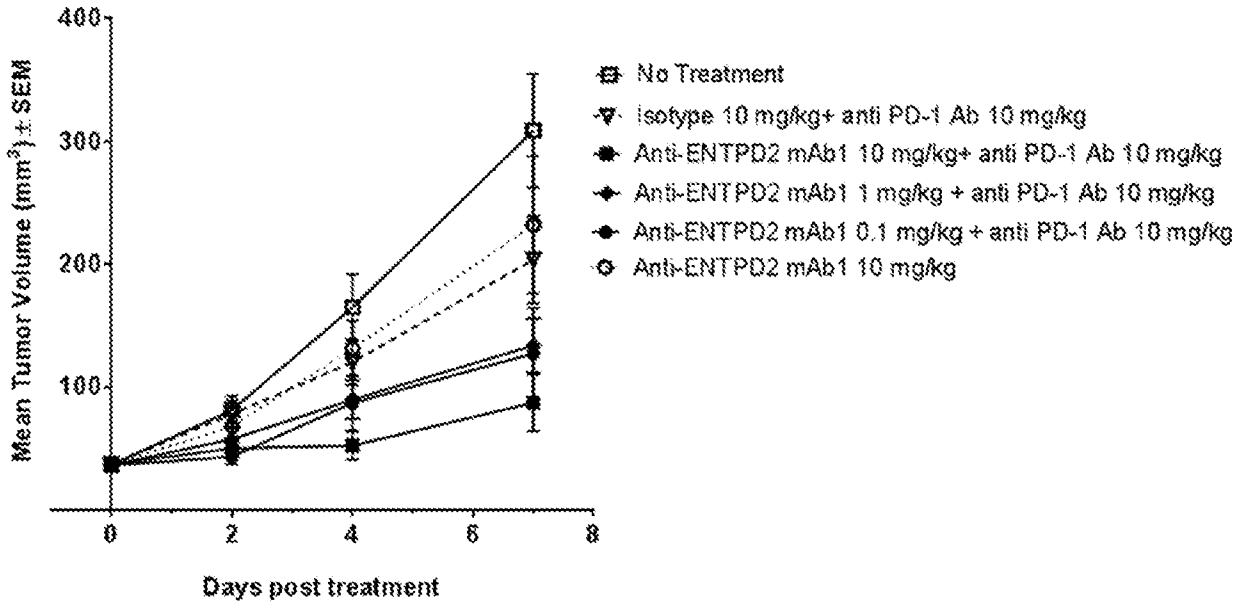

400
300
200
100
0
2
4
6
8
Mean Tumor Volume (mm³) ± SEM
Days post treatment
No Treatment
Isotype 10 mg/kg+ anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb1 10 mg/kg+ anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb1 1 mg/kg + anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb1 0.1 mg/kg + anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb1 10 mg/kg

FIG. 12B

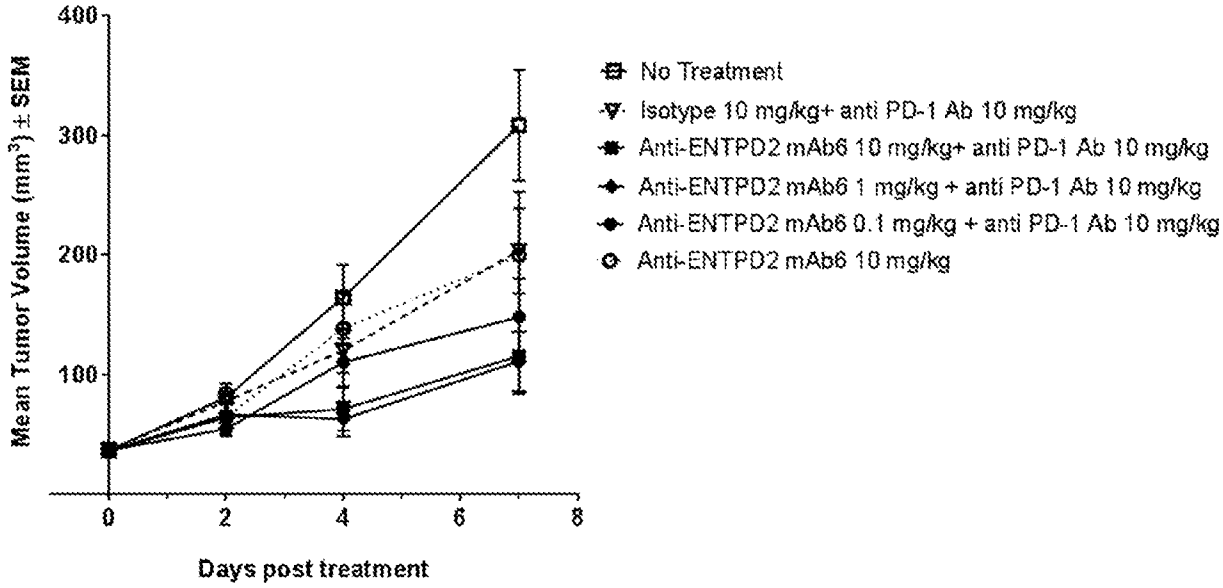

400
300
200
100
0
2
4
6
8
Mean Tumor Volume (mm3) ± SEM
Days post treatment
No Treatment
Isotype 10 mg/kg+ anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb6 10 mg/kg+ anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb6 1 mg/kg + anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb6 0.1 mg/kg + anti PD-1 Ab 10 mg/kg
Anti-ENTPD2 mAb6 10 mg/kg

FIG. 13A

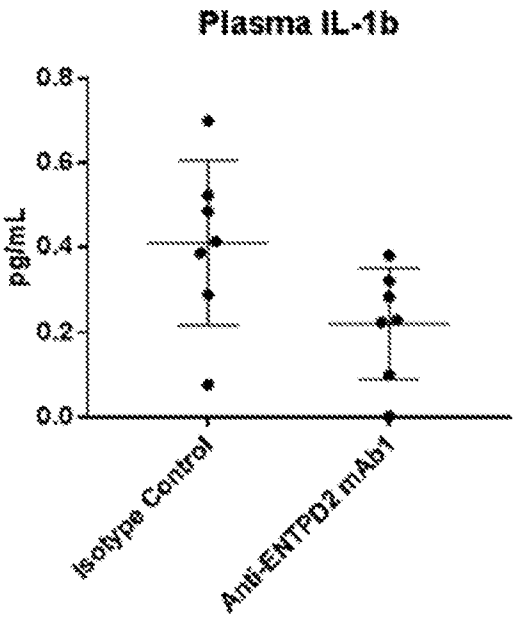


FIG. 13B

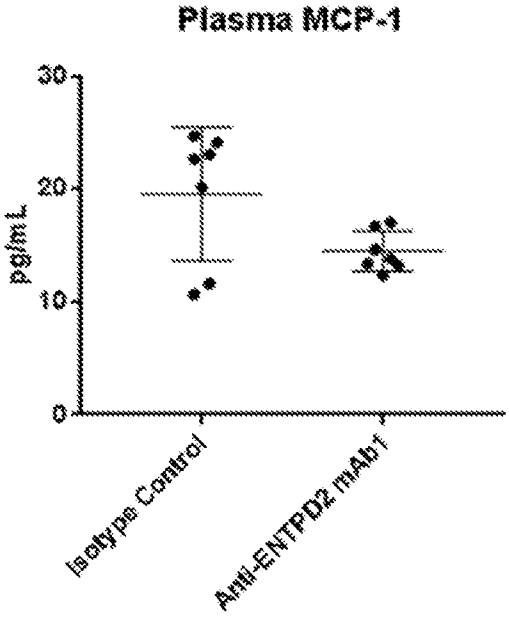


FIG. 13C

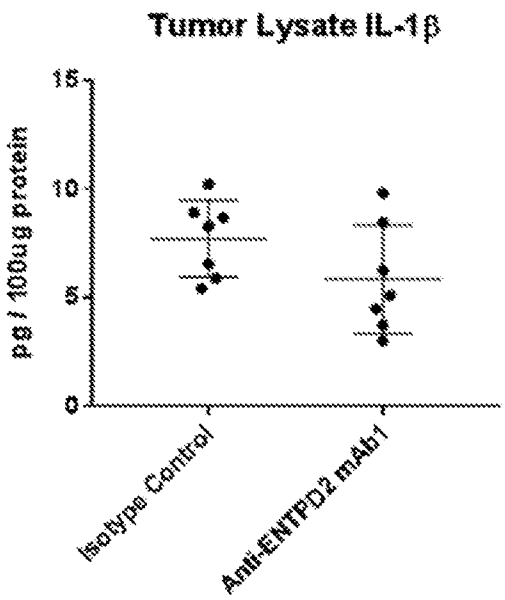


FIG. 13D

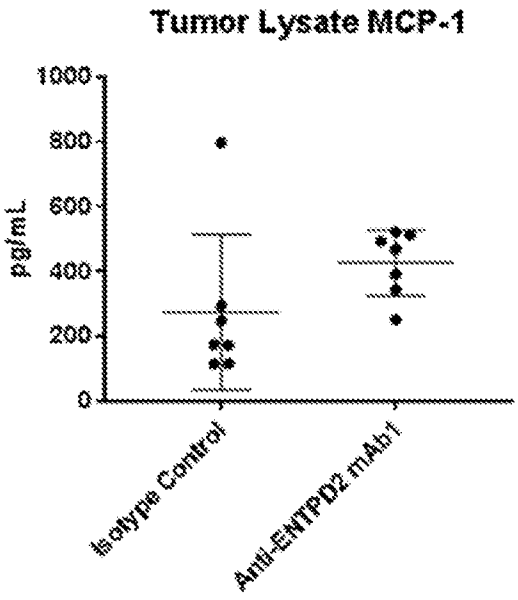


FIG. 14

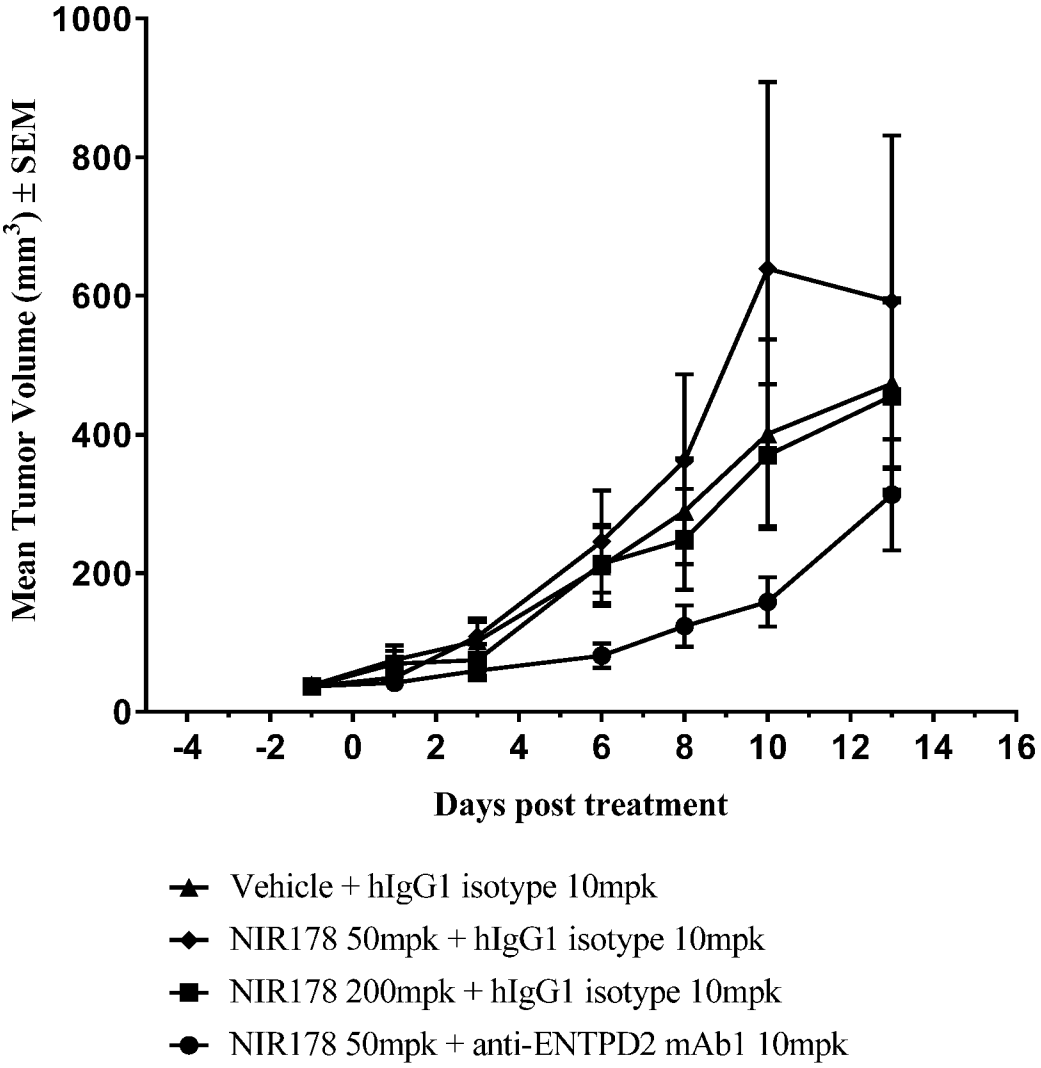

1000
800
600
400
200
0
Mean Tumor Volume (mm3) ± SEM
-4
-2
0
2
4
6
8
10
12
14
16
Days post treatment
Vehicle + hIgG1 isotype 10mpk
NIR178 50mpk + hIgG1 isotype 10mpk
NIR178 200mpk + hIgG1 isotype 10mpk
NIR178 50mpk + anti-ENTPD2 mAb1 10mpk

FIG. 15

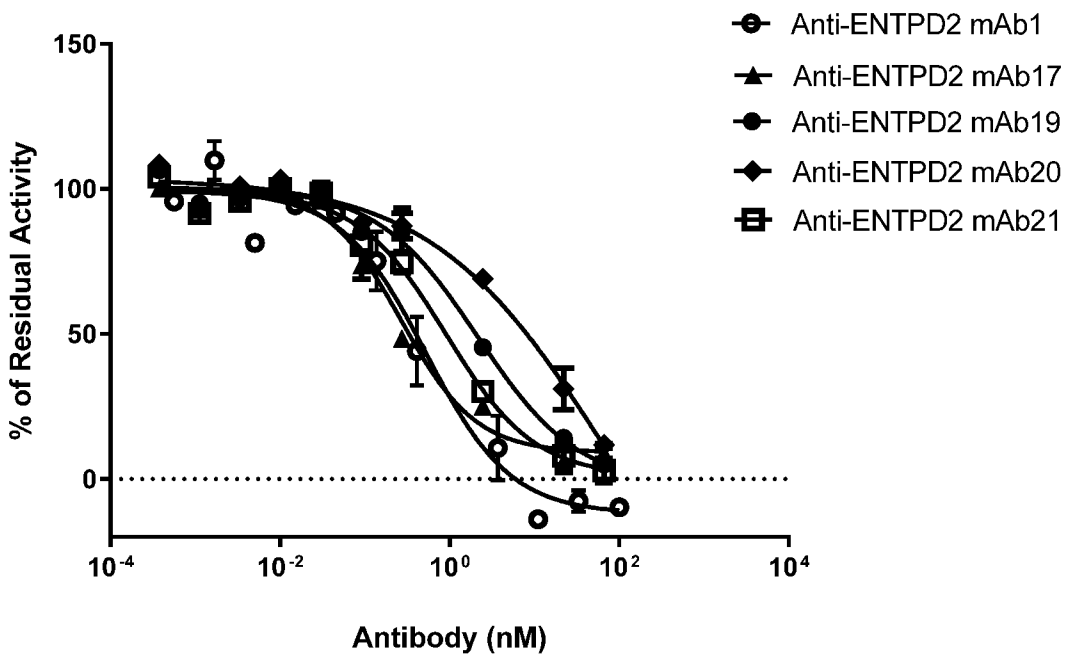

Anti-ENTPD2 mAb1
Anti-ENTPD2 mAb17
Anti-ENTPD2 mAb19
Anti-ENTPD2 mAb20
Anti-ENTPD2 mAb21
% of Residual Activity
150
100
50
0
10-4
10-2
100
102
104
Antibody (nM)

FIG. 16A

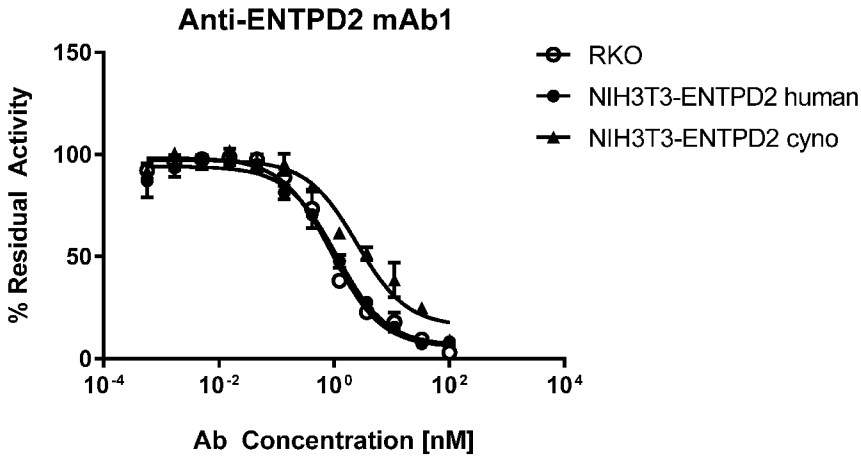


FIG. 16B

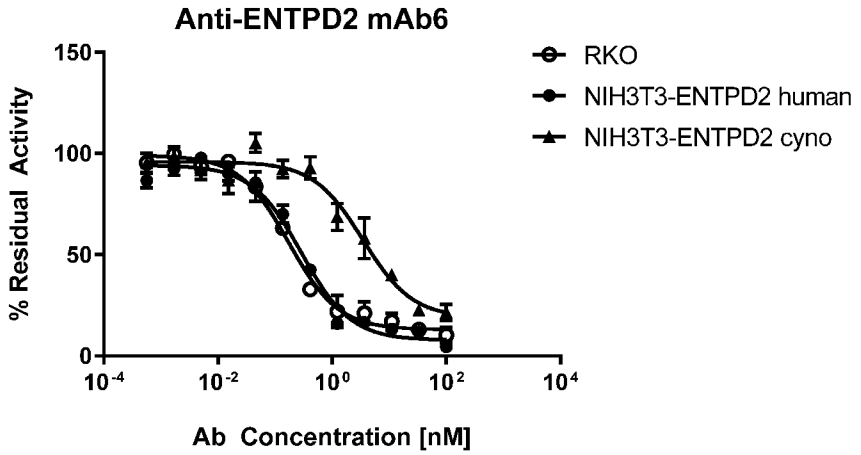
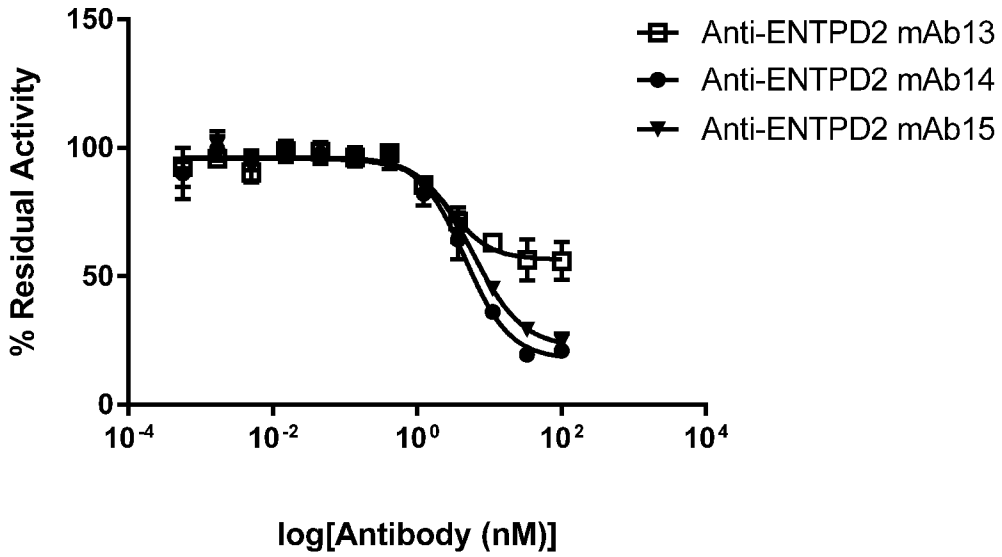


FIG. 17


150
100
50
0
% Residual Activity
10-4
10-2
100
102
104
log[Antibody (nM)]
Anti-ENTPD2 mAb13
Anti-ENTPD2 mAb14
Anti-ENTPD2 mAb15

SEQUENCE LISTING

<110> NOVARTIS AG

<120> ENTPD2 ANTIBODIES, COMBINATION THERAPIES, AND METHODS OF USING THE ANTIBODIES AND COMBINATION THERAPIES

<130> PAT058145-WO-PCT

<140>
<141>

<150> 62/677,850
<151> 2018-05-30

<160> 1015

<170> PatentIn version 3.5

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<213> Artificial Sequence

<220>
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1 5

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1 5 10 15

Gly

<210> 3
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<400> 3
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Asn Pro Lys Tyr Asp Ile
1 5

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<212> PRT
<213> Artificial Sequence

<220>
<221> source
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Gly Tyr Thr Phe Thr Asp Tyr Asn Met Asp
1 5 10

<210> 7
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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1 5

<210> 8
<211> 8
<212> PRT
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1 5

<210> 9

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

<220>
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1 5 10 15

Asp Val

<210> 10
<211> 125
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<213> Artificial Sequence

<220>
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1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

Lys Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Arg Thr Ala Tyr
65 70 75 80

```
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
            100                 105                 110


Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 11
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 11
gaagtgcagc tggtgcagtc tggcgccgaa gtgaagaagc ctggcgagtc cctgaagatc       60

tcctgcaagg cctccggcta caccttcacc gactacaaca tggactgggt gcgacagatg      120

cccggcaagg gcctggaatg gatgggcgac atcaacccta agtacgacat ctccacctac      180

aaccagcagt tcaagggcca agtgaccatc tccgccgaca agtccatccg gaccgcctac      240

ctgcagtggt cctccctgaa ggcctctgac accgccatgt actactgcgc cagacggggc      300

ttcttcctgt actacggcat caactactac tacttcgacg tgtggggcca gggcaccctc      360

gtgacagtgt catct                                                       375


<210> 12
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 12

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

Ser Leu Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Asn Met Asp Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

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

Lys Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Arg Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
            100                 105                 110

Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190
```

```
Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380
```

```
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400


Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415


Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430


Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445


Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210> 13
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 13
gaagtgcagc tggtgcagtc tggcgccgaa gtgaagaagc ctggcgagtc cctgaagatc       60

tcctgcaagg cctccggcta caccttcacc gactacaaca tggactgggt gcgacagatg      120

cccggcaagg gcctggaatg gatgggcgac atcaacccta agtacgacat ctccacctac      180

aaccagcagt tcaagggcca agtgaccatc tccgccgaca agtccatccg gaccgcctac      240

ctgcagtggt cctccctgaa ggcctctgac accgccatgt actactgcgc cagacggggc      300

ttcttcctgt actacggcat caactactac tacttcgacg tgtggggcca gggcaccctc      360

gtgacagtgt catctgctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc      420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag      480
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cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct 600

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccca agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

<210> 14
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 14
Ser Ala Ser Ser Ser Val Ser Tyr Ile His
1 5 10

<210> 15

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 15
Ser Thr Ser Asn Leu Ala Ser
1 5

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 16
His Gln Trp Ser Ser Tyr Pro Trp Thr
1 5

<210> 17
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 17
Ser Ser Ser Val Ser Tyr
1 5

<210> 18
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 18
Ser Thr Ser
1

<210> 19
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 19
Trp Ser Ser Tyr Pro Trp
1 5

<210> 20
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 20
Ser Ser Val Ser Tyr
1 5

<210> 21
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 21
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 22
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 22
gatatccagc tgacccagtc cccttccagc ctgtctgcct ctgtgggcga cagagtgaca 60

attacctgct ccgcctcctc ctccgtgtcc tacatccact ggttccagca gaagcccggc 120

aaggccccca agctgctgat ctactccacc tccaacctgg cctccggcgt gccctctaga 180

ttctccggct ctggctctgg cacctttttt accctgacca tctccagcct gcagcccgag 240

gacttcgcca cctacttttg ccaccagtgg tccagctacc cctggacctt tggccagggc 300

accaaggtgg aaatcaag 318

<210> 23
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 23
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr

115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 24
<211> 639
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 24
gatatccagc tgacccagtc cccttccagc ctgtctgcct ctgtgggcga cagagtgaca 60

attacctgct ccgcctcctc ctccgtgtcc tacatccact ggttccagca gaagcccggc 120

aaggccccca agctgctgat ctactccacc tccaacctgg cctccggcgt gccctctaga 180

ttctccggct ctggctctgg caccttttt accctgacca tctccagcct gcagcccgag 240

gacttcgcca cctacttttg ccaccagtgg tccagctacc cctggacctt tggccagggc 300

accaaggtgg aaatcaagcg tacggtggcc gctcccagcg tgttcatctt ccccccccagc 360

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 25
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 25
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ala Pro Gly Gln Arg Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
100 105 110

Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 26
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 26
caggtgcagc tggtgcagtc tggcgccgag gtggtgaaac ctggcgcctc cgtgaagatc 60

tcctgcaagg cctccggcta caccttcacc gactacaaca tggactgggt gaaacaggcc 120

cctggccagc ggctggaatg gatcggcgac atcaacccta agtacgacat ctccacctac 180

aaccagcagt tcaagggcaa ggccaccatc accgtggaca agtccgcctc caccgcctac 240

atggaactgt cctccctgcg gagcgaggac accgccgtgt actactgcgc cagacggggc 300

ttcttcctgt actacggcat caactactac tacttcgacg tgtggggcca gggcaccctg 360

gtgacagtgt cctcc 375

<210> 27
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 27
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala
1 5 10 15

```
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Asn Met Asp Trp Val Lys Gln Ala Pro Gly Gln Arg Leu Glu Trp Ile
        35                  40                  45

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

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
            100                 105                 110

Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205
```

```
Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400
```

```
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415


Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430


Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445


Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210> 28
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 28
caggtgcagc tggtgcagtc tggcgccgag gtggtgaaac ctggcgcctc cgtgaagatc       60

tcctgcaagg cctccggcta caccttcacc gactacaaca tggactgggt gaaacaggcc      120

cctggccagc ggctggaatg gatcggcgac atcaacccta agtacgacat ctccacctac      180

aaccagcagt tcaagggcaa ggccaccatc accgtggaca agtccgcctc caccgcctac      240

atggaactgt cctccctgcg gagcgaggac accgccgtgt actactgcgc cagacggggc      300

ttcttcctgt actacggcat caactactac tacttcgacg tgtggggcca gggcaccctg      360

gtgacagtgt cctccgctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc      420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag      480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc      540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct      600
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ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccca agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

<210> 29
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 29
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Arg Ile Thr Leu Ser Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Thr Leu Thr Ile Ser Ser Val Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 30
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 30
gagatcgtgc tgacccagtc ccctgccacc ctgtctgcca gccctggcga gcggatcacc 60

ctgtcctgct ccgcctcctc ctccgtgtcc tacatccact ggtatcagca gaagcccggc 120

caggcccctc ggctgctgat ctactccacc tccaacctgg cctccggcat ccctgccaga 180

ttctccggct ctggctccgg caccttttac accctgacca tctccagcgt ggaacccgag 240

gacgccgccg tgtactactg ccaccagtgg tccagctacc cctggacctt cggcggaggc 300

accaagctgg aaatcaag 318

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

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 31

```
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Ala Ser Pro Gly
1               5                  10                  15

Glu Arg Ile Thr Leu Ser Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        35                  40                  45

Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
    50                  55                  60

Gly Ser Gly Thr Phe Tyr Thr Leu Thr Ile Ser Ser Val Glu Pro Glu
65                  70                  75                  80

Asp Ala Ala Val Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
                85                  90                  95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175
```

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 32
<211> 639
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 32
gagatcgtgc tgacccagtc ccctgccacc ctgtctgcca gccctggcga gcggatcacc 60

ctgtcctgct ccgcctcctc ctccgtgtcc tacatccact ggtatcagca gaagcccggc 120

caggcccctc ggctgctgat ctactccacc tccaacctgg cctccggcat ccctgccaga 180

ttctccggct ctggctccgg caccttttac accctgacca tctccagcgt ggaacccgag 240

gacgccgccg tgtactactg ccaccagtgg tccagctacc cctggacctt cggcggaggc 300

accaagctgg aaatcaagcg tacggtggcc gctcccagcg tgttcatctt cccccccagc 360

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 33

<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 33
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ala Pro Gly Gln Arg Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
100 105 110

Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 34
<211> 375
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 34
caggtgcagc tggtgcagtc tggcgccgag gtggtgaaac ctggcgcctc cgtgaagatc 60

tcctgcaagg cctccggcta caccttcacc gactacaaca tggactgggt gaaacaggcc 120

cctggccagc ggctggaatg gatcggcgac atcaacccta agtacgacat ctccacctac 180

aaccagcagt tcaagggcaa ggccaccatc accgtggaca cctccgcctc caccgcctac 240

atggaactgt cctccctgcg gagcgaggac accgccgtgt actactgcgc cagacggggc 300

ttcttcctgt actacggcat caactactac tacttcgacg tgtggggcca gggcaccctg 360

gtgacagtgt cctcc 375

<210> 35
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 35
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ala Pro Gly Gln Arg Leu Glu Trp Ile
35 40 45

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

Lys Gly Lys Ala Thr Ile Thr Val Asp Thr Ser Ala Ser Thr Ala Tyr

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65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
            100                 105                 110

Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
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            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445

Leu Ser Leu Ser Pro Gly Lys
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450 455

<210> 36
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 36
caggtgcagc tggtgcagtc tggcgccgag gtggtgaaac ctggcgcctc cgtgaagatc 60

tcctgcaagg cctccggcta caccttcacc gactacaaca tggactgggt gaaacaggcc 120

cctggccagc ggctggaatg gatcggcgac atcaacccta agtacgacat ctccacctac 180

aaccagcagt tcaagggcaa ggccaccatc accgtggaca cctccgcctc caccgcctac 240

atggaactgt cctccctgcg gagcgaggac accgccgtgt actactgcgc cagacggggc 300

ttcttcctgt actacggcat caactactac tacttcgacg tgtggggcca gggcaccctg 360

gtgacagtgt cctccgctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc 420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag 480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct 600

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccca agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 37
Ser Gly Tyr Tyr Trp Asn
1 5

<210> 38
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 38
Tyr Ile Ser Tyr Asp Ala Asp Asn Asn Tyr Asn Pro Ser Leu Lys Asn
1 5 10 15

<210> 39
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 39
Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Arg Gly Ser Tyr Tyr Tyr
1   5   10   15

Val Met Asp Tyr
            20

<210> 40
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 40
Gly Tyr Ser Ile Thr Ser Gly Tyr
1   5

<210> 41
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 41
Ser Tyr Asp Ala Asp
1   5

<210> 42
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 42
Gly Tyr Ser Ile Thr Ser Gly Tyr Tyr Trp Asn
1 5 10

<210> 43
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 43
Gly Tyr Ser Ile Thr Ser Gly Tyr Tyr
1 5

<210> 44
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 44
Ile Ser Tyr Asp Ala Asp Asn
1 5

<210> 45
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 45
Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Arg Gly Ser Tyr
1   5   10   15

Tyr Tyr Val Met Asp Tyr
            20

<210> 46
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 46
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 Tyr Ser Ile Thr Ser Gly
            20   25   30

Tyr Tyr Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
        35   40   45

Ile Gly Tyr Ile Ser Tyr Asp Ala Asp Asn Asn Tyr Asn Pro Ser Leu
    50   55   60

Lys Asn Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65   70   75   80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Arg Gly Ser Tyr

100 105 110

Tyr Tyr Val Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115 120 125

Ser

<210> 47
<211> 387
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 47
cagatccagc tgcaggaatc tggccctggc ctggtgaaac cctcccagac cctgtccctg 60

acctgcaccg tgtccggcta ctccatcacc tccggctact actggaactg gatccggcag 120

caccccggca agggcctgga atggatcggc tacatctcct acgacgctga caacaactac 180

aaccccagcc tgaagaacag agtgaccatc tcccgggaca cctccaagaa ccagttctcc 240

ctgaagctgt cctccgtgac cgccgctgac accgccgtgt actactgcgc tggcggctac 300

tacagatacg gcctgggctc ctaccggggc tcctactact acgtgatgga ctactggggc 360

cagggcacca ccgtgaccgt gtcctct 387

<210> 48
<211> 459
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 48

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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 Tyr Ser Ile Thr Ser Gly
            20                  25                  30

Tyr Tyr Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Tyr Ile Ser Tyr Asp Ala Asp Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Asn Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Arg Gly Ser Tyr
            100                 105                 110

Tyr Tyr Val Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    130                 135                 140

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
145                 150                 155                 160

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

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            180                 185                 190
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Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        195                 200                 205

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    210                 215                 220

Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
225                 230                 235                 240

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
                245                 250                 255

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
            260                 265                 270

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
        275                 280                 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
    290                 295                 300

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305                 310                 315                 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
                325                 330                 335

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
            340                 345                 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
        355                 360                 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
    370                 375                 380
```

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
420 425 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 49
<211> 1377
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 49
cagatccagc tgcaggaatc tggccctggc ctggtgaaac cctcccagac cctgtccctg 60

acctgcaccg tgtccggcta ctccatcacc tccggctact actggaactg gatccggcag 120

caccccggca agggcctgga atggatcggc tacatctcct acgacgctga caacaactac 180

aaccccagcc tgaagaacag agtgaccatc tcccgggaca cctccaagaa ccagttctcc 240

ctgaagctgt cctccgtgac cgccgctgac accgccgtgt actactgcgc tggcggctac 300

tacagatacg gcctgggctc ctaccggggc tcctactact acgtgatgga ctactggggc 360

cagggcacca ccgtgaccgt gtcctctgct agcaccaagg gcccaagtgt gtttcccctg 420

gcccccagca gcaagtctac ttccggcgga actgctgccc tgggttgcct ggtgaaggac 480

tacttccccg agcccgtgac agtgtcctgg aactctgggg ctctgacttc cggcgtgcac 540

accttccccg ccgtgctgca gagcagcggc ctgtacagcc tgagcagcgt ggtgacagtg 600

ccctccagct ctctgggaac ccagacctat atctgcaacg tgaaccacaa gcccagcaac 660

accaaggtgg acaagagagt ggagcccaag agctgcgaca agacccacac ctgccccccc 720

tgcccagctc cagaactgct gggagggcct tccgtgttcc tgttcccccc caagcccaag 780

gacaccctga tgatcagcag gacccccgag gtgacctgcg tggtggtgga cgtgtcccac 840

gaggacccag aggtgaagtt caactggtac gtggacggcg tggaggtgca caacgccaag 900

accaagccca gagaggagca gtacaacagc acctacaggg tggtgtccgt gctgaccgtg 960

ctgcaccagg actggctgaa cggcaaagaa tacaagtgca aagtctccaa caaggccctg 1020

ccagccccaa tcgaaaagac aatcagcaag gccaagggcc agccacggga gccccaggtg 1080

tacaccctgc cccccagccg ggaggagatg accaagaacc aggtgtccct gacctgtctg 1140

gtgaagggct tctaccccag cgatatcgcc gtggagtggg agagcaacgg ccagcccgag 1200

aacaactaca agaccacccc cccagtgctg gacagcgacg gcagcttctt cctgtacagc 1260

aagctgaccg tggacaagtc caggtggcag cagggcaacg tgttcagctg cagcgtgatg 1320

cacgaggccc tgcacaacca ctacacccag aagtccctga gcctgagccc cggcaag 1377

<210> 50
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 50
Lys Ala Ser Gln Ser Val Asp Tyr Glu Gly His Ser Tyr Met Asn
1 5 10 15

<210> 51
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 51
Ala Ala Ser Asn Leu Glu Ser
1   5

<210> 52
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 52
Gln Gln Ser Asn Glu Asp Pro Pro Thr
1   5

<210> 53
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 53
Ser Gln Ser Val Asp Tyr Glu Gly His Ser Tyr
1   5   10

<210> 54
<211> 3
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 54
Ala Ala Ser
1

<210> 55
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 55
Ser Asn Glu Asp Pro Pro
1   5

<210> 56
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 56
Gln Ser Val Asp Tyr Glu Gly His Ser Tyr
1   5   10

<210> 57
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 57
Glu Thr Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Glu
            20   25   30

Gly His Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
        35   40   45

Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
    50   55   60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65   70   75   80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105   110

<210> 58
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 58
gagacagtgc tgacccagtc ccctgccacc ctgtccgtgt ctcccggcga gagagccacc   60

atcagctgca aggcctccca gtccgtggac tacgaaggcc attcctacat gaactggtat   120

cagcagaagc ccggccaggc ccctcggctg ctgatctacg ccgcctccaa cctggaatcc   180

ggcatccctg cccggttctc cggctctggc tctggcaccg acttcaccct gaccatctcc   240

agcgtggaac ccgaggacgc cgccacctac tactgccagc agtccaacga ggacccccc 300

accttcggcg gaggcaccaa gctggaaatc aag 333

<210> 59
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 59
Glu Thr Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Glu
20 25 30

Gly His Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
35 40 45

Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

```
Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140


Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175


Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190


His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 60
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 60
gagacagtgc tgacccagtc ccctgccacc ctgtccgtgt ctcccggcga gagagccacc       60

atcagctgca aggcctccca gtccgtggac tacgaaggcc attcctacat gaactggtat      120

cagcagaagc ccggccaggc ccctcggctg ctgatctacg ccgcctccaa cctggaatcc      180

ggcatccctg cccggttctc cggctctggc tctggcaccg acttcaccct gaccatctcc      240

agcgtggaac ccgaggacgc cgccacctac tactgccagc agtccaacga ggacccccccc      300

accttcggcg gaggcaccaa gctggaaatc aagcgtacgg tggccgctcc cagcgtgttc      360
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atcttccccc ccagcgacga gcagctgaag agtggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 61
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 61
Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asn Ser Tyr Met Asn
1 5 10 15

<210> 62
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 62
Ser Gln Ser Val Asp Tyr Asp Gly Asn Ser Tyr
1 5 10

<210> 63
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 63
Gln Ser Val Asp Tyr Asp Gly Asn Ser Tyr
1 5 10

<210> 64
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 64
Glu Thr Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asn Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
35 40 45

Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 65

<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 65
gagacagtgc tgacccagtc ccctgccacc ctgtccgtgt ctcccggcga gagagccacc 60

atcagctgca aggcctccca gtccgtggac tacgacggca actcctacat gaactggtat 120

cagcagaagc ccggccaggc ccctcggctg ctgatctacg ccgcctccaa cctggaatcc 180

ggcatccctg cccggttctc cggctctggc tctggcaccg acttcaccct gaccatctcc 240

agcgtggaac ccgaggacgc cgccacctac tactgccagc agtccaacga ggaccccccc 300

accttcggcg gaggcaccaa gctggaaatc aag 333

<210> 66
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 66
Glu Thr Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asn Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
35 40 45

Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

```
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 67
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
```

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 67
gagacagtgc tgacccagtc ccctgccacc ctgtccgtgt ctcccggcga gagagccacc 60

atcagctgca aggcctccca gtccgtggac tacgacggca actcctacat gaactggtat 120

cagcagaagc ccggccaggc ccctcggctg ctgatctacg ccgcctccaa cctggaatcc 180

ggcatccctg cccggttctc cggctctggc tctggcaccg acttcaccct gaccatctcc 240

agcgtggaac ccgaggacgc cgccacctac tactgccagc agtccaacga ggacccccc 300

accttcggcg gaggcaccaa gctggaaatc aagcgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agtggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 68
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 68
Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Ser Gly Ser Tyr Tyr Tyr
1 5 10 15

Val Met Asp Tyr
20

<210> 69

<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 69
Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Ser Gly Ser Tyr
1 5 10 15

Tyr Tyr Val Met Asp Tyr
20

<210> 70
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 70
Gln Val 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 Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Tyr Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
35 40 45

Met Gly Tyr Ile Ser Tyr Asp Ala Asp Asn Asn Tyr Asn Pro Ser Leu
50 55 60

Lys Asn Arg Ile Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Ser Gly Ser Tyr
100 105 110

Tyr Tyr Val Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115 120 125

Ser

<210> 71
<211> 387
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 71
caggtgcagc tgcaggaatc tggccctggc ctggtgaaac cctcccagac cctgtccctg 60

acctgcaccg tgtccggcta ctccatcacc tccggctact actggaactg gatccggcag 120

caccccggca agggcctgga atggatgggc tacatctcct acgacgctga caacaactac 180

aaccccagcc tgaagaacag aatcaccatc tcccgggaca cctccaagaa ccagttctcc 240

ctgaagctgt cctccgtgac cgccgctgac accgccgtgt actactgcgc tggcggctac 300

tacagatacg gcctgggctc ctactccggc tcctactact acgtgatgga ctactggggc 360

cagggcacca ccgtgaccgt gtcctct 387

<210> 72
<211> 459
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 72

```
Gln Val 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 Tyr Ser Ile Thr Ser Gly
            20                  25                  30

Tyr Tyr Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Met Gly Tyr Ile Ser Tyr Asp Ala Asp Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Asn Arg Ile Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Ser Gly Ser Tyr
            100                 105                 110

Tyr Tyr Val Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    130                 135                 140

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
145                 150                 155                 160

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
                165                 170                 175
```

```
Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            180                 185                 190

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        195                 200                 205

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    210                 215                 220

Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
225                 230                 235                 240

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
                245                 250                 255

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
            260                 265                 270

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
        275                 280                 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
    290                 295                 300

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305                 310                 315                 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
                325                 330                 335

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
            340                 345                 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
        355                 360                 365
```

```
Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
    370                 375                 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385                 390                 395                 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
                405                 410                 415

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
            420                 425                 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
        435                 440                 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210> 73
<211> 1377
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 73
caggtgcagc tgcaggaatc tggccctggc ctggtgaaac cctcccagac cctgtccctg       60

acctgcaccg tgtccggcta ctccatcacc tccggctact actggaactg gatccggcag      120

caccccggca agggcctgga atggatgggc tacatctcct acgacgctga caacaactac      180

aaccccagcc tgaagaacag aatcaccatc tcccgggaca cctccaagaa ccagttctcc      240

ctgaagctgt cctccgtgac cgccgctgac accgccgtgt actactgcgc tggcggctac      300

tacagatacg gcctgggctc ctactccggc tcctactact acgtgatgga ctactggggc      360
```

cagggcacca ccgtgaccgt gtcctctgct agcaccaagg gcccaagtgt gtttcccctg 420

gcccccagca gcaagtctac ttccggcgga actgctgccc tgggttgcct ggtgaaggac 480

tacttccccg agcccgtgac agtgtcctgg aactctgggg ctctgacttc cggcgtgcac 540

accttccccg ccgtgctgca gagcagcggc ctgtacagcc tgagcagcgt ggtgacagtg 600

ccctccagct ctctgggaac ccagacctat atctgcaacg tgaaccacaa gcccagcaac 660

accaaggtgg acaagagagt ggagcccaag agctgcgaca agacccacac ctgccccccc 720

tgcccagctc cagaactgct gggagggcct tccgtgttcc tgttcccccc caagcccaag 780

gacaccctga tgatcagcag gacccccgag gtgacctgcg tggtggtgga cgtgtcccac 840

gaggacccag aggtgaagtt caactggtac gtggacggcg tggaggtgca caacgccaag 900

accaagccca gagaggagca gtacaacagc acctacaggg tggtgtccgt gctgaccgtg 960

ctgcaccagg actggctgaa cggcaaagaa tacaagtgca aagtctccaa caaggccctg 1020

ccagccccaa tcgaaaagac aatcagcaag gccaagggcc agccacggga gccccaggtg 1080

tacaccctgc cccccagccg ggaggagatg accaagaacc aggtgtccct gacctgtctg 1140

gtgaagggct tctaccccag cgatatcgcc gtggagtggg agagcaacgg ccagcccgag 1200

aacaactaca agaccacccc cccagtgctg gacagcgacg gcagcttctt cctgtacagc 1260

aagctgaccg tggacaagtc caggtggcag cagggcaacg tgttcagctg cagcgtgatg 1320

cacgaggccc tgcacaacca ctacacccag aagtccctga gcctgagccc cggcaag 1377

<210> 74
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 74
Asp Thr Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Val Gly

```
1               5                   10                  15

Asp Arg Ala Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Asp Tyr Glu
            20                  25                  30

Gly His Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Ser
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 75
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 75

```
gacacccaga tgacccagtc cccctcctcc ctgtccgtgt ccgtgggcga cagagccacc       60

atcacatgca aggcctccca gtccgtggac tacgaaggcc attcctacat gaactggtat      120

cagcagaagc ccggcaaggc ccccaagctg ctgatctacg ccgcctccaa cctggaatcc      180

ggcgtgccct ccagattctc cggctccggc tctggcaccg acttcaccct gaccatctcc      240

agcgtgcagc ccgaggactt cgccacctac tactgccagc agtccaacga ggacccccccc      300
```

accttcggcg gaggcaccaa gctggaaatc aag 333

<210> 76
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 76
Asp Thr Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Val Gly
1 5 10 15

Asp Arg Ala Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Asp Tyr Glu
20 25 30

Gly His Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Ser
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

```
Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175


Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190


His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 77
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 77
gacacccaga tgacccagtc cccctcctcc ctgtccgtgt ccgtgggcga cagagccacc       60

atcacatgca aggcctccca gtccgtggac tacgaaggcc attcctacat gaactggtat      120

cagcagaagc ccggcaaggc ccccaagctg ctgatctacg ccgcctccaa cctggaatcc      180

ggcgtgccct ccagattctc cggctccggc tctggcaccg acttcaccct gaccatctcc      240

agcgtgcagc ccgaggactt cgccacctac tactgccagc agtccaacga ggacccccccc      300

accttcggcg gaggcaccaa gctggaaatc aagcgtacgg tggccgctcc cagcgtgttc      360

atcttccccc ccagcgacga gcagctgaag agtggcaccg ccagcgtggt gtgcctgctg      420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc      480
```

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 78
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 78
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Glu Ile Thr Leu Ser Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Thr Leu Thr Ile Ser Ser Val Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 79

<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 79
gagatcgtgc tgacccagtc ccctgccacc ctgtctgcca gccctggcga ggagatcacc 60

ctgtcctgct ccgcctcctc ctccgtgtcc tacatccact ggtatcagca gaagcccggc 120

caggcccctc ggctgctgat ctactccacc tccaacctgg cctccggcat ccctgccaga 180

ttctccggct ctggctccgg caccttttac accctgacca tctccagcgt ggaacccgag 240

gacgccgccg tgtactactg ccaccagtgg tccagctacc cctggacctt cggcggaggc 300

accaagctgg aaatcaag 318

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 80
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Glu Ile Thr Leu Ser Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

```
Gly Ser Gly Thr Phe Tyr Thr Leu Thr Ile Ser Ser Val Glu Pro Glu
65                  70                  75                  80

Asp Ala Ala Val Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
                85                  90                  95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205

Asn Arg Gly Glu Cys
    210


<210> 81
<211> 639
<212> DNA
<213> Artificial Sequence

<220>
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<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 81
gagatcgtgc tgacccagtc ccctgccacc ctgtctgcca gccctggcga ggagatcacc 60

ctgtcctgct ccgcctcctc ctccgtgtcc tacatccact ggtatcagca gaagcccggc 120

caggcccctc ggctgctgat ctactccacc tccaacctgg cctccggcat ccctgccaga 180

ttctccggct ctggctccgg caccttttac accctgacca tctccagcgt ggaacccgag 240

gacgccgccg tgtactactg ccaccagtgg tccagctacc cctggacctt cggcggaggc 300

accaagctgg aaatcaagcg tacggtggcc gctcccagcg tgttcatctt cccccccagc 360

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 82
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 82
Ser Ser Ser Ala Ala Trp Asn
1 5

<210> 83
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 83
Arg Ile Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser Val
1   5   10   15

Lys Ser

<210> 84
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 84
Gly Ser Tyr Val Thr Ser Ser Tyr Glu Gly Phe Asp Tyr
1   5   10

<210> 85
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 85
Gly Asp Ser Val Ser Ser Ser Ser Ala
1   5

<210> 86
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 86
Tyr Tyr Arg Ser Lys Trp Tyr
1   5

<210> 87
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 87
Gly Asp Ser Val Ser Ser Ser Ser Ala Ala Trp Asn
1   5   10

<210> 88
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 88
Gly Asp Ser Val Ser Ser Ser Ser Ala Ala
1   5   10

<210> 89
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 89
Ile Tyr Tyr Arg Ser Lys Trp Tyr Asn
1 5

<210> 90
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 90
Ala Arg Gly Ser Tyr Val Thr Ser Ser Tyr Glu Gly Phe Asp Tyr
1 5 10 15

<210> 91
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 91
Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Ser
20 25 30

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

Trp Leu Gly Arg Ile Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50 55 60

Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Gly Ser Tyr Val Thr Ser Ser Tyr Glu Gly Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 92
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 92
caggtgcaat tgcagcagag cggtccgggc ctggtgaaac cgagccagac cctgagcctg 60

acctgcgcga tttccggaga tagcgtgagc tctagctctg ctgcttggaa ctggattcgt 120

cagagcccga gccgtggcct cgagtggctg ggccgtatct actaccgtag caaatggtac 180

aacgactatg ccgtgagcgt gaaaagccgc attaccatta acccggatac ttcgaaaaac 240

cagtttagcc tgcaactgaa cagcgtgacc ccggaagata cggccgtgta ttattgcgcg 300

cgtggttctt acgttacttc ttcttacgaa ggtttcgatt actggggcca aggcaccctg 360

gtgactgtta gctca 375

<210> 93
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 93
Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Ser
20 25 30

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

Trp Leu Gly Arg Ile Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50 55 60

Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Gly Ser Tyr Val Thr Ser Ser Tyr Glu Gly Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
115 120 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
130 135 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145 150 155 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His

```
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
```

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        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445

Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210> 94
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 94
caggtgcaat tgcagcagag cggtccgggc ctggtgaaac cgagccagac cctgagcctg       60

acctgcgcga tttccggaga tagcgtgagc tctagctctg ctgcttggaa ctggattcgt      120

cagagcccga gccgtggcct cgagtggctg ggccgtatct actaccgtag caaatggtac      180

aacgactatg ccgtgagcgt gaaaagccgc attaccatta acccggatac ttcgaaaaac      240

cagtttagcc tgcaactgaa cagcgtgacc ccggaagata cggccgtgta ttattgcgcg      300
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cgtggttctt acgttacttc ttcttacgaa ggtttcgatt actggggcca aggcaccctg 360

gtgactgtta gctcagcctc caccaagggt ccatcggtct tccccctggc accctcctcc 420

aagagcacct ctgggggcac agcggccctg ggctgcctgg tcaaggacta cttccccgaa 480

ccggtgacgg tgtcgtggaa ctcaggcgcc ctgaccagcg gcgtgcacac cttcccggct 540

gtcctacagt cctcaggact ctactccctc agcagcgtgg tgaccgtgcc ctccagcagc 600

ttgggcaccc agacctacat ctgcaacgtg aatcacaagc ccagcaacac caaggtggac 660

aagagagttg agcccaaatc ttgtgacaaa actcacacat gcccaccgtg cccagcacct 720

gaactcctgg ggggaccgtc agtcttcctc ttccccccaa aacccaagga caccctcatg 780

atctcccgga cccctgaggt cacatgcgtg gtggtggacg tgagccacga agaccctgag 840

gtcaagttca actggtacgt ggacggcgtg gaggtgcata atgccaagac aaagccgcgg 900

gaggagcagt acaacagcac gtaccgggtg gtcagcgtcc tcaccgtcct gcaccaggac 960

tggctgaatg gcaaggagta caagtgcaag gtctccaaca aagccctccc agcccccatc 1020

gagaaaacca tctccaaagc caaagggcag ccccgagaac cacaggtgta caccctgccc 1080

ccatcccggg aggagatgac caagaaccag gtcagcctga cctgcctggt caaaggcttc 1140

tatcccagcg acatcgccgt ggagtgggag agcaatgggc agccggagaa caactacaag 1200

accacgcctc ccgtgctgga ctccgacggc tccttcttcc tctacagcaa gctcaccgtg 1260

gacaagagca ggtggcagca ggggaacgtc ttctcatgct ccgtgatgca tgaggctctg 1320

cacaaccact acacgcagaa gagcctctcc ctgtctccgg gtaaa 1365

<210> 95
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 95

Ser Gly Asp Asn Leu Pro Glu Lys Tyr Ala Tyr
1   5   10

<210> 96
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 96
Asp Asp Asn Lys Arg Pro Ser
1   5

<210> 97
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 97
Gln Ser Tyr Gly Lys Trp Gly Trp Thr Trp Val
1   5   10

<210> 98
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 98
Asp Asn Leu Pro Glu Lys Tyr
1   5

<210> 99
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 99
Asp Asp Asn
1

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 100
Tyr Gly Lys Trp Gly Trp Thr Trp
1   5

<210> 101
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 101
Asn Leu Pro Glu Lys Tyr
1   5

<210> 102
<211> 108

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 102
Ser Tyr Glu Leu Thr Gln Pro Leu Ser Val Ser Val Ala Leu Gly Gln
1 5 10 15

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

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Asp Asp Asn 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 Arg Ala Gln Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Gly Lys Trp Gly Trp Thr
85 90 95

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

<210> 103
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 103

agctacgaac tgacccagcc gctgtccgtg agcgtggctc tgggccagac cgcgcggatt 60

acctgtagcg gcgataacct gccggaaaaa tacgcttact ggtaccagca gaaaccgggc 120

caggcgccgg tgctggtgat ctacgacgac aacaaacgtc cgagcggcat cccggaacgt 180

tttagcggat ccaacagcgg caacaccgcg accctgacca ttagccgcgc ccaggcggga 240

gacgaagcgg attattactg ccagtcttac ggtaaatggg gttggacttg ggtgtttggc 300

ggcggcacga agttaaccgt ccta 324

<210> 104
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 104
Ser Tyr Glu Leu Thr Gln Pro Leu Ser Val Ser Val Ala Leu Gly Gln
1 5 10 15

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

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Asp Asp Asn 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 Arg Ala Gln Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Gly Lys Trp Gly Trp Thr
85 90 95

```
Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys
            100                 105                 110


Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln
        115                 120                 125


Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly
    130                 135                 140


Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly
145                 150                 155                 160


Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala
                165                 170                 175


Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser
            180                 185                 190


Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val
        195                 200                 205


Ala Pro Thr Glu Cys Ser
    210


<210> 105
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 105
agctacgaac tgacccagcc gctgtccgtg agcgtggctc tgggccagac cgcgcggatt       60

acctgtagcg gcgataacct gccggaaaaa tacgcttact ggtaccagca gaaaccgggc      120

caggcgccgg tgctggtgat ctacgacgac aacaaacgtc cgagcggcat cccggaacgt      180
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tttagcggat ccaacagcgg caacaccgcg accctgacca ttagccgcgc ccaggcggga 240

gacgaagcgg attattactg ccagtcttac ggtaaatggg gttggacttg ggtgtttggc 300

ggcggcacga agttaaccgt cctaggtcag cccaaggctg ccccctcggt cactctgttc 360

ccgccctcct ctgaggagct tcaagccaac aaggccacac tggtgtgtct cataagtgac 420

ttctacccgg gagccgtgac agtggcctgg aaggcagata gcagccccgt caaggcggga 480

gtggagacca ccacaccctc caaacaaagc aacaacaagt acgcggccag cagctatctg 540

agcctgacgc ctgagcagtg gaagtcccac agaagctaca gctgccaggt cacgcatgaa 600

gggagcaccg tggagaagac agtggcccct acagaatgtt ca 642

<210> 106
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 106
Ser Tyr Ala Val Ser
1 5

<210> 107
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 107
Arg Ile Val Pro Trp Leu Gly His Thr Gln Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 108
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 108
Glu Ser Pro Gly Tyr Arg Tyr Ser Phe Asp Val
1 5 10

<210> 109
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 109
Gly Gly Thr Phe Asp Ser Tyr
1 5

<210> 110
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 110
Val Pro Trp Leu Gly His
1 5

<210> 111
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 111
Gly Gly Thr Phe Asp Ser Tyr Ala Val Ser
1 5 10

<210> 112
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 112
Gly Gly Thr Phe Asp Ser Tyr Ala
1 5

<210> 113
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 113
Ile Val Pro Trp Leu Gly His Thr
1 5

<210> 114
<211> 13

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 114
Ala Arg Glu Ser Pro Gly Tyr Arg Tyr Ser Phe Asp Val
1 5 10

<210> 115
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 115
Gln Val 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 Ala Ser Gly Gly Thr Phe Asp Ser Tyr
20 25 30

Ala Val Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Val Pro Trp Leu Gly His Thr Gln Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ser Pro Gly Tyr Arg Tyr Ser Phe Asp Val Trp Asp Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 116
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 116
caggtgcaat tggtgcagag cggtgccgaa gtgaaaaaac cgggcagcag cgtgaaagtt 60

agctgcaaag catccggagg gacgtttgac tcttacgctg tttcttgggt gcgccaggcc 120

ccgggccagg gcctcgagtg gatgggccgt atcgttccgt ggctgggcca tactcagtac 180

gcccagaaat ttcagggccg ggtgaccatt accgccgatg aaagcaccag caccgcctat 240

atggaactga gcagcctgcg cagcgaagat acggccgtgt attattgcgc gcgtgaatct 300

ccgggttacc gttactcttt cgatgtttgg gaccaaggca ccctggtgac tgttagctca 360

<210> 117
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 117
Gln Val 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 Ala Ser Gly Gly Thr Phe Asp Ser Tyr

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            20                  25                  30

Ala Val Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Val Pro Trp Leu Gly His Thr Gln Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Ser Pro Gly Tyr Arg Tyr Ser Phe Asp Val Trp Asp Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
```

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    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

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

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
```

405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 118
<211> 1350
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 118
caggtgcaat tggtgcagag cggtgccgaa gtgaaaaaac cgggcagcag cgtgaaagtt 60

agctgcaaag catccggagg gacgtttgac tcttacgctg tttcttgggt gcgccaggcc 120

ccgggccagg gcctcgagtg gatgggccgt atcgttccgt ggctgggcca tactcagtac 180

gcccagaaat ttcagggccg ggtgaccatt accgccgatg aaagcaccag caccgcctat 240

atggaactga gcagcctgcg cagcgaagat acggccgtgt attattgcgc gcgtgaatct 300

ccgggttacc gttactcttt cgatgtttgg gaccaaggca ccctggtgac tgttagctca 360

gcctccacca agggtccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 720

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 780

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 900

agcacgtacc gggtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 1080

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa 1350

<210> 119
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 119
Ser Gly Asp Ala Ile Gly Glu Lys Tyr Val Tyr
1 5 10

<210> 120
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 120
Asp Asp Asn Asn Arg Pro Ser
1 5

<210> 121
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 121
Ala Ser Tyr Asp Leu Gln Gln Ala Arg Trp Val
1 5 10

<210> 122
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 122
Asp Ala Ile Gly Glu Lys Tyr
1 5

<210> 123
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 123

Tyr Asp Leu Gln Gln Ala Arg Trp
1 5

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 124
Ala Ile Gly Glu Lys Tyr
1 5

<210> 125
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 125
Ser Tyr Glu Leu Thr Gln Pro Leu Ser Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Ile Gly Glu Lys Tyr Val
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Asp Asp Asn Asn 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 Arg Ala Gln Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Tyr Asp Leu Gln Gln Ala Arg
85 90 95

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

<210> 126
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 126
agctacgaac tgacccagcc gctgtccgtg agcgtggctc tgggccagac cgcgcggatt 60

acctgtagcg gcgatgctat cggtgaaaaa tacgtttact ggtaccagca gaaaccgggc 120

caggcgccgg tgctggtgat ctacgacgac aacaaccgtc cgagcggcat cccggaacgt 180

tttagcggat ccaacagcgg caacaccgcg accctgacca ttagccgcgc ccaggcggga 240

gacgaagcgg attattactg cgcttcttac gacctgcagc aggctcgttg ggtgtttggc 300

ggcggcacga agttaaccgt ccta 324

<210> 127
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 127
Ser Tyr Glu Leu Thr Gln Pro Leu Ser Val Ser Val Ala Leu Gly Gln
1 5 10 15

```
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Ile Gly Glu Lys Tyr Val
            20                  25                  30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
        35                  40                  45

Asp Asp Asn Asn 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 Arg Ala Gln Ala Gly
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Tyr Asp Leu Gln Gln Ala Arg
                85                  90                  95

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys
            100                 105                 110

Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln
        115                 120                 125

Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly
    130                 135                 140

Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly
145                 150                 155                 160

Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala
                165                 170                 175

Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser
            180                 185                 190

Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val
        195                 200                 205
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Ala Pro Thr Glu Cys Ser
210

<210> 128
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 128
agctacgaac tgacccagcc gctgtccgtg agcgtggctc tgggccagac cgcgcggatt 60

acctgtagcg gcgatgctat cggtgaaaaa tacgtttact ggtaccagca gaaaccgggc 120

caggcgccgg tgctggtgat ctacgacgac aacaaccgtc cgagcggcat cccggaacgt 180

tttagcggat ccaacagcgg caacaccgcg accctgacca ttagccgcgc ccaggcggga 240

gacgaagcgg attattactg cgcttcttac gacctgcagc aggctcgttg ggtgtttggc 300

ggcggcacga agttaaccgt cctaggtcag cccaaggctg ccccctcggt cactctgttc 360

ccgccctcct ctgaggagct tcaagccaac aaggccacac tggtgtgtct cataagtgac 420

ttctacccgg gagccgtgac agtggcctgg aaggcagata gcagccccgt caaggcggga 480

gtggagacca ccacaccctc caaacaaagc aacaacaagt acgcggccag cagctatctg 540

agcctgacgc ctgagcagtg gaagtcccac agaagctaca gctgccaggt cacgcatgaa 600

gggagcaccg tggagaagac agtggcccct acagaatgtt ca 642

<210> 129
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 129
Arg Ile Val Pro Trp Leu Gly Phe Thr Arg Tyr Ala Gln Lys Phe Gln
1   5   10   15

Gly

<210> 130
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 130
Val Pro Trp Leu Gly Phe
1   5

<210> 131
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 131
Ile Val Pro Trp Leu Gly Phe Thr
1   5

<210> 132
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 132
Gln Val 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 Ala Ser Gly Gly Thr Phe Asp Ser Tyr
20 25 30

Ala Val Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Val Pro Trp Leu Gly Phe Thr Arg Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ser Pro Gly Tyr Arg Tyr Ser Phe Asp Val Trp Asp Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 133
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 133
caggtgcaat tggtgcagag cggtgccgaa gtgaaaaaac cgggcagcag cgtgaaagtt 60

agctgcaaag catccggagg gacgtttgac tcttacgctg tttcttgggt gcgccaggcc 120

ccgggccagg gcctcgagtg gatgggccgt atcgttccgt ggctgggctt cactcgttac 180

gcccagaaat ttcagggccg ggtgaccatt accgccgatg aaagcaccag caccgcctat 240

atggaactga gcagcctgcg cagcgaagat acggccgtgt attattgcgc gcgtgaatct 300

ccgggttacc gttactcttt cgatgtttgg gaccaaggca ccctggtgac tgttagctca 360

<210> 134
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 134
Gln Val 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 Ala Ser Gly Gly Thr Phe Asp Ser Tyr
20 25 30

Ala Val Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Val Pro Trp Leu Gly Phe Thr Arg Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ser Pro Gly Tyr Arg Tyr Ser Phe Asp Val Trp Asp Gln
100 105 110

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Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

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

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Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450
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<210> 135
<211> 1350
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 135
caggtgcaat tggtgcagag cggtgccgaa gtgaaaaaac cgggcagcag cgtgaaagtt 60

agctgcaaag catccggagg gacgtttgac tcttacgctg tttcttgggt gcgccaggcc 120

ccgggccagg gcctcgagtg gatgggccgt atcgttccgt ggctgggctt cactcgttac 180

gcccagaaat ttcagggccg ggtgaccatt accgccgatg aaagcaccag caccgcctat 240

atggaactga gcagcctgcg cagcgaagat acggccgtgt attattgcgc gcgtgaatct 300

ccgggttacc gttactcttt cgatgtttgg gaccaaggca ccctggtgac tgttagctca 360

gcctccacca agggtccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 720

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 780

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 900

agcacgtacc gggtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 1080

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa 1350

<210> 136
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 136
Ser Tyr Ala Met Ser
1 5

<210> 137
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 137
Val Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 138
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 138
Gly Asp Asp Tyr Gly Asp Asp Tyr Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 139
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 139
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 140
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 140
Ser Gly Ser Gly Gly Ser
1 5

<210> 141
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 141
Gly Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5 10

<210> 142
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 142
Gly Phe Thr Phe Ser Ser Tyr Ala
1 5

<210> 143
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 143
Ile Ser Gly Ser Gly Gly Ser Thr
1 5

<210> 144
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 144
Ala Arg Gly Asp Asp Tyr Gly Asp Asp Tyr Tyr Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> 145
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 145
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Ser Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

Ala Arg Gly Asp Asp Tyr Gly Asp Asp Tyr Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 146
<211> 372

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 146
gaggtgcagc tgttggagtc tgggggaggc ttggtacagt ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gagaggggat 300

gactacggtg acgactacta ctactacggt atggacgtct ggggccaagg gaccacggtc 360

accgtctcct ca 372

<210> 147
<211> 454
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 147
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Ser Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val

```
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

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

Ala Arg Gly Asp Asp Tyr Gly Asp Asp Tyr Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
        115                 120                 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
    130                 135                 140

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145                 150                 155                 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
                165                 170                 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
            180                 185                 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
        195                 200                 205

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
    210                 215                 220

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
225                 230                 235                 240

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
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                245                 250                 255

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
            260                 265                 270

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
        275                 280                 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
    290                 295                 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305                 310                 315                 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
                325                 330                 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
            340                 345                 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
        355                 360                 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
    370                 375                 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385                 390                 395                 400

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
                405                 410                 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
            420                 425                 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
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435 440 445

Ser Leu Ser Pro Gly Lys
450

<210> 148
<211> 1362
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 148
gaggtgcagc tgttggagtc tgggggaggc ttggtacagt ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gagaggggat 300

gactacggtg acgactacta ctactacggt atggacgtct ggggccaagg gaccacggtc 360

accgtctcct cagctagcac caagggccca agtgtgtttc ccctggcccc cagcagcaag 420

tctacttccg gcggaactgc tgccctgggt tgcctggtga aggactactt ccccgagccc 480

gtgacagtgt cctggaactc tggggctctg acttccggcg tgcacacctt ccccgccgtg 540

ctgcagagca gcggcctgta cagcctgagc agcgtggtga cagtgccctc cagctctctg 600

ggaacccaga cctatatctg caacgtgaac cacaagccca gcaacaccaa ggtggacaag 660

agagtggagc ccaagagctg cgacaagacc cacacctgcc ccccctgccc agctccagaa 720

ctgctgggag ggccttccgt gttcctgttc cccccaagc ccaaggacac cctgatgatc 780

agcaggaccc ccgaggtgac ctgcgtggtg gtggacgtgt cccacgagga cccagaggtg 840

aagttcaact ggtacgtgga cggcgtggag gtgcacaacg ccaagaccaa gcccagagag 900

gagcagtaca acagcaccta cagggtggtg tccgtgctga ccgtgctgca ccaggactgg 960

ctgaacggca aagaatacaa gtgcaaagtc tccaacaagg ccctgccagc cccaatcgaa 1020

aagacaatca gcaaggccaa gggccagcca cgggagcccc aggtgtacac cctgcccccc 1080

agccgggagg agatgaccaa gaaccaggtg tccctgacct gtctggtgaa gggcttctac 1140

cccagcgata tcgccgtgga gtgggagagc aacggccagc ccgagaacaa ctacaagacc 1200

acccccccag tgctggacag cgacggcagc ttcttcctgt acagcaagct gaccgtggac 1260

aagtccaggt ggcagcaggg caacgtgttc agctgcagcg tgatgcacga ggccctgcac 1320

aaccactaca cccagaagtc cctgagcctg agccccggca ag 1362

<210> 149
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 149
Arg Ser Ser Gln Ser Leu Leu His Gly Asn Arg Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 150
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 150
Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 151

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 151
Met Gln Ala Leu Gln Thr Pro Pro Thr
1 5

<210> 152
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 152
Ser Gln Ser Leu Leu His Gly Asn Arg Tyr Asn Tyr
1 5 10

<210> 153
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 153
Leu Gly Ser
1

<210> 154
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 154
Ala Leu Gln Thr Pro Pro
1 5

<210> 155
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 155
Gln Ser Leu Leu His Gly Asn Arg Tyr Asn Tyr
1 5 10

<210> 156
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 156
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Gly
20 25 30

Asn Arg Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 157
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 157
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60

atctcctgca ggtctagtca gagcctcctg catggtaatc gatacaacta tttggattgg 120

tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180

tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240

agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct 300

ccgacgttcg gccaagggac caaggtggaa atcaaa 336

<210> 158
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 158
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Gly
20 25 30

Asn Arg Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 159
<211> 657
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 159
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60

atctcctgca ggtctagtca gagcctcctg catggtaatc gatacaacta tttggattgg 120

tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180

tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240

agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct 300

ccgacgttcg gccaagggac caaggtggaa atcaaacgaa ctgtggctgc accaagcgtg 360

ttcatcttcc cccccagcga cgagcagctg aagagtggca ccgccagcgt ggtgtgcctg 420

ctgaacaact tctacccccg ggaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

agcggcaaca gccaggagag cgtcaccgag caggacagca aggactccac ctacagcctg 540

agcagcaccc tgaccctgag caaggccgac tacgagaagc ataaggtgta cgcctgcgag 600

gtgacccacc agggcctgtc cagccccgtg accaagagct tcaacagggg cgagtgc 657

<210> 160
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 160
Ser Cys Ser Met Asn
1 5

<210> 161
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 161
Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 162
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 162
Asp Gln Gly Asn Trp Asn Tyr Asp Asp Tyr Tyr Asn Gly Leu Asp Val
1 5 10 15

<210> 163

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 163
Gly Phe Thr Phe Asn Ser Cys
1 5

<210> 164
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 164
Ser Ser Ser Ser Ser Thr
1 5

<210> 165
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 165
Gly Phe Thr Phe Asn Ser Cys Ser Met Asn
1 5 10

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 166
Gly Phe Thr Phe Asn Ser Cys Ser
1 5

<210> 167
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 167
Ile Ser Ser Ser Ser Ser Thr Ile
1 5

<210> 168
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 168
Ala Arg Asp Gln Gly Asn Trp Asn Tyr Asp Asp Tyr Tyr Asn Gly Leu
1 5 10 15

Asp Val

<210> 169
<211> 125
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 169
Glu Val Leu Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Cys
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

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

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

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 170
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 170
gaggtgctgc tggtggagtc tgggggaggc ttggtacagc ctgggggGTC cctgagactc 60

tcctgtgcag cctctgggtt caccttcaat agctgtagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtttcatac attagtagta gtagtagtac catttactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctcactgtat 240

ctgcaaatga acagcctgaa agacgaggac acggctgtgt attactgtgc gagagatcag 300

ggtaactgga actacgacga ctactacaac ggtttggacg tctggggcca agggaccacg 360

gtcaccgtct cctca 375

<210> 171
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 171
Glu Val Leu Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Cys
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

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

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

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270
```

```
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285


Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300


Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320


Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335


Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350


Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365


Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380


Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400


Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415


Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430


Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445


Leu Ser Leu Ser Pro Gly Lys
    450                 455
```

<210> 172
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 172
gaggtgctgc tggtggagtc tgggggaggc ttggtacagc ctgggggGTC cctgagactc 60

tcctgtgcag cctctgggtt caccttcaat agctgtagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtttcatac attagtagta gtagtagtac catttactac 180

gcagactctg tgaagggccg attcaccatc tccagagaca atgccaagaa ctcactgtat 240

ctgcaaatga acagcctgaa agacgaggac acggctgtgt attactgtgc gagagatcag 300

ggtaactgga actacgacga ctactacaac ggtttggacg tctggggcca agggaccacg 360

gtcaccgtct cctcagctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc 420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag 480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct 600

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccccA agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

<210> 173
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 173
Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 174
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 174
Met Gln Ala Leu Gln Thr Pro Leu Thr
1 5

<210> 175
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 175
Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
1 5 10

<210> 176
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 176
Ala Leu Gln Thr Pro Leu
1 5

<210> 177
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 177
Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
1 5 10

<210> 178
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 178
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 179
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 179
gatattgtga tgactcagtc tccactctcc ctgcccgtca ctcctggaga gccggcctcc 60

atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg 120

tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180

tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240

agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct 300

ctcactttcg gcggagggac caaggtggag atcaaa 336

<210> 180
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 180
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

```
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140


Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160


Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175


Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190


Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205


Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 181
<211> 657
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 181
gatattgtga tgactcagtc tccactctcc ctgcccgtca ctcctggaga gccggcctcc       60

atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg      120

tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc      180

tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc      240

agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct      300

ctcactttcg gcggagggac caaggtggag atcaaacgta cggtggccgc tcccagcgtg      360

ttcatcttcc cccccagcga cgagcagctg aagagtggca ccgccagcgt ggtgtgcctg      420
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ctgaacaact tctacccccg ggaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

agcggcaaca gccaggagag cgtcaccgag caggacagca aggactccac ctacagcctg 540

agcagcaccc tgaccctgag caaggccgac tacgagaagc ataaggtgta cgcctgcgag 600

gtgacccacc agggcctgtc cagccccgtg accaagagct tcaacagggg cgagtgc 657

<210> 182
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 182
His Tyr Gly Met Asn
1 5

<210> 183
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 183
Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 184
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 184
Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
1   5   10

<210> 185
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 185
Gly Tyr Thr Phe Thr His Tyr
1   5

<210> 186
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 186
Asn Thr Asp Thr Gly Asn
1   5

<210> 187
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 187
Gly Tyr Thr Phe Thr His Tyr Gly Met Asn
1 5 10

<210> 188
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 188
Gly Tyr Thr Phe Thr His Tyr Gly
1 5

<210> 189
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 189
Ile Asn Thr Asp Thr Gly Asn Pro
1 5

<210> 190
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 190
Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
1   5   10   15

<210> 191
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 191
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Gln Pro Gly Gln
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
            20   25   30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
        35   40   45

Gly Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe
    50   55   60

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

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

Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 192
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 192
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc 60

tcctgcaagg cttcagggta caccttcaca cactatggga tgaactgggt gaagcaggca 120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat 180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat 240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga 300

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctca 369

<210> 193
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 193
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Gln Pro Gly Gln
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

```
Gly Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe
    50                  55                  60

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

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

Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr Ala
        115                 120                 125

Pro Ser Val Tyr Pro Leu Ala Pro Val Cys Gly Asp Thr Thr Gly Ser
    130                 135                 140

Ser Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
145                 150                 155                 160

Thr Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
                165                 170                 175

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
            180                 185                 190

Val Thr Ser Ser Thr Trp Pro Ser Gln Ser Ile Thr Cys Asn Val Ala
        195                 200                 205

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Glu Pro Arg Gly
    210                 215                 220

Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu
225                 230                 235                 240
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```
Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val
                245                 250                 255


Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val
            260                 265                 270


Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val
        275                 280                 285


Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
    290                 295                 300


Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met
305                 310                 315                 320


Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala
                325                 330                 335


Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
            340                 345                 350


Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
        355                 360                 365


Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
    370                 375                 380


Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
385                 390                 395                 400


Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
                405                 410                 415


Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser
            420                 425                 430
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Val Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser
435 440 445

Arg Thr Pro Gly Lys
450

<210> 194
<211> 1359
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 194
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc 60

tcctgcaagg cttcagggta caccttcaca cactatggga tgaactgggt gaagcaggca 120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat 180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat 240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga 300

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctcag ccaagaccac cgcccccagc gtgtaccccc tggcccccgt gtgcggcgat 420

accaccggca gcagcgtgac cctgggctgc ctggtgaagg gctacttccc cgagcccgtg 480

accctgacct ggaacagcgg ctccctgagc agcggcgtgc acaccttccc cgccgtgctg 540

cagagcgacc tgtacaccct gtccagctcc gtgaccgtga caagcagcac ctggcccagc 600

cagagcatca cctgcaacgt ggcccacccc gccagcagca ccaaggtgga caagaagatc 660

gagcccaggg gccccaccat caagccctgc ccccctgca agtgcccagc ccccaacctg 720

ctgggcggac ccagcgtgtt catcttcccc cccaagatca aggacgtgct gatgatcagc 780

ctgagcccca tcgtgacctg cgtggtggtg gacgtgagcg aggacgaccc cgacgtgcag 840

atcagctggt tcgtgaacaa cgtggaggtg cacaccgccc agacccagac ccaccgggag 900

gactacaaca gcaccctgcg cgtcgtgtcc gccctgccca tccagcacca ggactggatg 960

agcggcaaag aattcaagtg caaggtgaac aacaaggacc tgcctgcccc catcgagcgg 1020

accatcagca agcccaaggg cagcgtgaga gccccccagg tgtacgtgct gccccctccc 1080

gaggaagaga tgaccaagaa acaggtgaca ctgacctgca tggtgaccga cttcatgccc 1140

gaggacatct acgtggagtg gaccaacaac ggcaagaccg agctgaacta caagaacacc 1200

gagcctgtgc tggacagcga cggcagctac ttcatgtaca gcaagctgcg ggtggagaag 1260

aaaaactggg tggagcggaa cagctacagc tgcagcgtgg tgcacgaggg cctgcacaac 1320

caccacacca ccaagagctt cagccggacc cccggcaag 1359

<210> 195
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 195
Lys Ser Ser Gln Ser Leu Phe Asn Ser Asn Thr Asn Lys Asn Tyr Leu
1 5 10 15

Asn

<210> 196
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 196
Tyr Ala Ser Thr Arg His Thr
1 5

<210> 197
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 197
Gln Gln Trp Tyr Ser Tyr Pro Trp Thr
1 5

<210> 198
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 198
Ser Gln Ser Leu Phe Asn Ser Asn Thr Asn Lys Asn Tyr
1 5 10

<210> 199
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 199
Tyr Ala Ser
1

<210> 200
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 200
Trp Tyr Ser Tyr Pro Trp
1 5

<210> 201
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 201
Gln Ser Leu Phe Asn Ser Asn Thr Asn Lys Asn Tyr
1 5 10

<210> 202
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 202
Asp Ile Met Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Lys Ala Thr Ile Thr Cys Lys Ser Ser Gln Ser Leu Phe Asn Ser

20 25 30

Asn Thr Asn Lys Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Phe Tyr Tyr Ala Ser Thr Arg His Thr Gly Val
50 55 60

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

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

Trp Tyr Ser Tyr Pro Trp Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 203
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 203
gacatcatga tgacccagtc tccatcatcc ctgagtgtgt cagcaggaga gaaagccact 60

atcacctgca agtccagtca gagtcttttc aacagtaaca ccaacaagaa ctacttgaac 120

tggtacctgc agaaaccagg gcagtctcct aaactgctgt tctattatgc atccactagg 180

catactgggg tccctgatcg cttcataggc agtggatctg ggacagattt cactctcacc 240

atcaccagtg tccaggatga agacctggca gattattact gtcagcagtg gtatagctac 300

ccgtggacgt tcggacctgg caccaagctg gaaatcaaa 339

<210> 204
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 204
Asp Ile Met Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Lys Ala Thr Ile Thr Cys Lys Ser Ser Gln Ser Leu Phe Asn Ser
20 25 30

Asn Thr Asn Lys Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Phe Tyr Tyr Ala Ser Thr Arg His Thr Gly Val
50 55 60

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

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

Trp Tyr Ser Tyr Pro Trp Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile
100 105 110

Lys Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser
115 120 125

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

```
Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu
145                 150                 155                 160


Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp
                165                 170                 175


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


Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr
        195                 200                 205


Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
    210                 215                 220


<210> 205
<211> 660
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 205
gacatcatga tgacccagtc tccatcatcc ctgagtgtgt cagcaggaga gaaagccact       60

atcacctgca agtccagtca gagtcttttc aacagtaaca ccaacaagaa ctacttgaac      120

tggtacctgc agaaaccagg gcagtctcct aaactgctgt tctattatgc atccactagg      180

catactgggg tccctgatcg cttcataggc agtggatctg ggacagattt cactctcacc      240

atcaccagtg tccaggatga agacctggca gattattact gtcagcagtg gtatagctac      300

ccgtggacgt tcggacctgg caccaagctg gaaatcaaac gcgctgatgc cgcccctacc      360

gtgagcatct tccccccccag cagcgagcag ctgaccagcg gcggagccag cgtggtgtgc      420

ttcctgaaca acttctaccc caaggacatc aacgtgaagt ggaagatcga cggcagcgag      480
```

cggcagaacg gcgtgctgaa cagctggacc gaccaggaca gcaaggactc cacctacagc 540

atgagcagca ccctgaccct gaccaaggac gagtacgagc ggcacaacag ctacacctgc 600

gaggccaccc acaagaccag caccagcccc atcgtgaaga gcttcaaccg gaacgagtgc 660

<210> 206
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 206
Gly Tyr Thr Phe Trp His Tyr
1 5

<210> 207
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 207
Gly Tyr Thr Phe Trp His Tyr Gly Met Asn
1 5 10

<210> 208
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 208
Gly Tyr Thr Phe Trp His Tyr Gly
1 5

<210> 209
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 209
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Gln Pro Gly Gln
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Trp His Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe
50 55 60

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

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

Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 210
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc 60

tcctgcaagg cttcagggta caccttctgg cactatggga tgaactgggt gaagcaggca 120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat 180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat 240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga 300

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctca 369

<210> 211
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 211
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Gln Pro Gly Gln
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Trp His Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

```
Gly Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe
    50                  55                  60

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

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

Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr Ala
        115                 120                 125

Pro Ser Val Tyr Pro Leu Ala Pro Val Cys Gly Asp Thr Thr Gly Ser
    130                 135                 140

Ser Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
145                 150                 155                 160

Thr Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
                165                 170                 175

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
            180                 185                 190

Val Thr Ser Ser Thr Trp Pro Ser Gln Ser Ile Thr Cys Asn Val Ala
        195                 200                 205

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Glu Pro Arg Gly
    210                 215                 220

Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu
225                 230                 235                 240
```

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Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val
                245                 250                 255


Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val
            260                 265                 270


Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val
        275                 280                 285


Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
    290                 295                 300


Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met
305                 310                 315                 320


Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala
                325                 330                 335


Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
            340                 345                 350


Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
        355                 360                 365


Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
    370                 375                 380


Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
385                 390                 395                 400


Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
                405                 410                 415


Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser
            420                 425                 430
```

Val Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser
435 440 445

Arg Thr Pro Gly Lys
450

<210> 212
<211> 1359
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 212
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc 60

tcctgcaagg cttcagggta caccttctgg cactatggga tgaactgggt gaagcaggca 120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat 180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat 240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga 300

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctcag ccaagaccac cgcccccagc gtgtaccccc tggcccccgt gtgcggcgat 420

accaccggca gcagcgtgac cctgggctgc ctggtgaagg gctacttccc cgagcccgtg 480

accctgacct ggaacagcgg ctccctgagc agcggcgtgc acaccttccc cgccgtgctg 540

cagagcgacc tgtacaccct gtccagctcc gtgaccgtga caagcagcac ctggcccagc 600

cagagcatca cctgcaacgt ggcccacccc gccagcagca ccaaggtgga caagaagatc 660

gagcccaggg gccccaccat caagccctgc ccccctgca agtgcccagc ccccaacctg 720

ctgggcggac ccagcgtgtt catcttcccc cccaagatca aggacgtgct gatgatcagc 780

ctgagcccca tcgtgacctg cgtggtggtg gacgtgagcg aggacgaccc cgacgtgcag 840

atcagctggt tcgtgaacaa cgtggaggtg cacaccgccc agacccagac ccaccgggag 900

gactacaaca gcaccctgcg cgtcgtgtcc gccctgccca tccagcacca ggactggatg 960

agcggcaaag aattcaagtg caaggtgaac aacaaggacc tgcctgcccc catcgagcgg 1020

accatcagca agcccaaggg cagcgtgaga gccccccagg tgtacgtgct gccccctccc 1080

gaggaagaga tgaccaagaa acaggtgaca ctgacctgca tggtgaccga cttcatgccc 1140

gaggacatct acgtggagtg gaccaacaac ggcaagaccg agctgaacta caagaacacc 1200

gagcctgtgc tggacagcga cggcagctac ttcatgtaca gcaagctgcg ggtggagaag 1260

aaaaactggg tggagcggaa cagctacagc tgcagcgtgg tgcacgaggg cctgcacaac 1320

caccacacca ccaagagctt cagccggacc cccggcaag 1359

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 213
Gly Tyr Thr Phe His His Tyr
1 5

<210> 214
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 214
Gly Tyr Thr Phe His His Tyr Gly Met Asn
1 5 10

<210> 215
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 215
Gly Tyr Thr Phe His His Tyr Gly
1 5

<210> 216
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 216
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Gln Pro Gly Gln
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe His His Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe
50 55 60

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

Leu Gln Ile Ser Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Tyr Cys

85 90 95

Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 217
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 217
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc 60

tcctgcaagg cttcagggta caccttccac cactatggga tgaactgggt gaagcaggca 120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat 180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat 240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga 300

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctca 369

<210> 218
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 218

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe His His Tyr
            20                  25                  30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Asp Thr Gly Asn Pro Thr Tyr Ala Asp Asp Phe
    50                  55                  60

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

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

Val Arg Tyr Gly Thr Leu Tyr Ser Gly Tyr Gly Phe Phe Phe Asp Ser
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr Ala
        115                 120                 125

Pro Ser Val Tyr Pro Leu Ala Pro Val Cys Gly Asp Thr Thr Gly Ser
    130                 135                 140

Ser Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
145                 150                 155                 160

Thr Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
                165                 170                 175

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
            180                 185                 190
```

```
Val Thr Ser Ser Thr Trp Pro Ser Gln Ser Ile Thr Cys Asn Val Ala
        195                 200                 205

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Glu Pro Arg Gly
    210                 215                 220

Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu
225                 230                 235                 240

Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val
                245                 250                 255

Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val
            260                 265                 270

Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val
        275                 280                 285

Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
    290                 295                 300

Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met
305                 310                 315                 320

Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala
                325                 330                 335

Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
            340                 345                 350

Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
        355                 360                 365

Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
    370                 375                 380
```

Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
385 390 395 400

Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
405 410 415

Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser
420 425 430

Val Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser
435 440 445

Arg Thr Pro Gly Lys
450

<210> 219
<211> 1359
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 219
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc 60

tcctgcaagg cttcagggta caccttccac cactatggga tgaactgggt gaagcaggca 120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat 180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat 240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga 300

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctcag ccaagaccac cgcccccagc gtgtaccccc tggcccccgt gtgcggcgat 420

accaccggca gcagcgtgac cctgggctgc ctggtgaagg gctacttccc cgagcccgtg 480

accctgacct ggaacagcgg ctccctgagc agcggcgtgc acaccttccc cgccgtgctg 540

cagagcgacc tgtacaccct gtccagctcc gtgaccgtga caagcagcac ctggcccagc 600

cagagcatca cctgcaacgt ggcccacccc gccagcagca ccaaggtgga caagaagatc 660

gagcccaggg gccccaccat caagccctgc ccccccctgca agtgcccagc ccccaacctg 720

ctgggcggac ccagcgtgtt catcttcccc cccaagatca aggacgtgct gatgatcagc 780

ctgagcccca tcgtgacctg cgtggtggtg gacgtgagcg aggacgaccc cgacgtgcag 840

atcagctggt tcgtgaacaa cgtggaggtg cacaccgccc agacccagac ccaccgggag 900

gactacaaca gcaccctgcg cgtcgtgtcc gccctgccca tccagcacca ggactggatg 960

agcggcaaag aattcaagtg caaggtgaac aacaaggacc tgcctgcccc catcgagcgg 1020

accatcagca agcccaaggg cagcgtgaga gccccccagg tgtacgtgct gccccctccc 1080

gaggaagaga tgaccaagaa acaggtgaca ctgacctgca tggtgaccga cttcatgccc 1140

gaggacatct acgtggagtg gaccaacaac ggcaagaccg agctgaacta caagaacacc 1200

gagcctgtgc tggacagcga cggcagctac ttcatgtaca gcaagctgcg ggtggagaag 1260

aaaaactggg tggagcggaa cagctacagc tgcagcgtgg tgcacgaggg cctgcacaac 1320

caccacacca ccaagagctt cagccggacc cccggcaag 1359

<210> 220
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 220
Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu Lys Asn
1 5 10 15

<210> 221
<211> 15
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 221
Gly Tyr Tyr Arg Tyr Gly Leu Ser Tyr Tyr Tyr Val Met Asp Tyr
1 5 10 15

<210> 222
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 222
Ser Tyr Asp Gly Asp
1 5

<210> 223
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 223
Ile Ser Tyr Asp Gly Asp Asn
1 5

<210> 224
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 224
Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Ser Tyr Tyr Tyr Val Met Asp
1 5 10 15

Tyr

<210> 225
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 225
Asp 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 Tyr Ser Ile Thr Ser Gly
20 25 30

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

Met Gly Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu
50 55 60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

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

```
Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Ser Tyr Tyr Tyr Val Met Asp
            100                 105                 110


Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
        115                 120


<210> 226
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 226
gatatacagc ttcaggagtc aggacctggc ctcgtgaaac cttctcagtc tctgtctctc       60

acctgctctg tcactggcta ctccatcacc agtggttatt actggaactg gatccggcag      120

tttccaggaa acaaactgga atggatgggc tacataagct acgacggtga caataactac      180

aacccatctc tcaaaaatcg aatctccatc actcgtgaca catctaagaa ccagtttttc      240

ctgaagttga gttctgtgac tactgaggac acagctacat attactgtgc aggaggctac      300

tataggtacg gcctgtcgta ttactatgtt atggactact ggggtcaagg aacctcagtc      360

accgtctcct ca                                                          372


<210> 227
<211> 454
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 227
Asp 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 Tyr Ser Ile Thr Ser Gly
            20                  25                  30

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

Met Gly Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu
    50                  55                  60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65                  70                  75                  80

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

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Ser Tyr Tyr Tyr Val Met Asp
            100                 105                 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys
        115                 120                 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
    130                 135                 140

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145                 150                 155                 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
                165                 170                 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
            180                 185                 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
        195                 200                 205
```

```
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
    210                 215                 220

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
225                 230                 235                 240

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
                245                 250                 255

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
            260                 265                 270

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
        275                 280                 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
    290                 295                 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305                 310                 315                 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
                325                 330                 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
            340                 345                 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
        355                 360                 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
    370                 375                 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385                 390                 395                 400
```

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445

Ser Leu Ser Pro Gly Lys
450

<210> 228
<211> 1362
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 228
gatatacagc ttcaggagtc aggacctggc ctcgtgaaac cttctcagtc tctgtctctc 60

acctgctctg tcactggcta ctccatcacc agtggttatt actggaactg gatccggcag 120

tttccaggaa acaaactgga atggatgggc tacataagct acgacggtga caataactac 180

aacccatctc tcaaaaatcg aatctccatc actcgtgaca catctaagaa ccagtttttc 240

ctgaagttga gttctgtgac tactgaggac acagctacat attactgtgc aggaggctac 300

tataggtacg gcctgtcgta ttactatgtt atggactact ggggtcaagg aacctcagtc 360

accgtctcct cagctagcac caagggccca agtgtgtttc ccctggcccc cagcagcaag 420

tctacttccg gcggaactgc tgccctgggt tgcctggtga aggactactt ccccgagccc 480

gtgacagtgt cctggaactc tggggctctg acttccggcg tgcacacctt ccccgccgtg 540

ctgcagagca gcggcctgta cagcctgagc agcgtggtga cagtgccctc cagctctctg 600

ggaacccaga cctatatctg caacgtgaac cacaagccca gcaacaccaa ggtggacaag 660

agagtggagc ccaagagctg cgacaagacc cacacctgcc ccccctgccc agctccagaa 720

ctgctgggag ggccttccgt gttcctgttc ccccccaagc ccaaggacac cctgatgatc 780

agcaggaccc ccgaggtgac ctgcgtggtg gtggacgtgt cccacgagga cccagaggtg 840

aagttcaact ggtacgtgga cggcgtggag gtgcacaacg ccaagaccaa gcccagagag 900

gagcagtaca acagcaccta cagggtggtg tccgtgctga ccgtgctgca ccaggactgg 960

ctgaacggca aagaatacaa gtgcaaagtc tccaacaagg ccctgccagc cccaatcgaa 1020

aagacaatca gcaaggccaa gggccagcca cgggagcccc aggtgtacac cctgcccccc 1080

agccgggagg agatgaccaa gaaccaggtg tccctgacct gtctggtgaa gggcttctac 1140

cccagcgata tcgccgtgga gtgggagagc aacggccagc ccgagaacaa ctacaagacc 1200

acccccccag tgctggacag cgacggcagc ttcttcctgt acagcaagct gaccgtggac 1260

aagtccaggt ggcagcaggg caacgtgttc agctgcagcg tgatgcacga ggccctgcac 1320

aaccactaca cccagaagtc cctgagcctg agccccggca ag 1362

<210> 229
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 229
Asp Thr Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asn Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 230
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 230
gacactgtgc tgacccaatc tccagcctct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggta atagttatat gaactggtac 120

caacagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 180

gggatcccag ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggagg aggaggatgc tgcaacctat tactgtcagc aaagtaatga ggatcctccg 300

acgttcggtg gaggcaccaa gctggaaatc aaa 333

<210> 231
<211> 218
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 231

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Asp Thr Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1               5                  10                  15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
            20                  25                  30

Gly Asn Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65                  70                  75                  80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175
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Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 232
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 232
gacactgtgc tgacccaatc tccagcctct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggta atagttatat gaactggtac 120

caacagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 180

gggatcccag ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggagg aggaggatgc tgcaacctat tactgtcagc aaagtaatga ggatcctccg 300

acgttcggtg gaggcaccaa gctggaaatc aaacgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agtggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 233

<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 233
Glu Val Gln Leu Gln Gln Phe Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
100 105 110

Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 234
<211> 375
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 234
gaggtccaac tgcaacagtt tggagctgaa ctggtgaagc ctggggcttc agtgaagata 60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggagat attaatccta agtatgatat ttctacctac 180

aatcagcaat tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggagctcc gcagcctgac atctgaggac actgcagtct attattgtgc aagaagaggc 300

ttttttcttt actacggtat taactactat tacttcgatg tctggggcgc agggaccacg 360

gtcaccgtct cctca 375

<210> 235
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 235
Glu Val Gln Leu Gln Gln Phe Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

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

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr

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65                  70                  75                  80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
            100                 105                 110

Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
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            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445

Leu Ser Leu Ser Pro Gly Lys
```

450 455

<210> 236
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 236
gaggtccaac tgcaacagtt tggagctgaa ctggtgaagc ctggggcttc agtgaagata 60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggagat attaatccta agtatgatat ttctacctac 180

aatcagcaat tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggagctcc gcagcctgac atctgaggac actgcagtct attattgtgc aagaagaggc 300

ttttttcttt actacggtat taactactat tacttcgatg tctggggcgc agggaccacg 360

gtcaccgtct cctcagctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc 420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag 480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct 600

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccca agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

<210> 237
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 237
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Thr Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 238
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 238
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctctagggga ggagatcacc 60

ctaacctgca gtgccagctc gagtgtaagt tacatacact ggtaccagca gaagtcaggc 120

acttctccca cactcttgat ttatagcaca tccaatctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtagttatc catggacgtt cggtggaggc 300

accaagctgg aaatcaaa 318

<210> 239
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 239
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Thr Leu Leu Ile Tyr

35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 240

<211> 639
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 240
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctctagggga ggagatcacc 60

ctaacctgca gtgccagctc gagtgtaagt tacatacact ggtaccagca gaagtcaggc 120

acttctccca cactcttgat ttatagcaca tccaatctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtagttatc catggacgtt cggtggaggc 300

accaagctgg aaatcaaacg tacggtggcc gctcccagcg tgttcatctt cccccccagc 360

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 241
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 241
Asp 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 Tyr Ser Ile Thr Ser Gly
20 25 30

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

Met Gly Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu
50 55 60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

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

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Ser Gly Ser Tyr
100 105 110

Tyr Tyr Val Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
115 120 125

Ser

<210> 242
<211> 387
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 242
gatatacagc ttcaggagtc aggacctggc ctcgtgaaac cttctcagtc tctgtctctc 60

acctgctctg tcactggcta ctccatcacc agtggttatt actggaactg gatccggcag 120

tttccaggaa acaaactgga atggatgggc tacataagct acgacggtga caataactac 180

aacccatctc tcaaaaatcg aatctccatc actcgtgaca catctaagaa ccagtttttc 240

ctgaagttga gttctgtgac tactgaggac acagctacat attactgtgc aggaggctac 300

tataggtacg gcctgggctc ctactccggc tcgtattact atgttatgga ctactggggt 360

caaggaacct cagtcaccgt ctcctca 387

<210> 243
<211> 459
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 243
Asp 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 Tyr Ser Ile Thr Ser Gly
20 25 30

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

Met Gly Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu
50 55 60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

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

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Gly Ser Tyr Ser Gly Ser Tyr
100 105 110

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Tyr Tyr Val Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
        115                 120                 125


Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
    130                 135                 140


Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
145                 150                 155                 160


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


Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
            180                 185                 190


Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
        195                 200                 205


Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
    210                 215                 220


Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
225                 230                 235                 240


Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
                245                 250                 255


Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
            260                 265                 270


Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
        275                 280                 285


Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
    290                 295                 300
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Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305                 310                 315                 320


Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
                325                 330                 335


Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
            340                 345                 350


Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
        355                 360                 365


Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
    370                 375                 380


Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385                 390                 395                 400


Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
                405                 410                 415


Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
            420                 425                 430


Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
        435                 440                 445


Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210> 244
<211> 1377
<212> DNA
<213> Artificial Sequence

<220>
<221> source
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<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 244
gatatacagc ttcaggagtc aggacctggc ctcgtgaaac cttctcagtc tctgtctctc 60

acctgctctg tcactggcta ctccatcacc agtggttatt actggaactg gatccggcag 120

tttccaggaa acaaactgga atggatgggc tacataagct acgacggtga caataactac 180

aacccatctc tcaaaaatcg aatctccatc actcgtgaca catctaagaa ccagtttttc 240

ctgaagttga gttctgtgac tactgaggac acagctacat attactgtgc aggaggctac 300

tataggtacg gcctgggctc ctactccggc tcgtattact atgttatgga ctactggggt 360

caaggaacct cagtcaccgt ctcctcagct agcaccaagg gcccaagtgt gtttcccctg 420

gcccccagca gcaagtctac ttccggcgga actgctgccc tgggttgcct ggtgaaggac 480

tacttccccg agcccgtgac agtgtcctgg aactctgggg ctctgacttc cggcgtgcac 540

accttccccg ccgtgctgca gagcagcggc ctgtacagcc tgagcagcgt ggtgacagtg 600

ccctccagct ctctgggaac ccagacctat atctgcaacg tgaaccacaa gcccagcaac 660

accaaggtgg acaagagagt ggagcccaag agctgcgaca agacccacac ctgccccccc 720

tgcccagctc cagaactgct gggagggcct tccgtgttcc tgttcccccc caagcccaag 780

gacaccctga tgatcagcag gaccccgag gtgacctgcg tggtggtgga cgtgtcccac 840

gaggacccag aggtgaagtt caactggtac gtggacggcg tggaggtgca caacgccaag 900

accaagccca gagaggagca gtacaacagc acctacaggg tggtgtccgt gctgaccgtg 960

ctgcaccagg actggctgaa cggcaaagaa tacaagtgca aagtctccaa caaggccctg 1020

ccagccccaa tcgaaaagac aatcagcaag gccaagggcc agccacggga gccccaggtg 1080

tacaccctgc cccccagccg ggaggagatg accaagaacc aggtgtccct gacctgtctg 1140

gtgaagggct tctaccccag cgatatcgcc gtggagtggg agagcaacgg ccagcccgag 1200

aacaactaca agaccacccc cccagtgctg gacagcgacg gcagcttctt cctgtacagc 1260

aagctgaccg tggacaagtc caggtggcag cagggcaacg tgttcagctg cagcgtgatg 1320

cacgaggccc tgcacaacca ctacacccag aagtccctga gcctgagccc cggcaag 1377

<210> 245
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 245
Asp Ile Asn Pro Asn Tyr Asp Ile Thr Thr Tyr Asn Gln Arg Phe Lys
1 5 10 15

Gly

<210> 246
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 246
Arg Gly Phe Phe Pro Tyr Tyr Gly Asn Ser Tyr Tyr Tyr Phe Asp Val
1 5 10 15

<210> 247
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 247

Asn Pro Asn Tyr Asp Ile
1 5

<210> 248
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 248
Ile Asn Pro Asn Tyr Asp Ile Thr
1 5

<210> 249
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 249
Ala Arg Arg Gly Phe Phe Pro Tyr Tyr Gly Asn Ser Tyr Tyr Tyr Phe
1 5 10 15

Asp Val

<210> 250
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 250
Glu Val Gln Leu Gln Gln Phe Gly Ala Glu Leu Val Lys Pro Gly Thr
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

Gly Asp Ile Asn Pro Asn Tyr Asp Ile Thr Thr Tyr Asn Gln Arg Phe
50 55 60

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Phe Phe Pro Tyr Tyr Gly Asn Ser Tyr Tyr Tyr Phe
100 105 110

Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 251
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 251
gaggtccagc tgcaacagtt tggagctgag ctggtgaagc ctgggacttc agtgaagata 60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggagat attaatccta actatgatat tactacctac 180

aaccagaggt tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggagctcc gcagcctgac atctgaggac actgcagtct attactgtgc aagaagagga 300

ttttttcctt attacggtaa tagctactat tacttcgatg tctggggcgc agggaccacg 360

gtcaccgtct cctca 375

<210> 252
<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 252
Glu Val Gln Leu Gln Gln Phe Gly Ala Glu Leu Val Lys Pro Gly Thr
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

Gly Asp Ile Asn Pro Asn Tyr Asp Ile Thr Thr Tyr Asn Gln Arg Phe
50 55 60

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Phe Phe Pro Tyr Tyr Gly Asn Ser Tyr Tyr Tyr Phe
100 105 110

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Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300
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Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445

Leu Ser Leu Ser Pro Gly Lys
    450                 455
```

<210> 253
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 253
gaggtccagc tgcaacagtt tggagctgag ctggtgaagc ctgggacttc agtgaagata 60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggagat attaatccta actatgatat tactacctac 180

aaccagaggt tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggagctcc gcagcctgac atctgaggac actgcagtct attactgtgc aagaagagga 300

ttttttcctt attacggtaa tagctactat tacttcgatg tctggggcgc agggaccacg 360

gtcaccgtct cctcagctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc 420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag 480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct 600

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccca agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

<210> 254
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 254
Ser Ala Ser Ser Ser Val Ser Tyr Met His
1 5 10

<210> 255
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 255
His Gln Trp Ser Asn Tyr Pro Trp Thr
1 5

<210> 256
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 256
Trp Ser Asn Tyr Pro Trp
1 5

<210> 257
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 257
Gln Ile Val Leu Thr Gln Ser Pro Thr Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Asn Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 258
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 258
caaattgttc tcacccagtc tccaacaatc atgtctgcat ctctagggga ggagatcacc 60

cttacctgca gtgccagctc gagtgtaagt tacatgcact ggtaccagca gaagtcaggc 120

acttctccca aactcttgat ttatagcaca tccaacctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtaattatc catggacgtt cggtggaggc 300

accaagctgg aaatcaaa 318

<210> 259
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 259
Gln Ile Val Leu Thr Gln Ser Pro Thr Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Asn Tyr Pro Trp Thr

85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 260
<211> 639
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 260
caaattgttc tcacccagtc tccaacaatc atgtctgcat ctctagggga ggagatcacc 60

cttacctgca gtgccagctc gagtgtaagt tacatgcact ggtaccagca gaagtcaggc 120

acttctccca aactcttgat ttatagcaca tccaacctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtaattatc catggacgtt cggtggaggc 300

accaagctgg aaatcaaacg tacggtggcc gctcccagcg tgttcatctt cccccccagc 360

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 261
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 261
Asp Ile Asn Pro Asn Tyr Asp Ile Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 262
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 262
Arg Gly Phe Phe Leu Tyr Tyr Gly Ser Ser Tyr Tyr Tyr Phe Asp Val
1 5 10 15

<210> 263
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 263
Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ser Ser Tyr Tyr Tyr Phe
1 5 10 15

Asp Val

<210> 264
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 264
Glu Val Gln Leu Gln Gln Phe Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ser Ser Tyr Tyr Tyr Phe
100 105 110

Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 265
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 265
gaggtccagc tgcaacagtt tggagctgag ctggtgaagc ctggggcttc agtgaagata 60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggagat attaatccta actatgatat tactagctac 180

aaccagaagt tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggagctcc gcagcctgac atctgaggac actgcagtct attactgtgc aagaagaggg 300

ttttttcttt actacggtag tagctactat tacttcgatg tctggggcgc agggaccacg 360

gtcaccgtct cctca 375

<210> 266

<211> 455
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 266

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


Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35                  40                  45


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


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


Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ser Ser Tyr Tyr Tyr Phe
            100                 105                 110


Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125


Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140


Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160
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```
Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225                 230                 235                 240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350
```

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
355 360 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
370 375 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385 390 395 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
405 410 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
420 425 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
435 440 445

Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 267
<211> 1365
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 267
gaggtccagc tgcaacagtt tggagctgag ctggtgaagc ctggggcttc agtgaagata 60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggagat attaatccta actatgatat tactagctac 180

aaccagaagt tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggagctcc gcagcctgac atctgaggac actgcagtct attactgtgc aagaagaggg 300

ttttttcttt actacggtag tagctactat tacttcgatg tctggggcgc agggaccacg 360

gtcaccgtct cctcagctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc 420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag 480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct 600

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgcgacaag acccacacct gccccccctg cccagctcca 720

gaactgctgg gagggccttc cgtgttcctg ttcccccca agcccaagga caccctgatg 780

atcagcagga cccccgaggt gacctgcgtg gtggtggacg tgtcccacga ggacccagag 840

gtgaagttca actggtacgt ggacggcgtg gaggtgcaca acgccaagac caagcccaga 900

gaggagcagt acaacagcac ctacagggtg gtgtccgtgc tgaccgtgct gcaccaggac 960

tggctgaacg gcaaagaata caagtgcaaa gtctccaaca aggccctgcc agccccaatc 1020

gaaaagacaa tcagcaaggc caagggccag ccacgggagc cccaggtgta caccctgccc 1080

cccagccggg aggagatgac caagaaccag gtgtccctga cctgtctggt gaagggcttc 1140

taccccagcg atatcgccgt ggagtgggag agcaacggcc agcccgagaa caactacaag 1200

accacccccc cagtgctgga cagcgacggc agcttcttcc tgtacagcaa gctgaccgtg 1260

gacaagtcca ggtggcagca gggcaacgtg ttcagctgca gcgtgatgca cgaggccctg 1320

cacaaccact acacccagaa gtccctgagc ctgagccccg gcaag 1365

<210> 268
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 268
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 269
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 269
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctctagggga ggagatcacc 60

ctaacctgca gtgccagctc gagtgtaagt tacatgcact ggtaccagca gaagtcaggc 120

acttctccca aactcttgat ttatagcaca tccaacctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtagttatc catggacgtt cggtggaggc 300

accaagctgg aaatcaaa 318

<210> 270
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 270
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

```
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140


Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160


Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175


Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190


Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205


Asn Arg Gly Glu Cys
    210


<210> 271
<211> 639
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 271
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctctagggga ggagatcacc       60

ctaacctgca gtgccagctc gagtgtaagt tacatgcact ggtaccagca gaagtcaggc      120

acttctccca aactcttgat ttatagcaca tccaacctgg cttctggagt cccttctcgc      180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa     240

gatgctgccg attattactg ccatcagtgg agtagttatc catggacgtt cggtggaggc      300

accaagctgg aaatcaaacg tacggtggcc gctcccagcg tgttcatctt cccccccagc      360
```

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 272
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 272
Glu Tyr Thr Met His
1 5

<210> 273
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 273
Gly Ile Asn Pro Asn Asn Gly Ile Thr Thr Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 274
<211> 17

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 274
Arg Gly Phe Pro Ile Tyr Tyr Tyr Gly Thr Ser Leu Tyr Tyr Phe Asp
1 5 10 15

Tyr

<210> 275
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 275
Gly Tyr Thr Phe Thr Glu Tyr
1 5

<210> 276
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 276
Asn Pro Asn Asn Gly Ile
1 5

<210> 277

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 277
Gly Tyr Thr Phe Thr Glu Tyr Thr Met His
1 5 10

<210> 278
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 278
Gly Tyr Thr Phe Thr Glu Tyr Thr
1 5

<210> 279
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 279
Ile Asn Pro Asn Asn Gly Ile Thr
1 5

<210> 280
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 280
Ala Arg Arg Gly Phe Pro Ile Tyr Tyr Tyr Gly Thr Ser Leu Tyr Tyr
1   5   10   15

Phe Asp Tyr

<210> 281
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 281
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Glu Tyr
            20   25   30

Thr Met His Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35   40   45

Gly Gly Ile Asn Pro Asn Asn Gly Ile Thr Thr Tyr Asn Gln Lys Phe
    50   55   60

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

Met Asp Leu Arg Ser Leu Thr Ser Glu Gly Ser Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Arg Gly Phe Pro Ile Tyr Tyr Tyr Gly Thr Ser Leu Tyr Tyr
100 105 110

Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
115 120 125

<210> 282
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 282
gaggtccagc tgcaacagtc tggacctgag ctggtgaagc ctggggcttc agtgaagata 60

tcctgcaaga cttctggata cacattcact gaatacacca tgcactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggaggt attaatccta acaatggtat tactacttac 180

aaccagaagt tcaagggcaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggacctcc gcagcctgac atctgagggt tctgcagtct attactgtgc aagaagggga 300

ttccctattt attactacgg tactagcctc tactactttg actactgggg ccaaggcacc 360

actctcacag tctcctca 378

<210> 283
<211> 456
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 283
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala

```
1               5                   10                  15

Ser Val Lys Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Glu Tyr
            20                  25                  30

Thr Met His Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35                  40                  45

Gly Gly Ile Asn Pro Asn Asn Gly Ile Thr Thr Tyr Asn Gln Lys Phe
    50                  55                  60

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

Met Asp Leu Arg Ser Leu Thr Ser Glu Gly Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Phe Pro Ile Tyr Tyr Tyr Gly Thr Ser Leu Tyr Tyr
            100                 105                 110

Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Ala Ser
        115                 120                 125

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
    130                 135                 140

Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
```

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        195                 200                 205

Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val
    210                 215                 220

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225                 230                 235                 240

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
                245                 250                 255

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            260                 265                 270

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
        275                 280                 285

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    290                 295                 300

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
305                 310                 315                 320

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
                325                 330                 335

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
            340                 345                 350

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
        355                 360                 365

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    370                 375                 380

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
```

385 390 395 400

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
405 410 415

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
420 425 430

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
435 440 445

Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 284
<211> 1368
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 284
gaggtccagc tgcaacagtc tggacctgag ctggtgaagc ctggggcttc agtgaagata 60

tcctgcaaga cttctggata cacattcact gaatacacca tgcactgggt gaagcagagc 120

catggaaaga gccttgagtg gattggaggt attaatccta acaatggtat tactacttac 180

aaccagaagt tcaagggcaa ggccacattg actgtagaca agtcctccag cacagcctac 240

atggacctcc gcagcctgac atctgagggt tctgcagtct attactgtgc aagaagggga 300

ttccctattt attactacgg tactagcctc tactactttg actactgggg ccaaggcacc 360

actctcacag tctcctcagc tagcaccaag ggcccaagtg tgtttccct ggcccccagc 420

agcaagtcta cttccggcgg aactgctgcc ctgggttgcc tggtgaagga ctacttcccc 480

gagcccgtga cagtgtcctg gaactctggg gctctgactt ccggcgtgca caccttcccc 540

gccgtgctgc agagcagcgg cctgtacagc ctgagcagcg tggtgacagt gccctccagc 600

tctctgggaa cccagaccta tatctgcaac gtgaaccaca agcccagcaa caccaaggtg 660

gacaagagag tggagcccaa gagctgcgac aagacccaca cctgcccccc ctgcccagct 720

ccagaactgc tgggagggcc ttccgtgttc ctgttccccc ccaagcccaa ggacaccctg 780

atgatcagca ggacccccga ggtgacctgc gtggtggtgg acgtgtccca cgaggaccca 840

gaggtgaagt tcaactggta cgtggacggc gtggaggtgc acaacgccaa gaccaagccc 900

agagaggagc agtacaacag cacctacagg gtggtgtccg tgctgaccgt gctgcaccag 960

gactggctga acggcaaaga atacaagtgc aaagtctcca acaaggccct gccagcccca 1020

atcgaaaaga caatcagcaa ggccaagggc cagccacggg agccccaggt gtacaccctg 1080

ccccccagcc gggaggagat gaccaagaac caggtgtccc tgacctgtct ggtgaagggc 1140

ttctacccca gcgatatcgc cgtggagtgg gagagcaacg gccagcccga gaacaactac 1200

aagaccaccc ccccagtgct ggacagcgac ggcagcttct tcctgtacag caagctgacc 1260

gtggacaagt ccaggtggca gcagggcaac gtgttcagct gcagcgtgat gcacgaggcc 1320

ctgcacaacc actacaccca gaagtccctg agcctgagcc ccggcaag 1368

<210> 285
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 285
Thr Thr Ser Asn Leu Ala Ser
1 5

<210> 286
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 286
Thr Thr Ser
1

<210> 287
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 287
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Arg Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 288
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 288
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctctagggga ggagatcacc 60

ctaacctgca gtgccagctc gagtgtaagt tacatgcact ggtaccagca gaggtcaggc 120

acttctccca aactcttgat ttataccaca tccaacctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtagttatc cgtggacgtt cggtggaggc 300

accaagctgg aaatcaaa 318

<210> 289
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 289
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Arg Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

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Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65                  70                  75                  80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
                85                  90                  95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205

Asn Arg Gly Glu Cys
    210
```

<210> 290
<211> 639
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 290
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctctagggga ggagatcacc 60

ctaacctgca gtgccagctc gagtgtaagt tacatgcact ggtaccagca gaggtcaggc 120

acttctccca aactcttgat ttataccaca tccaacctgg cttctggagt cccttctcgc 180

ttcagtggca gtgggtctgg gacctttttat tctctcacaa tcagcagtgt ggaggctgaa 240

gatgctgccg attattactg ccatcagtgg agtagttatc cgtggacgtt cggtggaggc 300

accaagctgg aaatcaaacg tacggtggcc gctcccagcg tgttcatctt ccccccccagc 360

gacgagcagc tgaagagtgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtcaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 540

agcaaggccg actacgagaa gcataaggtg tacgcctgcg aggtgaccca ccagggcctg 600

tccagccccg tgaccaagag cttcaacagg ggcgagtgc 639

<210> 291
<211> 495
<212> PRT
<213> Homo sapiens

<400> 291
Met Ala Gly Lys Val Arg Ser Leu Leu Pro Pro Leu Leu Leu Ala Ala
1 5 10 15

Ala Gly Leu Ala Gly Leu Leu Leu Leu Cys Val Pro Thr Arg Asp Val
20 25 30

Arg Glu Pro Pro Ala Leu Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser
35 40 45

```
Ser His Thr Ser Met Phe Ile Tyr Lys Trp Pro Ala Asp Lys Glu Asn
    50                  55                  60

Asp Thr Gly Ile Val Gly Gln His Ser Ser Cys Asp Val Pro Gly Gly
65                  70                  75                  80

Gly Ile Ser Ser Tyr Ala Asp Asn Pro Ser Gly Ala Ser Gln Ser Leu
                85                  90                  95

Val Gly Cys Leu Glu Gln Ala Leu Gln Asp Val Pro Lys Glu Arg His
            100                 105                 110

Ala Gly Thr Pro Leu Tyr Leu Gly Ala Thr Ala Gly Met Arg Leu Leu
        115                 120                 125

Asn Leu Thr Asn Pro Glu Ala Ser Thr Ser Val Leu Met Ala Val Thr
    130                 135                 140

His Thr Leu Thr Gln Tyr Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu
145                 150                 155                 160

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

Leu Glu Asn Phe Ile Lys Tyr Gly Trp Val Gly Arg Trp Phe Arg Pro
            180                 185                 190

Arg Lys Gly Thr Leu Gly Ala Met Asp Leu Gly Gly Ala Ser Thr Gln
        195                 200                 205

Ile Thr Phe Glu Thr Thr Ser Pro Ala Glu Asp Arg Ala Ser Glu Val
    210                 215                 220

Gln Leu His Leu Tyr Gly Gln His Tyr Arg Val Tyr Thr His Ser Phe
225                 230                 235                 240
```

```
Leu Cys Tyr Gly Arg Asp Gln Val Leu Gln Arg Leu Leu Ala Ser Ala
                245                 250                 255

Leu Gln Thr His Gly Phe His Pro Cys Trp Pro Arg Gly Phe Ser Thr
            260                 265                 270

Gln Val Leu Leu Gly Asp Val Tyr Gln Ser Pro Cys Thr Met Ala Gln
        275                 280                 285

Arg Pro Gln Asn Phe Asn Ser Ser Ala Arg Val Ser Leu Ser Gly Ser
    290                 295                 300

Ser Asp Pro His Leu Cys Arg Asp Leu Val Ser Gly Leu Phe Ser Phe
305                 310                 315                 320

Ser Ser Cys Pro Phe Ser Arg Cys Ser Phe Asn Gly Val Phe Gln Pro
                325                 330                 335

Pro Val Ala Gly Asn Phe Val Ala Phe Ser Ala Phe Phe Tyr Thr Val
            340                 345                 350

Asp Phe Leu Arg Thr Ser Met Gly Leu Pro Val Ala Thr Leu Gln Gln
        355                 360                 365

Leu Glu Ala Ala Ala Val Asn Val Cys Asn Gln Thr Trp Ala Gln Leu
    370                 375                 380

Gln Ala Arg Val Pro Gly Gln Arg Ala Arg Leu Ala Asp Tyr Cys Ala
385                 390                 395                 400

Gly Ala Met Phe Val Gln Gln Leu Leu Ser Arg Gly Tyr Gly Phe Asp
                405                 410                 415

Glu Arg Ala Phe Gly Gly Val Ile Phe Gln Lys Lys Ala Ala Asp Thr
            420                 425                 430
```

```
Ala Val Gly Trp Ala Leu Gly Tyr Met Leu Asn Leu Thr Asn Leu Ile
        435                 440                 445


Pro Ala Asp Pro Pro Gly Leu Arg Lys Gly Thr Asp Phe Ser Ser Trp
    450                 455                 460


Val Val Leu Leu Leu Leu Phe Ala Ser Ala Leu Leu Ala Ala Leu Val
465                 470                 475                 480


Leu Leu Leu Arg Gln Val His Ser Ala Lys Leu Pro Ser Thr Ile
                485                 490                 495


<210> 292
<211> 2156
<212> DNA
<213> Homo sapiens

<400> 292
ggctccccgc actctccggg tccacgcatc gtcctcccgc gcgcccgccc gcccatggcc       60

gggaaggtgc ggtcactgct gccgccgctg ctgctggccg ccgcgggcct cgccggcctc      120

ctactgctgt gcgtccccac ccgcgacgtc cgggagccgc ccgccctcaa gtatggcatc      180

gtcctggacg ctggttcttc acacacgtcc atgtttatct acaagtggcc ggcagacaag      240

gagaacgaca caggcattgt gggccagcac agctcctgtg atgttccagg tgggggcatc      300

tccagctatg cagacaaccc ttctggggcc agccagagtc ttgttggatg cctcgaacag      360

gcgcttcagg atgtgcccaa agagagacac gcgggcacac ccctctacct gggagccaca      420

gcgggtatgc gcctgctcaa cctgaccaat ccagaggcct cgaccagtgt gctcatggca      480

gtgactcaca cactgaccca gtaccccttt gacttccggg gtgcacgcat cctctcgggc      540

caggaagagg gggtgtttgg ctgggtgact gccaactacc tgctggagaa cttcatcaag      600

tacggctggg tgggccggtg gttccggcca cggaagggga cactgggggc catggacctg      660

gggggtgcct ctacccagat cacttttgag acaaccagtc cagctgagga cagagccagc      720

gaggtccagc tgcatctcta cggccagcac taccgagtct acacccacag cttcctctgc      780
```

tatggccgtg accaggtcct ccagaggctg ctggccagcg ccctccagac ccacggcttc 840

caccctgct ggccgagggg cttttccacc caagtgctgc tcggggatgt gtaccagtca 900

ccatgcacca tggcccagcg gccccagaac ttcaacagca gtgccagggt cagcctgtca 960

gggagcagtg acccccacct ctgccgagat ctggtttctg ggctcttcag cttctcctcc 1020

tgccccttct cccgatgctc tttcaatggg gtcttccagc ccccagtggc tgggaacttt 1080

gtggccttct ctgccttctt ctacactgtg gacttttgc ggacttcgat ggggctgccc 1140

gtggccaccc tgcagcagct ggaggcagcc gcagtgaatg tctgcaacca gacctgggct 1200

cagctgcaag ctcgggtgcc agggcaacgg gcccgcctgg ccgactactg cgccggggcc 1260

atgttcgtgc agcagctgct gagtcgcggc tacggcttcg acgagcgcgc cttcggcggc 1320

gtgatcttcc agaagaaggc cgcggacact gcagtgggct gggcgctcgg ctacatgctg 1380

aacctgacca acctgatccc cgccgacccg ccggggctgc gcaagggcac agacttcagc 1440

tcctgggtcg tcctcctgct gctcttcgcc tccgcgctcc tggctgcgct tgtcctgctg 1500

ctgcgtcagg tgcactccgc caagctgcca agcaccattt aggggccgac gggggcagct 1560

gccccatccc tcccccaacc cctgtatccc caccccgtac tcccaccct cccacaaccc 1620

ctgtacctcc caccctgta tccccacccc tccacccacc cctctcccaa cctctctccc 1680

cgcccctgta tcctgcattc ctccacccac cctctatccc ccaccgctcc accccaccac 1740

tgtcttctcc atccttccac cccaccctca gcgtctctgc ccctaaggca gcccaggaaa 1800

taggaactga gactctggta cccacaggag cctgggtggg caaagagcgc tcaatccagc 1860

tccttgaacc cctccagccc gcttcagcct gggcatcact gcaggccccg tgctcctcct 1920

cctcctcctc agggctgggt ctccagagag tggggccttg gtcctgagaa tcagccctta 1980

gaggctcctt ctgtgtagtc tgggtctgta ctggggaggg tcacagccca cgggctggca 2040

gccagcccag cacctacttg taaaaatttt gtaataaaaa gtttttccta gagacgtgaa 2100

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 2156

<210> 293
<211> 472
<212> PRT
<213> Homo sapiens

<400> 293

```
Met Ala Gly Lys Val Arg Ser Leu Leu Pro Pro Leu Leu Leu Ala Ala
1               5                  10                  15

Ala Gly Leu Ala Gly Leu Leu Leu Leu Cys Val Pro Thr Arg Asp Val
            20                  25                  30

Arg Glu Pro Pro Ala Leu Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser
        35                  40                  45

Ser His Thr Ser Met Phe Ile Tyr Lys Trp Pro Ala Asp Lys Glu Asn
    50                  55                  60

Asp Thr Gly Ile Val Gly Gln His Ser Ser Cys Asp Val Pro Gly Gly
65                  70                  75                  80

Gly Ile Ser Ser Tyr Ala Asp Asn Pro Ser Gly Ala Ser Gln Ser Leu
                85                  90                  95

Val Gly Cys Leu Glu Gln Ala Leu Gln Asp Val Pro Lys Glu Arg His
            100                 105                 110

Ala Gly Thr Pro Leu Tyr Leu Gly Ala Thr Ala Gly Met Arg Leu Leu
        115                 120                 125

Asn Leu Thr Asn Pro Glu Ala Ser Thr Ser Val Leu Met Ala Val Thr
    130                 135                 140

His Thr Leu Thr Gln Tyr Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu
145                 150                 155                 160

Ser Gly Gln Glu Glu Gly Val Phe Gly Trp Val Thr Ala Asn Tyr Leu
                165                 170                 175
```

```
Leu Glu Asn Phe Ile Lys Tyr Gly Trp Val Gly Arg Trp Phe Arg Pro
            180                 185                 190

Arg Lys Gly Thr Leu Gly Ala Met Asp Leu Gly Gly Ala Ser Thr Gln
        195                 200                 205

Ile Thr Phe Glu Thr Thr Ser Pro Ala Glu Asp Arg Ala Ser Glu Val
    210                 215                 220

Gln Leu His Leu Tyr Gly Gln His Tyr Arg Val Tyr Thr His Ser Phe
225                 230                 235                 240

Leu Cys Tyr Gly Arg Asp Gln Val Leu Gln Arg Leu Leu Ala Ser Ala
                245                 250                 255

Leu Gln Thr His Gly Phe His Pro Cys Trp Pro Arg Gly Phe Ser Thr
            260                 265                 270

Gln Val Leu Leu Gly Asp Val Tyr Gln Ser Pro Cys Thr Met Ala Gln
        275                 280                 285

Arg Pro Gln Asn Phe Asn Ser Ser Ala Arg Val Ser Leu Ser Gly Ser
    290                 295                 300

Ser Asp Pro His Leu Cys Arg Asp Leu Val Ser Gly Leu Phe Ser Phe
305                 310                 315                 320

Ser Ser Cys Pro Phe Ser Arg Cys Ser Phe Asn Gly Val Phe Gln Pro
                325                 330                 335

Pro Val Ala Gly Asn Phe Val Ala Phe Ser Ala Phe Phe Tyr Thr Val
            340                 345                 350

Asp Phe Leu Arg Thr Ser Met Gly Leu Pro Val Ala Thr Leu Gln Gln
        355                 360                 365
```

```
Leu Glu Ala Ala Ala Val Asn Val Cys Asn Gln Thr Trp Ala Gln Gln
    370                 375                 380

Leu Leu Ser Arg Gly Tyr Gly Phe Asp Glu Arg Ala Phe Gly Gly Val
385                 390                 395                 400

Ile Phe Gln Lys Lys Ala Ala Asp Thr Ala Val Gly Trp Ala Leu Gly
                405                 410                 415

Tyr Met Leu Asn Leu Thr Asn Leu Ile Pro Ala Asp Pro Pro Gly Leu
            420                 425                 430

Arg Lys Gly Thr Asp Phe Ser Ser Trp Val Val Leu Leu Leu Leu Phe
        435                 440                 445

Ala Ser Ala Leu Leu Ala Ala Leu Val Leu Leu Leu Arg Gln Val His
    450                 455                 460

Ser Ala Lys Leu Pro Ser Thr Ile
465                 470
```

<210> 294
<211> 2087
<212> DNA
<213> Homo sapiens

<400> 294
ggctccccgc actctccggg tccacgcatc gtcctcccgc gcgcccgccc gcccatggcc 60

gggaaggtgc ggtcactgct gccgccgctg ctgctggccg ccgcgggcct cgccggcctc 120

ctactgctgt gcgtccccac ccgcgacgtc cgggagccgc ccgccctcaa gtatggcatc 180

gtcctggacg ctggttcttc acacacgtcc atgtttatct acaagtggcc ggcagacaag 240

gagaacgaca caggcattgt gggccagcac agctcctgtg atgttccagg tgggggcatc 300

tccagctatg cagacaaccc ttctggggcc agccagagtc ttgttggatg cctcgaacag 360

gcgcttcagg atgtgcccaa agagagacac gcgggcacac ccctctacct gggagccaca 420

gcgggtatgc gcctgctcaa cctgaccaat ccagaggcct cgaccagtgt gctcatggca 480

gtgactcaca cactgaccca gtaccccttt gacttccggg gtgcacgcat cctctcgggc 540

caggaagagg gggtgtttgg ctgggtgact gccaactacc tgctggagaa cttcatcaag 600

tacggctggg tgggccggtg gttccggcca cggaagggga cactgggggc catggacctg 660

gggggtgcct ctacccagat cacttttgag acaaccagtc cagctgagga cagagccagc 720

gaggtccagc tgcatctcta cggccagcac taccgagtct acacccacag cttcctctgc 780

tatggccgtg accaggtcct ccagaggctg ctggccagcg ccctccagac ccacggcttc 840

caccctgct ggccgagggg cttttccacc caagtgctgc tcggggatgt gtaccagtca 900

ccatgcacca tggcccagcg gccccagaac ttcaacagca gtgccagggt cagcctgtca 960

gggagcagtg acccccacct ctgccgagat ctggtttctg ggctcttcag cttctcctcc 1020

tgccccttct cccgatgctc tttcaatggg gtcttccagc ccccagtggc tgggaacttt 1080

gtggccttct ctgccttctt ctacactgtg gacttttgc ggacttcgat ggggctgccc 1140

gtggccaccc tgcagcagct ggaggcagcc gcagtgaatg tctgcaacca gacctgggct 1200

cagcagctgc tgagtcgcgg ctacggcttc gacgagcgcg ccttcggcgg cgtgatcttc 1260

cagaagaagg ccgcggacac tgcagtgggc tgggcgctcg gctacatgct gaacctgacc 1320

aacctgatcc ccgccgaccc gccggggctg cgcaagggca cagacttcag ctcctgggtc 1380

gtcctcctgc tgctcttcgc ctccgcgctc ctggctgcgc ttgtcctgct gctgcgtcag 1440

gtgcactccg ccaagctgcc aagcaccatt taggggccga cgggggcagc tgccccatcc 1500

ctcccccaac ccctgtatcc ccaccccgta ctcccacccc tcccacaacc cctgtacctc 1560

ccacccctgt atccccaccc ctccacccac ccctctccca acctctctcc ccgcccctgt 1620

atcctgcatt cctccaccca ccctctatcc cccaccgctc caccccacca ctgtcttctc 1680

catccttcca ccccaccctc agcgtctctg cccctaaggc agcccaggaa ataggaactg 1740

agactctggt acccacagga gcctgggtgg gcaaagagcg ctcaatccag ctccttgaac 1800

ccctccagcc cgcttcagcc tgggcatcac tgcaggcccc gtgctcctcc tcctcctcct 1860

cagggctggg tctccagaga gtggggcctt ggtcctgaga atcagccctt agaggctcct 1920

tctgtgtagt ctgggtctgt actggggagg gtcacagccc acgggctggc agccagccca 1980

gcacctactt gtaaaaattt tgtaataaaa agtttttcct agagacgtga aaaaaaaaaa 2040

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 2087

<210> 295
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 295
Glu Val 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 Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Tyr Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

Ala Arg Leu Gly Tyr Gly Arg Val Asp Glu Trp Gly Arg Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
        115

<210> 296
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 296
Gln Ser 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 Ser Leu Ser Asn Ile Gly Arg Asn
            20   25   30

Pro Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35   40   45

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

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

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp Ser His
                85   90   95

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

<210> 297
<211> 447
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 297
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

```
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys
    210                 215                 220

Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350
```

```
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365


Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380


Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser
385                 390                 395                 400


Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> 298
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 298
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
        35                  40                  45


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
```

```
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

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

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210


<210> 299
<211> 121
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 299
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 300
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 300
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 301
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 301
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
20 25 30

```
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

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

Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
```

<210> 302
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 302
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 303
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 303
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Gly Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

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

Ser Gly Pro Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp His Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 304
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 304
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Val Ile Leu Tyr Asp Gly Ser Asn Lys Tyr Tyr Pro Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


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


Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
            100                 105                 110


Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120


<210> 305
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 305
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30
```

```
Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
        35                  40                  45


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


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


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 306
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 306
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Val Ile Trp Tyr Asp Glu Ser Asn Lys Tyr Tyr Pro Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
```

65 70 75 80

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

Ala Arg Gly Gly Ser Ser Trp Tyr Pro Asp Ser Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 307
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 307
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 308
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 308
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

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

Val Arg Ser Gly Ser Tyr Asn Tyr Tyr Tyr Tyr Gly Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Arg
115 120

<210> 309
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 309
Gln Ser 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 Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

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

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

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

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

<210> 310
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 310
Gln Val 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 Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Leu Trp Glu Val Arg Ala Leu Pro Ser Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 311
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 311
Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

```
Thr Ala Arg Ile Thr Cys Gly Ala Asn Asp Ile Gly Ser Lys Ser Val
            20                  25                  30


His Trp Tyr Gln Gln Lys Ala Gly Gln Ala Pro Val Leu Val Val Ser
        35                  40                  45


Glu Asp Ile Ile Arg Pro Ser Gly Ile Pro Glu Arg Ile Ser Gly Ser
    50                  55                  60


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


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


Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
            100                 105


<210> 312
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 312
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu
            20                  25                  30


Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln
        35                  40                  45
```

```
Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr
    50                  55                  60

Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
                85                  90                  95

Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140

Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser
145                 150                 155                 160

Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
        195                 200                 205

Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys
    210                 215                 220

Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys
225                 230                 235                 240
```

```
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430
```

```
Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445


Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460


Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480


Gln Ala Leu Pro Pro Arg
                485


<210> 313
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 313
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1               5                   10                  15


Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45


Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80
```

```
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270
```

```
Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
    290                 295                 300

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
305                 310                 315                 320

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
                325                 330                 335

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
            340                 345                 350

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
        355                 360                 365

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
    370                 375                 380

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
385                 390                 395                 400

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
                405                 410                 415

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
            420                 425                 430

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
        435                 440                 445

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
    450                 455                 460
```

Arg
465

<210> 314
<211> 449
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 314
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met Lys Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Met
35 40 45

Gly Asp Ile Ile Pro Ser Asn Gly Ala Thr Phe Tyr Asn Gln Lys Phe
50 55 60

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser His Leu Leu Arg Ala Ser Trp Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala

```
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
225                 230                 235                 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp
            260                 265                 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val
    290                 295                 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
```

325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 315
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 315
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
```

```
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
                245                 250                 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
            260                 265                 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385                 390                 395                 400
```

```
Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415


Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            420                 425                 430


Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
        435                 440                 445


Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    450                 455                 460


Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465                 470                 475                 480


Leu Ser Pro Gly Lys
                485


<210> 316
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 316
Asp Phe Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asn Thr
            20                  25                  30


Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
        35                  40                  45
```

```
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65                  70                  75                  80

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

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
            100                 105                 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140

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

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220
```

<210> 317
<211> 450
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 317
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
100 105 110

Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

```
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175


Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190


Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205


Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220


Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
225                 230                 235                 240


Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255


Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270


Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285


Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg
    290                 295                 300


Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320


Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335


Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350
```

```
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365


Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380


Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400


Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415


Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His
            420                 425                 430


Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445


Gly Lys
    450


<210> 318
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 318
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30


Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
```

```
        35                  40                  45

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
    50                  55                  60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65                  70                  75                  80

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
```

```
225                 230                 235                 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
                245                 250                 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
            260                 265                 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        275                 280                 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    290                 295                 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305                 310                 315                 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                325                 330                 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            340                 345                 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        355                 360                 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    370                 375                 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385                 390                 395                 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                405                 410                 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
```

420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 319
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 319
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Pro Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

```
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
                85                  90                  95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205

Asn Arg Gly Glu Cys
    210
```

<210> 320

<400> 320
000

<210> 321

<400> 321
000

<210> 322

<400> 322
000

<210> 323

<400> 323
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<210> 324

<400> 324
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<210> 325

<400> 325
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<210> 326

<400> 326
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<210> 327

<400> 327
000

<210> 328
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 328
Glu Val Lys Leu Glu Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Ser Ile Thr Ser Gly
            20 25 30

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

Met Ser Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu
    50 55 60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

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

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Ser Tyr Tyr Tyr Val Met Asp
            100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ala
        115 120

<210> 329
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 329
gaagtgaagc tggagcagtc aggacctggc ctcgtgaaac cttctcagtc tctgtctctc 60

acctgctctg tcactggcta ctccatcacc agtggttatt actggaactg gatccggcag 120

tttccaggaa acaaactgga atggatgagc tacataagct acgacggtga caataactac 180

aacccatctc tcaaaaatcg aatctccatc actcgtgaca catctaagaa ccagtttttc 240

ctgaagttga gttctgtgac tactgaggac acagctacat attactgtgc aggaggctac 300

tataggtacg gcctgtcgta ttactatgtt atggactact ggggtcaagg aacctcagtc 360

acagtctccg ca 372

<210> 330
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 330
Glu Val Lys Leu Glu Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Ser Ile Thr Ser Gly
20 25 30

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

Met Ser Tyr Ile Ser Tyr Asp Gly Asp Asn Asn Tyr Asn Pro Ser Leu
50 55 60

Lys Asn Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

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

Ala Gly Gly Tyr Tyr Arg Tyr Gly Leu Ser Tyr Tyr Tyr Val Met Asp
100 105 110

```
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ala Ala Ser Thr Lys
        115                 120                 125


Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
    130                 135                 140


Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145                 150                 155                 160


Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
                165                 170                 175


Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
            180                 185                 190


Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
        195                 200                 205


Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
    210                 215                 220


Lys Ser Cys
225


<210> 331
<211> 681
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 331
gaagtgaagc tggagcagtc aggacctggc ctcgtgaaac cttctcagtc tctgtctctc       60

acctgctctg tcactggcta ctccatcacc agtggttatt actggaactg gatccggcag      120
```

tttccaggaa acaaactgga atggatgagc tacataagct acgacggtga caataactac 180

aacccatctc tcaaaaatcg aatctccatc actcgtgaca catctaagaa ccagtttttc 240

ctgaagttga gttctgtgac tactgaggac acagctacat attactgtgc aggaggctac 300

tataggtacg gcctgtcgta ttactatgtt atggactact ggggtcaagg aacctcagtc 360

acagtctccg cagctagcac caagggccca agtgtgtttc ccctggcccc cagcagcaag 420

tctacttccg gcggaactgc tgccctgggt tgcctggtga aggactactt ccccgagccc 480

gtgacagtgt cctggaactc tggggctctg acttccggcg tgcacacctt ccccgccgtg 540

ctgcagagca gcggcctgta cagcctgagc agcgtggtga cagtgccctc cagctctctg 600

ggaacccaga cctatatctg caacgtgaac cacaagccca gcaacaccaa ggtggacaag 660

agagtggagc ccaagagctg c 681

<210> 332
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 332
Asp Ile Lys Met Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asn Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 333
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 333
gatattaaga tgacccaatc tccagcctct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggta atagttatat gaactggtac 120

caacagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 180

gggatcccag ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggagg aggaggatgc tgcaacctat tactgtcagc aaagtaatga ggatcctccg 300

acgttcggtg gaggcaccaa gctggaactc aaa 333

<210> 334
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 334

```
Asp Ile Lys Met Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1               5                  10                  15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
            20                  25                  30

Gly Asn Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65                  70                  75                  80

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

Glu Asp Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190
```

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 335
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 335
gatattaaga tgacccaatc tccagcctct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggta atagttatat gaactggtac 120

caacagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 180

gggatcccag ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggagg aggaggatgc tgcaacctat tactgtcagc aaagtaatga ggatcctccg 300

acgttcggtg gaggcaccaa gctggaactc aaacgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agtggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 336
<211> 228
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 336

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

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35                  40                  45

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

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Gly Phe Phe Leu Tyr Tyr Gly Ile Asn Tyr Tyr Tyr Phe
            100                 105                 110

Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
    130                 135                 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175
```

```
Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190


Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
        195                 200                 205


Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220


Pro Lys Ser Cys
225


<210> 337
<211> 684
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 337
gaggtccaac tgcaacagtt tggagctgaa ctggtgaagc ctggggcttc agtgaagata       60

tcctgcaagg cttctggcta cacattcact gactacaaca tggactgggt gaagcagagc      120

catggaaaga gccttgagtg gattggagat attaatccta agtatgatat ttctacctac      180

aatcagcaat tcaagggaaa ggccacattg actgtagaca agtcctccag cacagcctac      240

atggagctcc gcagcctgac atctgaggac actgcagtct attattgtgc aagaagaggc      300

ttttttcttt actacggtat taactactat tacttcgatg tctggggcgc agggaccacg      360

gtcaccgtct cctcagctag caccaagggc ccaagtgtgt ttcccctggc ccccagcagc      420

aagtctactt ccggcggaac tgctgccctg ggttgcctgg tgaaggacta cttccccgag      480

cccgtgacag tgtcctggaa ctctggggct ctgacttccg gcgtgcacac cttccccgcc      540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgacagtgcc ctccagctct      600
```

ctgggaaccc agacctatat ctgcaacgtg aaccacaagc ccagcaacac caaggtggac 660

aagagagtgg agcccaagag ctgc 684

<210> 338
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 338

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

```
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
    130                 135                 140


Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145                 150                 155                 160


Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
                165                 170                 175


Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
            180                 185                 190


Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
        195                 200                 205


Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
    210                 215                 220


Ser Cys
225


<210> 339
<211> 678
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 339
caggtccagc tggtgcagtc aggagctgag ctgaagcagc ctggacagtc ggtgaagatc       60

tcctgcaagg cttcagggta caccttcaca cactatggga tgaactgggt gaagcaggca      120

ccaggacagg gtctaaagtg gatgggctgg atcaacactg acactgggaa tccaacatat      180

gctgatgact tcaaaggacg gtttgtcttc tccttggaca cctctgtcag cactgcatat      240

ctgcagatca gcaacctcaa gaatgaagac acggccacgt attactgtgt gagatatgga      300
```

accctatata gcggatatgg gttttttttt gattcctggg gccaagggac cctggtcacc 360

gtctcctcag ctagcaccaa gggcccaagt gtgtttcccc tggcccccag cagcaagtct 420

acttccggcg gaactgctgc cctgggttgc ctggtgaagg actacttccc cgagcccgtg 480

acagtgtcct ggaactctgg ggctctgact tccggcgtgc acaccttccc cgccgtgctg 540

cagagcagcg gcctgtacag cctgagcagc gtggtgacag tgccctccag ctctctggga 600

acccagacct atatctgcaa cgtgaaccac aagcccagca acaccaaggt ggacaagaga 660

gtggagccca agagctgc 678

<210> 340
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 340
Asp Ile Met Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Lys Ala Thr Ile Thr Cys Lys Ser Ser Gln Ser Leu Phe Asn Ser
20 25 30

Asn Thr Asn Lys Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Phe Tyr Tyr Ala Ser Thr Arg His Thr Gly Val
50 55 60

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Thr Ser Val Gln Asp Glu Asp Leu Ala Asp Tyr Tyr Cys Gln Gln

85 90 95

Trp Tyr Ser Tyr Pro Trp Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile
100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

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

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
165 170 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 341
<211> 660
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 341
gacatcatga tgacccagtc tccatcatcc ctgagtgtgt cagcaggaga gaaagccact 60

atcacctgca agtccagtca gagtcttttc aacagtaaca ccaacaagaa ctacttgaac 120

tggtacctgc agaaaccagg gcagtctcct aaactgctgt tctattatgc atccactagg 180

catactgggg tccctgatcg cttcataggc agtggatctg ggacagattt cactctcacc 240

atcaccagtg tccaggatga agacctggca gattattact gtcagcagtg gtatagctac 300

ccgtggacgt tcggacctgg caccaagctg gaaatcaaac gtacggtggc cgctcccagc 360

gtgttcatct tccccccag cgacgagcag ctgaagagtg gcaccgccag cgtggtgtgc 420

ctgctgaaca acttctaccc ccgggaggcc aaggtgcagt ggaaggtgga caacgccctg 480

cagagcggca acagccagga gagcgtcacc gagcaggaca gcaaggactc cacctacagc 540

ctgagcagca ccctgaccct gagcaaggcc gactacgaga agcataaggt gtacgcctgc 600

gaggtgaccc accagggcct gtccagcccc gtgaccaaga gcttcaacag gggcgagtgc 660

<210> 342
<211> 1485
<212> DNA
<213> Homo sapiens

<400> 342
atggccggga aggtgcggtc actgctgccg ccgctgctgc tggccgccgc gggcctcgcc 60

ggcctcctac tgctgtgcgt ccccacccgc gacgtccggg agccgcccgc cctcaagtat 120

ggcatcgtcc tggacgctgg ttcttcacac acgtccatgt ttatctacaa gtggccggca 180

gacaaggaga acgacacagg cattgtgggc cagcacagct cctgtgatgt tccaggtggg 240

ggcatctcca gctatgcaga caacccttct ggggccagcc agagtcttgt tggatgcctc 300

gaacaggcgc ttcaggatgt gcccaaagag agacacgcgg gcacacccct ctacctggga 360

gccacagcgg gtatgcgcct gctcaacctg accaatccag aggcctcgac cagtgtgctc 420

atggcagtga ctcacacact gacccagtac ccctttgact tccggggtgc acgcatcctc 480

tcgggccagg aagagggggt gtttggctgg gtgactgcca actacctgct ggagaacttc 540

atcaagtacg gctgggtggg ccggtggttc cggccacgga aggggacact gggggccatg 600

gacctggggg gtgcctctac ccagatcact tttgagacaa ccagtccagc tgaggacaga 660

gccagcgagg tccagctgca tctctacggc cagcactacc gagtctacac ccacagcttc 720

ctctgctatg gccgtgacca ggtcctccag aggctgctgg ccagcgccct ccagacccac 780

ggcttccacc cctgctggcc gaggggcttt tccacccaag tgctgctcgg ggatgtgtac 840

cagtcaccat gcaccatggc ccagcggccc cagaacttca acagcagtgc cagggtcagc 900

ctgtcaggga gcagtgaccc ccacctctgc cgagatctgg tttctgggct cttcagcttc 960

tcctcctgcc ccttctcccg atgctctttc aatggggtct tccagccccc agtggctggg 1020

aactttgtgg ccttctctgc cttcttctac actgtggact ttttgcggac ttcgatgggg 1080

ctgcccgtgg ccaccctgca gcagctggag gcagccgcag tgaatgtctg caaccagacc 1140

tgggctcagc tgcaagctcg ggtgccaggg caacgggccc gcctggccga ctactgcgcc 1200

ggggccatgt tcgtgcagca gctgctgagt cgcggctacg gcttcgacga gcgcgccttc 1260

ggcggcgtga tcttccagaa gaaggccgcg gacactgcag tgggctgggc gctcggctac 1320

atgctgaacc tgaccaacct gatccccgcc gacccgccgg ggctgcgcaa gggcacagac 1380

ttcagctcct gggtcgtcct cctgctgctc ttcgcctccg cgctcctggc tgcgcttgtc 1440

ctgctgctgc gtcaggtgca ctccgccaag ctgccaagca ccatt 1485

<210> 343
<211> 495
<212> PRT
<213> Macaca fascicularis

<400> 343
Met Ala Gly Lys Val Arg Ser Leu Leu Pro Pro Leu Leu Leu Ala Ala
1 5 10 15

Ala Gly Leu Ala Gly Leu Leu Leu Leu Cys Val Pro Thr Arg Asp Ile
20 25 30

Arg Glu Pro Pro Ala Leu Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser
35 40 45

```
Ser His Thr Ser Met Phe Ile Tyr Lys Trp Pro Ala Asp Lys Glu Asn
    50                  55                  60

Asp Thr Gly Ile Val Gly Gln His Ser Ser Cys Asp Val Pro Gly Gly
65                  70                  75                  80

Gly Ile Ser Ser Tyr Ala Asp Asn Pro Ser Gly Ala Gly Gln Ser Leu
                85                  90                  95

Val Gly Cys Leu Glu Gln Ala Leu Arg Asp Val Pro Lys Glu Arg His
            100                 105                 110

Ala Gly Thr Pro Leu Tyr Leu Gly Ala Thr Ala Gly Met Arg Leu Leu
        115                 120                 125

Asn Leu Thr Asn Pro Glu Ala Ser Thr Ser Val Leu Thr Ala Val Thr
    130                 135                 140

His Thr Leu Thr Gln Tyr Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu
145                 150                 155                 160

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

Leu Glu Asn Phe Ile Lys Tyr Gly Trp Val Gly Arg Trp Phe Arg Pro
            180                 185                 190

Arg Lys Gly Thr Leu Gly Ala Met Asp Leu Gly Gly Ala Ser Thr Gln
        195                 200                 205

Ile Thr Phe Glu Thr Thr Ser Pro Ala Glu Asp Arg Ala Ser Glu Val
    210                 215                 220

Gln Leu Arg Leu Tyr Gly Gln His Tyr Arg Val Tyr Thr His Ser Phe
225                 230                 235                 240
```

```
Leu Cys Tyr Gly Arg Asp Gln Val Leu Gln Arg Leu Leu Ala Ser Ala
                245                 250                 255

Leu Gln Thr His Ser Phe His Pro Cys Trp Pro Arg Gly Phe Ser Thr
            260                 265                 270

His Val Leu Leu Gly Asp Val Tyr Gln Ser Pro Cys Thr Val Ala Gln
        275                 280                 285

Arg Pro Gln Thr Phe Asn Ser Ser Ala Arg Val Ser Leu Ser Gly Ser
    290                 295                 300

Ser Asp Pro His Leu Cys Arg Asp Leu Val Ser Gly Leu Phe Ser Phe
305                 310                 315                 320

Ser Ser Cys Pro Phe Ser Arg Cys Ser Phe Asn Gly Val Phe Gln Pro
                325                 330                 335

Pro Val Ala Gly Asn Phe Ile Ala Phe Ser Ala Phe Phe Tyr Thr Val
            340                 345                 350

Asn Phe Leu Arg Thr Ser Met Gly Leu Pro Val Ala Thr Leu Gln Gln
        355                 360                 365

Leu Glu Ala Ala Ala Val Asn Val Cys Asn Gln Thr Trp Ala Gln Leu
    370                 375                 380

Gln Ala Arg Val Pro Gly Gln Gln Ala His Leu Ala Asp Tyr Cys Ala
385                 390                 395                 400

Gly Ala Met Phe Val Gln Gln Leu Leu Ser Arg Gly Tyr Gly Phe Asp
                405                 410                 415

Glu Arg Ala Phe Gly Gly Val Ile Phe Gln Lys Lys Ala Ala Asp Thr
            420                 425                 430
```

Ala Val Gly Trp Ala Leu Gly Tyr Met Leu Asn Leu Thr Asn Leu Ile
435 440 445

Pro Ala Asp Pro Pro Gly Leu Arg Lys Gly Thr Asp Phe Ser Ser Trp
450 455 460

Val Val Leu Leu Leu Leu Phe Ala Ser Ala Leu Leu Ala Ala Leu Val
465 470 475 480

Leu Leu Leu His Gln Val His Ser Ala Lys Leu Pro Ser Thr Ile
485 490 495

<210> 344
<211> 1485
<212> DNA
<213> Macaca fascicularis

<400> 344
atggccggga aggtgcggtc actgctgccg ccgctgctgc tggccgccgc gggcctcgcc 60

ggcctcctac tgctgtgcgt gcccaccagg gacattaggg agcctcccgc tctgaaatac 120

ggcatcgtgc tggacgccgg aagcagccac acctccatgt tcatctacaa gtggcccgcc 180

gacaaggaga acgacacagg catcgtgggc cagcatagct cctgcgacgt gcctggaggc 240

ggcatctcca gctacgccga caatccttcc ggcgctggac agtccctggt gggatgtctg 300

gagcaggccc tgagggacgt gcctaaggag agacacgccg gcacccctct gtacctggga 360

gccacagccg gcatgagact cctgaatctg accaaccctg aggcctccac ctccgtcctg 420

acagccgtga cacataccct gacccagtac cccttcgatt tcaggggagc cagaatactg 480

agcggccagg aagaaggcgt gttcggatgg gtgaccgcca actacctcct ggagaacttc 540

atcaagtacg gctgggtggg caggtggttt agacccagga agggcaccct gggagctatg 600

gatctgggcg gagcttccac acagatcacc ttcgagacca cctcccccgc tgaggacaga 660

gcctccgagg tgcagctgag gctgtacggc cagcattaca gggtgtatac acacagcttc 720

ctgtgctacg gcagggacca ggtcctgcag agactgctcg cttccgccct gcagacccac 780

tccttccacc cttgctggcc taggggcttt agcacccatg tgctcctggg agatgtgtac 840

cagagcccct gcaccgtggc ccaaagaccc cagaccttta actcctccgc tagagtgagc 900

ctgagcggca gctccgatcc ccacctgtgt agggacctgg tcagcggact gttcagcttc 960

agcagctgcc ctttcagcag gtgcagcttc aatggcgtgt tccagcctcc cgtggccggc 1020

aacttcatcg ctttctccgc cttcttctac accgtcaact ttctgaggac aagcatggga 1080

ctgcccgtgg ctaccctcca acaactggag gccgccgccg tgaacgtgtg caaccagaca 1140

tgggcccaac tgcaggctag ggtgcccggc caacaggccc atctggctga ctactgtgcc 1200

ggcgccatgt tcgtgcagca gctgctgagc aggggctatg gattcgacga gagggccttc 1260

ggcggcgtca tcttccaaaa gaaggccgcc gatacagccg tgggctgggc tctgggctac 1320

atgctgaacc tgacaaacct gatccccgct gacccccccg gactgaggaa gggaaccgat 1380

ttcagcagct gggtcgtgct cctgctgctg tttgctagcg ccctgctcgc cgctctggtg 1440

ctgctgctgc accaggtgca ctccgccaag ctgcccagca ccatt 1485

<210> 345
<211> 495
<212> PRT
<213> Mus musculus

<400> 345
Met Ala Gly Lys Leu Val Ser Leu Val Pro Pro Leu Leu Leu Ala Ala
1 5 10 15

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

Arg Glu Pro Pro Ala Leu Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser
35 40 45

Ser His Thr Ser Met Phe Val Tyr Lys Trp Pro Ala Asp Lys Glu Asn
50 55 60

Asp Thr Gly Ile Val Gly Gln His Ser Ser Cys Asp Val Arg Gly Gly

```
65                  70                  75                  80

Gly Ile Ser Ser Tyr Ala Asn Asp Pro Ser Arg Ala Gly Gln Ser Leu
                85                  90                  95

Val Glu Cys Leu Glu Gln Ala Leu Arg Asp Val Pro Lys Asp Arg Tyr
            100                 105                 110

Ala Ser Thr Pro Leu Tyr Leu Gly Ala Thr Ala Gly Met Arg Leu Leu
        115                 120                 125

Asn Leu Thr Ser Pro Glu Ala Thr Ala Lys Val Leu Glu Ala Val Thr
    130                 135                 140

Gln Thr Leu Thr Arg Tyr Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu
145                 150                 155                 160

Ser Gly Gln Asp Glu Gly Val Phe Gly Trp Val Thr Ala Asn Tyr Leu
                165                 170                 175

Leu Glu Asn Phe Ile Lys Tyr Gly Trp Val Gly Arg Trp Ile Arg Pro
            180                 185                 190

Arg Lys Gly Thr Leu Gly Ala Met Asp Leu Gly Gly Ala Ser Thr Gln
        195                 200                 205

Ile Thr Phe Glu Thr Thr Ser Pro Ser Glu Asp Pro Asp Asn Glu Val
    210                 215                 220

His Leu Arg Leu Tyr Gly Gln His Tyr Arg Val Tyr Thr His Ser Phe
225                 230                 235                 240

Leu Cys Tyr Gly Arg Asp Gln Val Leu Gln Arg Leu Leu Ala Ser Ala
                245                 250                 255

Leu Gln Ile His Arg Phe His Pro Cys Trp Pro Lys Gly Tyr Ser Thr
```

```
            260                 265                 270

Gln Val Leu Leu Arg Glu Val Tyr Gln Ser Pro Cys Thr Met Gly Gln
        275                 280                 285

Arg Pro Gln Thr Phe Asn Ser Ser Ala Thr Val Ser Leu Ser Gly Thr
    290                 295                 300

Ser Asn Ala Ala Leu Cys Arg Asp Leu Val Ser Gly Leu Phe Asn Ile
305                 310                 315                 320

Ser Ser Cys Pro Phe Ser Gln Cys Ser Phe Asn Gly Val Phe Gln Pro
                325                 330                 335

Pro Val Ala Gly Asn Phe Ile Ala Phe Ser Ala Phe Tyr Tyr Thr Val
            340                 345                 350

Asp Phe Leu Lys Thr Val Met Gly Leu Pro Val Gly Thr Leu Lys Gln
        355                 360                 365

Leu Glu Asp Ala Thr Glu Thr Thr Cys Asn Gln Thr Trp Ala Glu Leu
    370                 375                 380

Gln Ala Arg Val Pro Gly Gln Gln Thr Arg Leu Pro Asp Tyr Cys Ala
385                 390                 395                 400

Val Ala Met Phe Ile His Gln Leu Leu Ser Arg Gly Tyr Arg Phe Asp
                405                 410                 415

Glu Arg Ser Phe Arg Gly Val Val Phe Glu Lys Lys Ala Ala Asp Thr
            420                 425                 430

Ala Val Gly Trp Ala Leu Gly Tyr Met Leu Asn Leu Thr Asn Leu Ile
        435                 440                 445

Pro Ala Asp Leu Pro Gly Leu Arg Lys Gly Thr His Phe Ser Ser Trp
```

450 455 460

Val Ala Leu Leu Leu Leu Phe Thr Val Leu Ile Leu Ala Ala Leu Val
465 470 475 480

Leu Leu Leu Arg Gln Val Arg Ser Ala Lys Ser Pro Gly Ala Leu
485 490 495

<210> 346
<211> 1485
<212> DNA
<213> Mus musculus

<400> 346
atggctggaa agttggtgtc actggtgcca cccctgctgc tggctgccgt gggcctcgcc 60

ggcctcctgc tactgtgcgt ccctacccaa gacgtccggg agccgcccgc cctcaagtat 120

ggcatcgttc tggatgctgg ctcttcacac acatccatgt ttgtctacaa gtggccagcg 180

gacaaggaaa atgacacagg tatcgtgggc cagcacagct cttgcgatgt tcgaggtggt 240

ggcatctcca gctacgcaaa tgacccttct agggcaggcc agagtctggt tgaatgtctt 300

gaacaggcac ttcgggatgt gcccaaagac agatatgcca gcactccact ctacctggga 360

gctacagcag gcatgcgcct actcaacctg accagcccag aggccacagc caaggtgctg 420

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<213> Rattus norvegicus

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35 40 45

Ser His Thr Ser Met Phe Val Tyr Lys Trp Pro Ala Asp Lys Glu Asn
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Asp Thr Gly Ile Val Gly Gln His Ser Ser Cys Asp Val Gln Gly Gly
65 70 75 80

Gly Ile Ser Ser Tyr Ala Asn Asp Pro Ser Lys Ala Gly Gln Ser Leu
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Val Arg Cys Leu Glu Gln Ala Leu Arg Asp Val Pro Arg Asp Arg His
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Ala Ser Thr Pro Leu Tyr Leu Gly Ala Thr Ala Gly Met Arg Leu Leu
        115                 120                 125

Asn Leu Thr Ser Pro Glu Ala Thr Ala Arg Val Leu Glu Ala Val Thr
    130                 135                 140

Gln Thr Leu Thr Gln Tyr Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu
145                 150                 155                 160

Ser Gly Gln Asp Glu Gly Val Phe Gly Trp Val Thr Ala Asn Tyr Leu
                165                 170                 175

Leu Glu Asn Phe Ile Lys Tyr Gly Trp Val Gly Arg Trp Ile Arg Pro
            180                 185                 190

Arg Lys Gly Thr Leu Gly Ala Met Asp Leu Gly Gly Ala Ser Thr Gln
        195                 200                 205

Ile Thr Phe Glu Thr Thr Ser Pro Ser Glu Asp Pro Gly Asn Glu Val
    210                 215                 220

His Leu Arg Leu Tyr Gly Gln His Tyr Arg Val Tyr Thr His Ser Phe
225                 230                 235                 240

Leu Cys Tyr Gly Arg Asp Gln Ile Leu Leu Arg Leu Leu Ala Ser Ala
                245                 250                 255

Leu Gln Ile His Arg Phe His Pro Cys Trp Pro Lys Gly Tyr Ser Thr
            260                 265                 270

Gln Val Leu Leu Gln Glu Val Tyr Gln Ser Pro Cys Thr Met Gly Gln
        275                 280                 285
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Arg Pro Arg Ala Phe Asn Gly Ser Ala Ile Val Ser Leu Ser Gly Thr
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Ser Asn Ala Thr Leu Cys Arg Asp Leu Val Ser Arg Leu Phe Asn Ile
305                 310                 315                 320

Ser Ser Cys Pro Phe Ser Gln Cys Ser Phe Asn Gly Val Phe Gln Pro
                325                 330                 335

Pro Val Thr Gly Asn Phe Ile Ala Phe Ser Ala Phe Tyr Tyr Thr Val
            340                 345                 350

Asp Phe Leu Thr Thr Val Met Gly Leu Pro Val Gly Thr Leu Lys Gln
        355                 360                 365

Leu Glu Glu Ala Thr Glu Ile Thr Cys Asn Gln Thr Trp Thr Glu Leu
    370                 375                 380

Gln Ala Arg Val Pro Gly Gln Lys Thr Arg Leu Ala Asp Tyr Cys Ala
385                 390                 395                 400

Val Ala Met Phe Ile His Gln Leu Leu Ser Arg Gly Tyr His Phe Asp
                405                 410                 415

Glu Arg Ser Phe Arg Glu Val Val Phe Gln Lys Lys Ala Ala Asp Thr
            420                 425                 430

Ala Val Gly Trp Ala Leu Gly Tyr Met Leu Asn Phe Thr Asn Leu Ile
        435                 440                 445

Pro Ala Asp Leu Pro Gly Leu Arg Lys Gly Thr His Phe Ser Ser Trp
    450                 455                 460

Val Ala Leu Leu Leu Leu Phe Thr Val Leu Ile Leu Ala Ala Leu Val
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<211> 510
<212> PRT
<213> Homo sapiens

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35 40 45

Tyr Gly Ile Val Leu Asp Ala Gly Ser Ser His Thr Ser Leu Tyr Ile
50 55 60

Tyr Lys Trp Pro Ala Glu Lys Glu Asn Asp Thr Gly Val Val His Gln
65 70 75 80

Val Glu Glu Cys Arg Val Lys Gly Pro Gly Ile Ser Lys Phe Val Gln
85 90 95

Lys Val Asn Glu Ile Gly Ile Tyr Leu Thr Asp Cys Met Glu Arg Ala
100 105 110

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Arg Glu Val Ile Pro Arg Ser Gln His Gln Glu Thr Pro Val Tyr Leu
        115                 120                 125

Gly Ala Thr Ala Gly Met Arg Leu Leu Arg Met Glu Ser Glu Glu Leu
    130                 135                 140

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

Phe Asp Phe Gln Gly Ala Arg Ile Ile Thr Gly Gln Glu Glu Gly Ala
                165                 170                 175

Tyr Gly Trp Ile Thr Ile Asn Tyr Leu Leu Gly Lys Phe Ser Gln Lys
            180                 185                 190

Thr Arg Trp Phe Ser Ile Val Pro Tyr Glu Thr Asn Asn Gln Glu Thr
        195                 200                 205

Phe Gly Ala Leu Asp Leu Gly Gly Ala Ser Thr Gln Val Thr Phe Val
    210                 215                 220

Pro Gln Asn Gln Thr Ile Glu Ser Pro Asp Asn Ala Leu Gln Phe Arg
225                 230                 235                 240

Leu Tyr Gly Lys Asp Tyr Asn Val Tyr Thr His Ser Phe Leu Cys Tyr
                245                 250                 255

Gly Lys Asp Gln Ala Leu Trp Gln Lys Leu Ala Lys Asp Ile Gln Val
            260                 265                 270

Ala Ser Asn Glu Ile Leu Arg Asp Pro Cys Phe His Pro Gly Tyr Lys
        275                 280                 285

Lys Val Val Asn Val Ser Asp Leu Tyr Lys Thr Pro Cys Thr Lys Arg
    290                 295                 300
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Phe Glu Met Thr Leu Pro Phe Gln Gln Phe Glu Ile Gln Gly Ile Gly
305                 310                 315                 320


Asn Tyr Gln Gln Cys His Gln Ser Ile Leu Glu Leu Phe Asn Thr Ser
                325                 330                 335


Tyr Cys Pro Tyr Ser Gln Cys Ala Phe Asn Gly Ile Phe Leu Pro Pro
            340                 345                 350


Leu Gln Gly Asp Phe Gly Ala Phe Ser Ala Phe Tyr Phe Val Met Lys
        355                 360                 365


Phe Leu Asn Leu Thr Ser Glu Lys Val Ser Gln Glu Lys Val Thr Glu
    370                 375                 380


Met Met Lys Lys Phe Cys Ala Gln Pro Trp Glu Glu Ile Lys Thr Ser
385                 390                 395                 400


Tyr Ala Gly Val Lys Glu Lys Tyr Leu Ser Glu Tyr Cys Phe Ser Gly
                405                 410                 415


Thr Tyr Ile Leu Ser Leu Leu Leu Gln Gly Tyr His Phe Thr Ala Asp
            420                 425                 430


Ser Trp Glu His Ile His Phe Ile Gly Lys Ile Gln Gly Ser Asp Ala
        435                 440                 445


Gly Trp Thr Leu Gly Tyr Met Leu Asn Leu Thr Asn Met Ile Pro Ala
    450                 455                 460


Glu Gln Pro Leu Ser Thr Pro Leu Ser His Ser Thr Tyr Val Phe Leu
465                 470                 475                 480


Met Val Leu Phe Ser Leu Val Leu Phe Thr Val Ala Ile Ile Gly Leu
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Leu Ile Phe His Lys Pro Ser Tyr Phe Trp Lys Asp Met Val
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<211> 1530
<212> DNA
<213> Homo sapiens

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<211> 510
<212> PRT
<213> Mus musculus

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Ile Ala Val Gly Leu Thr Gln Asn Lys Pro Leu Pro Glu Asn Val Lys
35 40 45

Tyr Gly Ile Val Leu Asp Ala Gly Ser Ser His Thr Asn Leu Tyr Ile
50 55 60

Tyr Lys Trp Pro Ala Glu Lys Glu Asn Asp Thr Gly Val Val Gln Gln
65 70 75 80

Leu Glu Glu Cys Gln Val Lys Gly Pro Gly Ile Ser Lys Tyr Ala Gln
85 90 95

Lys Thr Asp Glu Ile Gly Ala Tyr Leu Ala Glu Cys Met Glu Leu Ser
100 105 110

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Thr Glu Leu Ile Pro Thr Ser Lys His His Gln Thr Pro Val Tyr Leu
        115                 120                 125

Gly Ala Thr Ala Gly Met Arg Leu Leu Arg Met Glu Ser Glu Gln Ser
    130                 135                 140

Ala Asp Glu Val Leu Ala Ala Val Ser Thr Ser Leu Lys Ser Tyr Pro
145                 150                 155                 160

Phe Asp Phe Gln Gly Ala Lys Ile Ile Thr Gly Gln Glu Glu Gly Ala
                165                 170                 175

Tyr Gly Trp Ile Thr Ile Asn Tyr Leu Leu Gly Arg Phe Thr Gln Glu
            180                 185                 190

Gln Ser Trp Leu Ser Leu Ile Ser Asp Ser Gln Lys Gln Glu Thr Phe
        195                 200                 205

Gly Ala Leu Asp Leu Gly Gly Ala Ser Thr Gln Ile Thr Phe Val Pro
    210                 215                 220

Gln Asn Ser Thr Ile Glu Ser Pro Glu Asn Ser Leu Gln Phe Arg Leu
225                 230                 235                 240

Tyr Gly Glu Asp Tyr Thr Val Tyr Thr His Ser Phe Leu Cys Tyr Gly
                245                 250                 255

Lys Asp Gln Ala Leu Trp Gln Lys Leu Ala Lys Asp Ile Gln Val Ser
            260                 265                 270

Ser Gly Gly Val Leu Lys Asp Pro Cys Phe Asn Pro Gly Tyr Glu Lys
        275                 280                 285

Val Val Asn Val Ser Glu Leu Tyr Gly Thr Pro Cys Thr Lys Arg Phe
    290                 295                 300
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Glu Lys Lys Leu Pro Phe Asp Gln Phe Arg Ile Gln Gly Thr Gly Asp
305                 310                 315                 320

Tyr Glu Gln Cys His Gln Ser Ile Leu Glu Leu Phe Asn Asn Ser His
                325                 330                 335

Cys Pro Tyr Ser Gln Cys Ala Phe Asn Gly Val Phe Leu Pro Pro Leu
            340                 345                 350

His Gly Ser Phe Gly Ala Phe Ser Ala Phe Tyr Phe Val Met Asp Phe
        355                 360                 365

Phe Lys Lys Val Ala Lys Asn Ser Val Ile Ser Gln Glu Lys Met Thr
    370                 375                 380

Glu Ile Thr Lys Asn Phe Cys Ser Lys Ser Trp Glu Glu Thr Lys Thr
385                 390                 395                 400

Ser Tyr Pro Ser Val Lys Glu Lys Tyr Leu Ser Glu Tyr Cys Phe Ser
                405                 410                 415

Gly Ala Tyr Ile Leu Ser Leu Leu Gln Gly Tyr Asn Phe Thr Asp Ser
            420                 425                 430

Ser Trp Glu Gln Ile His Phe Met Gly Lys Ile Lys Asp Ser Asn Ala
        435                 440                 445

Gly Trp Thr Leu Gly Tyr Met Leu Asn Leu Thr Asn Met Ile Pro Ala
    450                 455                 460

Glu Gln Pro Leu Ser Pro Pro Leu Pro His Ser Thr Tyr Ile Gly Leu
465                 470                 475                 480

Met Val Leu Phe Ser Leu Leu Leu Val Ala Val Ala Ile Thr Gly Leu
                485                 490                 495
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Phe Ile Tyr Ser Lys Pro Ser Tyr Phe Trp Lys Glu Ala Val
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<212> DNA
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<210> 501
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 501
Thr Tyr Trp Met His
1 5

<210> 502
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 502
Asn Ile Tyr Pro Gly Thr Gly Gly Ser Asn Phe Asp Glu Lys Phe Lys
1 5 10 15

Asn

<210> 503
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 503
Trp Thr Thr Gly Thr Gly Ala Tyr
1 5

<210> 504
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 504
Gly Tyr Thr Phe Thr Thr Tyr
1 5

<210> 505
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 505
Tyr Pro Gly Thr Gly Gly
1 5

<210> 506
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 506
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

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

Trp Met His Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Asn Ile Tyr Pro Gly Thr Gly Gly Ser Asn Phe Asp Glu Lys Phe

50 55 60

Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Trp Thr Thr Gly Thr Gly Ala Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 507
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 507
gaggtgcagc tggtgcagtc aggcgccgaa gtgaagaagc ccggcgagtc actgagaatt 60

agctgtaaag gttcaggcta caccttcact acctactgga tgcactgggt ccgccaggct 120

accggtcaag gcctcgagtg gatgggtaat atctaccccg gcaccggcgg ctctaacttc 180

gacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcac taggtggact 300

accggcacag gcgcctactg gggtcaaggc actaccgtga ccgtgtctag c 351

<210> 508
<211> 443
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 508

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


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


Trp Met His Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


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


Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Thr Arg Trp Thr Thr Gly Thr Gly Ala Tyr Trp Gly Gln Gly Thr Thr
            100                 105                 110


Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125


Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
    130                 135                 140


Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160


Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175
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Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
    210                 215                 220

Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
225                 230                 235                 240

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
                245                 250                 255

Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
            260                 265                 270

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
        275                 280                 285

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
    290                 295                 300

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305                 310                 315                 320

Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
                325                 330                 335

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
            340                 345                 350

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
        355                 360                 365
```

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Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
    370                 375                 380

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
385                 390                 395                 400

Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
                405                 410                 415

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
            420                 425                 430

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440


<210> 509
<211> 1329
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 509
gaggtgcagc tggtgcagtc aggcgccgaa gtgaagaagc ccggcgagtc actgagaatt       60

agctgtaaag gttcaggcta caccttcact acctactgga tgcactgggt ccgccaggct      120

accggtcaag gcctcgagtg gatgggtaat atctaccccg gcaccggcgg ctctaacttc      180

gacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat      240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcac taggtggact      300

accggcacag gcgcctactg gggtcaaggc actaccgtga ccgtgtctag cgctagcact      360

aagggcccgt ccgtgttccc cctggcacct tgtagccgga gcactagcga atccaccgct      420

gccctcggct gcctggtcaa ggattacttc ccggagcccg tgaccgtgtc ctggaacagc      480
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ggagccctga cctccggagt gcacaccttc cccgctgtgc tgcagagctc cgggctgtac 540

tcgctgtcgt cggtggtcac ggtgccttca tctagcctgg gtaccaagac ctacacttgc 600

aacgtggacc acaagccttc caacactaag gtggacaagc gcgtcgaatc gaagtacggc 660

ccaccgtgcc cgccttgtcc cgcgccggag ttcctcggcg gtccctcggt ctttctgttc 720

ccaccgaagc ccaaggacac tttgatgatt tcccgcaccc ctgaagtgac atgcgtggtc 780

gtggacgtgt cacaggaaga tccggaggtg cagttcaatt ggtacgtgga tggcgtcgag 840

gtgcacaacg ccaaaaccaa gccgagggag gagcagttca actccactta ccgcgtcgtg 900

tccgtgctga cggtgctgca tcaggactgg ctgaacggga aggagtacaa gtgcaaagtg 960

tccaacaagg gacttcctag ctcaatcgaa aagaccatct cgaaagccaa gggacagccc 1020

cgggaacccc aagtgtatac cctgccaccg agccaggaag aaatgactaa gaaccaagtc 1080

tcattgactt gccttgtgaa gggcttctac ccatcggata tcgccgtgga atgggagtcc 1140

aacggccagc cggaaaacaa ctacaagacc acccctccgg tgctggactc agacggatcc 1200

ttcttcctct actcgcggct gaccgtggat aagagcagat ggcaggaggg aaatgtgttc 1260

agctgttctg tgatgcatga agccctgcac aaccactaca ctcagaagtc cctgtccctc 1320

tccctggga 1329

<210> 510
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 510
Lys Ser Ser Gln Ser Leu Leu Asp Ser Gly Asn Gln Lys Asn Phe Leu
1 5 10 15

Thr

<210> 511
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 511
Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 512
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 512
Gln Asn Asp Tyr Ser Tyr Pro Tyr Thr
1 5

<210> 513
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 513
Ser Gln Ser Leu Leu Asp Ser Gly Asn Gln Lys Asn Phe
1 5 10

<210> 514
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 514
Trp Ala Ser
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<210> 515
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 515
Asp Tyr Ser Tyr Pro Tyr
1   5

<210> 516
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 516
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20   25   30

```
Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Lys
        35                  40                  45


Ala Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60


Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65                  70                  75                  80


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


Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110


Lys
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<210> 517
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 517
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg taaagcccct aagctgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tgcagcccga ggatatcgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaag 339

<210> 518
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 518
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20   25   30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Lys
        35   40   45

Ala Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50   55   60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65   70   75   80

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

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100   105   110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115   120   125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130   135   140

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

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
165 170 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 519
<211> 660
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 519
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg taaagcccct aagctgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tgcagcccga ggatatcgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaagc gtacggtggc cgctcccagc 360

gtgttcatct tccccccag cgacgagcag ctgaagagcg gcaccgccag cgtggtgtgc 420

ctgctgaaca acttctaccc ccgggaggcc aaggtgcagt ggaaggtgga caacgccctg 420

cagagcggca acagccagga gagcgtcacc gagcaggaca gcaaggactc cacctacagc 540

ctgagcagca ccctgaccct gagcaaggcc gactacgaga agcataaggt gtacgcctgc 600

gaggtgaccc accagggcct gtccagcccc gtgaccaaga gcttcaacag gggcgagtgc 660

<210> 520
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 520
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ala Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65 70 75 80

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

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 521
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 521
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg tcaagccccc agactgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tggaagccga ggacgccgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaag 339

<210> 522
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 522
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Gly Asn Gln Lys Asn Phe Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

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Ala Pro Arg Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
    50                  55                  60

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr
65                  70                  75                  80

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

Asp Tyr Ser Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
            100                 105                 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140

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

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220
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<210> 523
<211> 660
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 523
gagatcgtcc tgactcagtc acccgctacc ctgagcctga gccctggcga gcgggctaca 60

ctgagctgta aatctagtca gtcactgctg gatagcggta atcagaagaa cttcctgacc 120

tggtatcagc agaagcccgg tcaagcccct agactgctga tctactgggc ctctactaga 180

gaatcaggcg tgccctctag gtttagcggt agcggtagtg gcaccgactt caccttcact 240

atctctagcc tggaagccga ggacgccgct acctactact gtcagaacga ctatagctac 300

ccctacacct tcggtcaagg cactaaggtc gagattaagc gtacggtggc cgctcccagc 360

gtgttcatct tccccccag cgacgagcag ctgaagagcg gcaccgccag cgtggtgtgc 420

ctgctgaaca acttctaccc ccgggaggcc aaggtgcagt ggaaggtgga caacgccctg 480

cagagcggca acagccagga gagcgtcacc gagcaggaca gcaaggactc cacctacagc 540

ctgagcagca ccctgaccct gagcaaggcc gactacgaga agcataaggt gtacgcctgc 600

gaggtgaccc accagggcct gtccagcccc gtgaccaaga gcttcaacag gggcgagtgc 660

<210> 524
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 524
acctactgga tgcac 15

<210> 525
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 525
aatatctacc ccggcaccgg cggctctaac ttcgacgaga agtttaagaa t 51

<210> 526
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 526
tggactaccg gcacaggcgc ctac 24

<210> 527
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 527
ggctacacct tcactaccta c 21

<210> 528
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 528
taccccggca ccggcggc 18

<210> 529
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 529
aaatctagtc agtcactgct ggatagcggt aatcagaaga acttcctgac c 51

<210> 530
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 530
tgggcctcta ctagagaatc a 21

<210> 531
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 531
cagaacgact atagctaccc ctacacc 27

<210> 532
<211> 39

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 532
agtcagtcac tgctggatag cggtaatcag aagaacttc 39

<210> 533
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 533
tgggcctct 9

<210> 534
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 534
gactatagct acccctac 18

<210> 535
<211> 440
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 535

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
            20                  25                  30


Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80


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


Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110


Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
        115                 120                 125


Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140


Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160


Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175


Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys
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            180                 185                 190

Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala
    210                 215                 220

Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
225                 230                 235                 240

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
                245                 250                 255

Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val
            260                 265                 270

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
        275                 280                 285

Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
    290                 295                 300

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
305                 310                 315                 320

Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
                325                 330                 335

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr
            340                 345                 350

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
        355                 360                 365

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
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370 375 380

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
385 390 395 400

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
405 410 415

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
420 425 430

Ser Leu Ser Leu Ser Leu Gly Lys
435 440

<210> 536
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 536
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

```
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210


<210> 537
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
```

<400> 537

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Gly Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
    50                  55                  60

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

Met Glu Leu Lys Ser Leu Gln Phe Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190
```

```
Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380
```

```
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400


Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415


Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430


His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440                 445


<210> 538
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 538
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
            20                  25                  30


Gly Tyr Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
        35                  40                  45


Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala
    50                  55                  60


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80
```

```
Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg
                85                  90                  95


Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110


Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125


Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140


Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175


Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190


His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 539
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 539
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
```

```
1               5                   10                  15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Gln Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Asp Ser Gly Glu Ser Thr Tyr Ala Glu Glu Phe
    50                  55                  60

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

Leu Gln Ile Thr Ser Leu Thr Ala Glu Asp Thr Gly Met Tyr Phe Cys
                85                  90                  95

Val Arg Val Gly Tyr Asp Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
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        195                 200                 205

Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
```

385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 540
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 540
Glu Ile Val 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 Ala Arg Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr
35 40 45

Arg Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Cys Leu Thr Ile Asn Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Phe Pro Leu Thr
85 90 95

```
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110


Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125


Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140


Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160


Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175


Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190


Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205


Asn Arg Gly Glu Cys
    210


<210> 541
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 541
Gly Tyr Thr Phe Thr Thr Tyr Trp Met His
1               5                   10
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<210> 542

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<210> 601
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 601
Ser Tyr Trp Met Tyr
1 5

<210> 602
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 602
Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe Lys
1 5 10 15

Asn

<210> 603
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 603
Asp Tyr Arg Lys Gly Leu Tyr Ala Met Asp Tyr
1 5 10

<210> 604
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 604
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 605
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 605
Asp Pro Asn Ser Gly Ser
1 5

<210> 606
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 606
Glu Val 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 Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Tyr Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
35 40 45

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

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

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

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

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 607
<211> 360
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 607
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

agagggcaaa gactggagtg gatcggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag gttcactatt agtagggata actctaagaa caccctgtac 240

ctgcagatga atagcctgag agccgaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

<210> 608
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 608
Glu Val 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 Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Tyr Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
35 40 45

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

```
Lys Asn Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


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


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


Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125


Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140


Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160


Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175


Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190


Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205


Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220


Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240


Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255
```

```
Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440                 445
```

<210> 609
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 609
Lys Ala Ser Gln Asp Val Gly Thr Ala Val Ala
1 5 10

<210> 610
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 610
Trp Ala Ser Thr Arg His Thr
1 5

<210> 611
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 611
Gln Gln Tyr Asn Ser Tyr Pro Leu Thr
1 5

<210> 612
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 612
Ser Gln Asp Val Gly Thr Ala
1 5

<210> 613
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 613
Trp Ala Ser
1

<210> 614
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 614
Tyr Asn Ser Tyr Pro Leu
1 5

<210> 615
<211> 1338
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 615
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

agagggcaaa gactggagtg gatcggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag gttcactatt agtagggata actctaagaa caccctgtac 240

ctgcagatga atagcctgag agccgaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

gctagcacta agggcccgtc cgtgttcccc ctggcacctt gtagccggag cactagcgaa 420

tccaccgctg ccctcggctg cctggtcaag gattacttcc cggagcccgt gaccgtgtcc 480

tggaacagcg gagccctgac ctccggagtg cacaccttcc ccgctgtgct gcagagctcc 540

gggctgtact cgctgtcgtc ggtggtcacg gtgccttcat ctagcctggg taccaagacc 600

tacacttgca acgtggacca caagccttcc aacactaagg tggacaagcg cgtcgaatcg 660

aagtacggcc caccgtgccc gccttgtccc gcgccggagt tcctcggcgg tccctcggtc 720

tttctgttcc caccgaagcc caaggacact ttgatgattt cccgcacccc tgaagtgaca 780

tgcgtggtcg tggacgtgtc acaggaagat ccggaggtgc agttcaattg gtacgtggat 840

ggcgtcgagg tgcacaacgc caaaaccaag ccgagggagg agcagttcaa ctccacttac 900

cgcgtcgtgt ccgtgctgac ggtgctgcat caggactggc tgaacgggaa ggagtacaag 960

tgcaaagtgt ccaacaaggg acttcctagc tcaatcgaaa agaccatctc gaaagccaag 1020

ggacagcccc gggaacccca agtgtatacc ctgccaccga gccaggaaga aatgactaag 1080

aaccaagtct cattgacttg ccttgtgaag ggcttctacc catcggatat cgccgtggaa 1140

tgggagtcca acggccagcc ggaaaacaac tacaagacca cccctccggt gctggactca 1200

gacggatcct tcttcctcta ctcgcggctg accgtggata agagcagatg gcaggaggga 1260

aatgtgttca gctgttctgt gatgcatgaa gccctgcaca accactacac tcagaagtcc 1320

ctgtccctct ccctggga 1338

<210> 616
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 616
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
20 25 30

Val Ala Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 617
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 617
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta aagcctctca ggacgtgggc accgccgtgg cctggtatct gcagaagcct 120

ggtcaatcac ctcagctgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgac ttcaccttca ctatctcttc actggaagcc 240

gaggacgccg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 618
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 618
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
20 25 30

Val Ala Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
```

<210> 619
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 619
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta aagcctctca ggacgtgggc accgccgtgg cctggtatct gcagaagcct 120

ggtcaatcac ctcagctgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgac ttcaccttca ctatctcttc actggaagcc 240

gaggacgccg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 620
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 620
Glu Val 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 Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Tyr Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Asn Ser Gly Ser Thr Lys Tyr Asn Glu Lys Phe

50 55 60

Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 621
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 621
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

accggtcaag gcctggagtg gatgggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

<210> 622
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 622
Glu Val 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 Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Tyr Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Lys Asn Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

```
Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365
```

```
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440                 445
```

<210> 623
<211> 1338
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 623
gaagtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctac cgtgaagatt 60

agctgtaaag tctcaggcta caccttcact agctactgga tgtactgggt ccgacaggct 120

accggtcaag gcctggagtg gatgggtaga atcgacccta atagcggctc tactaagtat 180

aacgagaagt ttaagaatag agtgactatc accgccgata agtctactag caccgcctat 240

atggaactgt ctagcctgag atcagaggac accgccgtct actactgcgc tagagactat 300

agaaagggcc tgtacgctat ggactactgg ggtcaaggca ctaccgtgac cgtgtcttca 360

gctagcacta agggcccgtc cgtgttcccc ctggcacctt gtagccggag cactagcgaa 420

tccaccgctg ccctcggctg cctggtcaag gattacttcc cggagcccgt gaccgtgtcc 480

tggaacagcg gagccctgac ctccggagtg cacaccttcc ccgctgtgct gcagagctcc 540

gggctgtact cgctgtcgtc ggtggtcacg gtgccttcat ctagcctggg taccaagacc 600

tacacttgca acgtggacca caagccttcc aacactaagg tggacaagcg cgtcgaatcg 660

aagtacggcc caccgtgccc gccttgtccc gcgccggagt tcctcggcgg tccctcggtc 720

tttctgttcc caccgaagcc caaggacact ttgatgattt cccgcacccc tgaagtgaca 780

tgcgtggtcg tggacgtgtc acaggaagat ccggaggtgc agttcaattg gtacgtggat 840

ggcgtcgagg tgcacaacgc caaaaccaag ccgagggagg agcagttcaa ctccacttac 900

cgcgtcgtgt ccgtgctgac ggtgctgcat caggactggc tgaacgggaa ggagtacaag 960

tgcaaagtgt ccaacaaggg acttcctagc tcaatcgaaa agaccatctc gaaagccaag 1020

ggacagcccc gggaacccca agtgtatacc ctgccaccga gccaggaaga aatgactaag 1080

aaccaagtct cattgacttg ccttgtgaag ggcttctacc catcggatat cgccgtggaa 1140

tgggagtcca acggccagcc ggaaaacaac tacaagacca cccctccggt gctggactca 1200

gacggatcct tcttcctcta ctcgcggctg accgtggata agagcagatg gcaggaggga 1260

aatgtgttca gctgttctgt gatgcatgaa gccctgcaca accactacac tcagaagtcc 1320

ctgtccctct ccctggga 1338

<210> 624
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 624
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Asp Val Gly Thr Ala

20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 625
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 625
gacgtcgtga tgactcagtc acccctgagc ctgcccgtga ccctggggca gcccgcctct 60

attagctgta aagcctctca ggacgtgggc accgccgtgg cctggtatca gcagaagcca 120

gggcaagccc ctagactgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctcttc actgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 626

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 626

```
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1               5                  10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Asp Val Gly Thr Ala
            20                  25                  30


Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
```

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 627
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 627
gacgtcgtga tgactcagtc acccctgagc ctgcccgtga ccctggggca gcccgcctct 60

attagctgta aagcctctca ggacgtgggc accgccgtgg cctggtatca gcagaagcca 120

gggcaagccc ctagactgct gatctactgg gcctctacta gacacaccgg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctcttc actgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tataatagct acccccctgac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 628
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 628
agctactgga tgtac 15

<210> 629
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 629
agaatcgacc ctaatagcgg ctctactaag tataacgaga agtttaagaa t 51

<210> 630
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 630
gactatagaa agggcctgta cgctatggac tac 33

<210> 631
<211> 21

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 631
ggctacacct tcactagcta c 21

<210> 632
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 632
gaccctaata gcggctct 18

<210> 633
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 633
aaagcctctc aggacgtggg caccgccgtg gcc 33

<210> 634
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

oligonucleotide"

<400> 634
tgggcctcta ctagacacac c 21

<210> 635
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 635
cagcagtata atagctaccc cctgacc 27

<210> 636
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 636
tctcaggacg tgggcaccgc c 21

<210> 637
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 637
tgggcctct 9

<210> 638
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 638
tataatagct acccccctg 18

<210> 639
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 639
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Ser
20 25 30

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

Ala Trp Ile Ser Pro Tyr Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

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

```
Ala Arg Arg His Trp Pro Gly Gly Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu 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 Lys 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 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 Tyr Thr Leu
            340                 345                 350


Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365


Leu 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 Tyr 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> 640
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
```

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 640
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala
            20   25   30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Leu Tyr His Pro Ala
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130   135   140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145   150   155   160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165   170   175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 641
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 641
Glu Val 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 Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

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

Ser Ser Ile Tyr Pro Ser Gly Gly Ile Thr Phe Tyr Ala Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

Ala Arg Ile Lys Leu Gly Thr Val Thr Thr Val Asp Tyr Trp Gly Gln

```
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
```

```
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450
```

<210> 642
<211> 216
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 642

```
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1               5                  10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20                  25                  30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

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

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

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

Ser Thr Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Gln
            100                 105                 110

Pro Lys Ala Asn Pro Thr Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
        115                 120                 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
    130                 135                 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Gly Ser Pro Val Lys
145                 150                 155                 160

Ala Gly Val Glu Thr Thr Lys Pro Ser Lys Gln Ser Asn Asn Lys Tyr
                165                 170                 175
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Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
            180                 185                 190


Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
        195                 200                 205


Thr Val Ala Pro Thr Glu Cys Ser
    210                 215


<210> 643
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 643
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
            20                  25                  30


Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


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

```
Ala Arg Glu Gly Gly Trp Phe Gly Glu Leu Ala Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125


Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140


Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160


Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175


Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190


Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205


Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
    210                 215                 220


Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly
225                 230                 235                 240


Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255


Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270


Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285
```

```
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300


Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320


Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile
                325                 330                 335


Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350


Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365


Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380


Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400


Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415


Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430


His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445


Pro Gly Lys
    450


<210> 644
<211> 215
<212> PRT
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<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 644
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Leu Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

```
Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175


Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190


Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205


Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 645
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 645
Gln Val 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 Thr Ser Gly Asp Thr Phe Ser Thr Tyr
            20                  25                  30


Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Gly Ile Ile Pro Ile Phe Gly Lys Ala His Tyr Ala Gln Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


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

Ala Arg Lys Phe His Phe Val Ser Gly Ser Pro Phe Gly Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 646
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 646
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

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

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 647
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 647
Gly Tyr Thr Phe Thr Ser Tyr Trp Met Tyr
1 5 10

<210> 648

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<210> 701

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 701
Asn Tyr Gly Met Asn
1 5

<210> 702
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 702
Trp Ile Asn Thr Asp Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 703
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 703
Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met Asp Tyr
1 5 10 15

<210> 704
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 704
Gly Phe Thr Leu Thr Asn Tyr
1 5

<210> 705
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 705
Asn Thr Asp Thr Gly Glu
1 5

<210> 706
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 706
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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

```
Gly Met Asn Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
        35                  40                  45


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


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


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


Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
            100                 105                 110


Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 707
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 707
caagtgcagc tggtgcagtc gggagccgaa gtgaagaagc ctggagcctc ggtgaaggtg       60

tcgtgcaagg catccggatt caccctcacc aattacggga tgaactgggt cagacaggcc      120

cggggtcaac ggctggagtg gatcggatgg attaacaccg acaccgggga gcctacctac      180

gcggacgatt tcaagggacg gttcgtgttc tccctcgaca cctccgtgtc caccgcctac      240

ctccaaatct cctcactgaa agcggaggac accgccgtgt actattgcgc gaggaacccg      300

ccctactact acggaaccaa caacgccgaa gccatggact actggggcca gggcaccact      360
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gtgactgtgt ccagc 375

<210> 708
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 708
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

aggggccagc ggctggaatg gatcggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctct 375

<210> 709
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 709
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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

```
Gly Met Asn Trp Val Arg Gln Ala Arg Gly Gln Arg Leu Glu Trp Ile
        35                  40                  45

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

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

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

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
            100                 105                 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
    130                 135                 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys
        195                 200                 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220
```

```
Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu
225                 230                 235                 240


Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255


Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270


Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285


Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300


Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320


Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser
                325                 330                 335


Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350


Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365


Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380


Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400


Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr
                405                 410                 415
```

Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Leu Gly
450

<210> 710
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 710
Ser Ser Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 711
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 711
Tyr Thr Ser Thr Leu His Leu
1 5

<210> 712
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 712
Gln Gln Tyr Tyr Asn Leu Pro Trp Thr
1 5

<210> 713
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 713
Ser Gln Asp Ile Ser Asn Tyr
1 5

<210> 714
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 714
Tyr Thr Ser
1

<210> 715
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 715
Tyr Tyr Asn Leu Pro Trp
1 5

<210> 716
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 716
caagtgcagc tggtgcagtc gggagccgaa gtgaagaagc ctggagcctc ggtgaaggtg 60

tcgtgcaagg catccggatt caccctcacc aattacggga tgaactgggt cagacaggcc 120

cggggtcaac ggctggagtg gatcggatgg attaacaccg acaccgggga gcctacctac 180

gcggacgatt tcaagggacg gttcgtgttc tccctcgaca cctccgtgtc caccgcctac 240

ctccaaatct cctcactgaa agcggaggac accgccgtgt actattgcgc gaggaacccg 300

ccctactact acggaaccaa caacgccgaa gccatggact actggggcca gggcaccact 360

gtgactgtgt ccagcgcgtc cactaagggc ccgtccgtgt tccccctggc accttgtagc 420

cggagcacta gcgaatccac cgctgccctc ggctgcctgg tcaaggatta cttcccggag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgacctccg gagtgcacac cttccccgct 540

gtgctgcaga gctccgggct gtactcgctg tcgtcggtgg tcacggtgcc ttcatctagc 600

ctgggtacca agacctacac ttgcaacgtg gaccacaagc cttccaacac taaggtggac 660

aagcgcgtcg aatcgaagta cggcccaccg tgcccgcctt gtcccgcgcc ggagttcctc 720

ggcggtccct cggtctttct gttcccaccg aagcccaagg acactttgat gatttcccgc 780

acccctgaag tgacatgcgt ggtcgtggac gtgtcacagg aagatccgga ggtgcagttc 840

aattggtacg tggatggcgt cgaggtgcac aacgccaaaa ccaagccgag ggaggagcag 900

ttcaactcca cttaccgcgt cgtgtccgtg ctgacggtgc tgcatcagga ctggctgaac 960

gggaaggagt acaagtgcaa agtgtccaac aagggacttc ctagctcaat cgaaaagacc 1020

atctcgaaag ccaagggaca gccccgggaa ccccaagtgt ataccctgcc accgagccag 1080

gaagaaatga ctaagaacca agtctcattg acttgccttg tgaagggctt ctacccatcg 1140

gatatcgccg tggaatggga gtccaacggc cagccggaaa acaactacaa gaccacccct 1200

ccggtgctgg actcagacgg atccttcttc ctctactcgc ggctgaccgt ggataagagc 1260

agatggcagg agggaaatgt gttcagctgt tctgtgatgc atgaagccct gcacaaccac 1320

tacactcaga agtccctgtc cctctccctg gga 1353

<210> 717
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 717
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

aggggccagc ggctggaatg gatcggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctctgcttc taccaagggg cccagcgtgt tccccctggc cccctgctcc 420

agaagcacca gcgagagcac agccgccctg ggctgcctgg tgaaggacta cttccccgag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgaccagcg gcgtgcacac cttccccgcc 540

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aagagggtgg agagcaagta cggcccaccc tgcccccct gcccagcccc cgagttcctg 720

ggcggaccca gcgtgttcct gttcccccc aagcccaagg acaccctgat gatcagcaga 780

acccccgagg tgacctgtgt ggtggtggac gtgtcccagg aggaccccga ggtccagttc 840

aactggtacg tggacggcgt ggaggtgcac aacgccaaga ccaagcccag agaggagcag 900

tttaacagca cctaccgggt ggtgtccgtg ctgaccgtgc tgcaccagga ctggctgaac 960

ggcaaagagt acaagtgtaa ggtctccaac aagggcctgc caagcagcat cgaaaagacc 1020

atcagcaagg ccaagggcca gcctagagag ccccaggtct acaccctgcc acccagccaa 1080

gaggagatga ccaagaacca ggtgtccctg acctgtctgg tgaagggctt ctacccaagc 1140

gacatcgccg tggagtggga gagcaacggc cagcccgaga acaactacaa gaccaccccc 1200

ccagtgctgg acagcgacgg cagcttcttc ctgtacagca ggctgaccgt ggacaagtcc 1260

agatggcagg agggcaacgt ctttagctgc tccgtgatgc acgaggccct gcacaaccac 1320

tacacccaga agagcctgag cctgtccctg ggc 1353

<210> 718
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 718
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 719
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 719
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gctctagtca ggatatctct aactacctga actggtatct gcagaagccc 120

ggtcaatcac ctcagctgct gatctactac actagcaccc tgcacctggg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctctag cctgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 720
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 720
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatct gcagaagccc 120

ggccagtccc ctcagctgct gatctactac acctccaccc tgcacctggg cgtgccctcc 180

agattttccg gctctggctc tggcaccgag tttaccctga ccatcagctc cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa g 321

<210> 721
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 721
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160


Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175


Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190


Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205


Phe Asn Arg Gly Glu Cys
    210


<210> 722
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 722
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact       60
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atcacctgta gctctagtca ggatatctct aactacctga actggtatct gcagaagccc 120

ggtcaatcac ctcagctgct gatctactac actagcaccc tgcacctggg cgtgccctct 180

aggtttagcg gtagcggtag tggcaccgag ttcaccctga ctatctctag cctgcagccc 240

gacgacttcg ctacctacta ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttcccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 723
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 723
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatct gcagaagccc 120

ggccagtccc ctcagctgct gatctactac acctccaccc tgcacctggg cgtgccctcc 180

agattttccg gctctggctc tggcaccgag tttaccctga ccatcagctc cctgcagccc 240

gacgacttcg ccacctacta ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa gcgtacggtg gccgctccca gcgtgttcat cttcccccca 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gtctgctgaa caacttctac 420

cccagggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gtgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 724
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 724
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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

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

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

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

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

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

115 120 125

<210> 725
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 725
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtc 60

agctgtaaag ctagtggctt caccctgact aactacggga tgaactgggt ccgccaggcc 120

ccaggtcaag gcctcgagtg gatgggctgg attaacaccg acaccggcga gcctacctac 180

gccgacgact ttaagggcag attcgtgttt agcctggaca ctagtgtgtc taccgcctac 240

ctgcagatct ctagcctgaa ggccgaggac accgccgtct actactgcgc tagaaacccc 300

ccctactact acggcactaa caacgccgag gctatggact actggggtca aggcactacc 360

gtgaccgtgt ctagc 375

<210> 726
<211> 375
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 726
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

cctggacagg gcctggaatg gatgggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctct 375

<210> 727
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 727
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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

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

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

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

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

Ala Arg Asn Pro Pro Tyr Tyr Tyr Gly Thr Asn Asn Ala Glu Ala Met
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
115 120 125

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Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
    130                 135                 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145                 150                 155                 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
                165                 170                 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
            180                 185                 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys
        195                 200                 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320
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Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser
                325                 330                 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr
                405                 410                 415

Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Leu Gly
    450


<210> 728
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"
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<400> 728

caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtc 60

agctgtaaag ctagtggctt caccctgact aactacggga tgaactgggt ccgccaggcc 120

ccaggtcaag gcctcgagtg gatgggctgg attaacaccg acaccggcga gcctacctac 180

gccgacgact ttaagggcag attcgtgttt agcctggaca ctagtgtgtc taccgcctac 240

ctgcagatct ctagcctgaa ggccgaggac accgccgtct actactgcgc tagaaacccc 300

ccctactact acggcactaa caacgccgag gctatggact actggggtca aggcactacc 360

gtgaccgtgt ctagcgctag cactaagggc ccgtccgtgt tccccctggc accttgtagc 420

cggagcacta gcgaatccac cgctgccctc ggctgcctgg tcaaggatta cttcccggag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgacctccg gagtgcacac cttccccgct 540

gtgctgcaga gctccgggct gtactcgctg tcgtcggtgg tcacggtgcc ttcatctagc 600

ctgggtacca agacctacac ttgcaacgtg gaccacaagc cttccaacac taaggtggac 660

aagcgcgtcg aatcgaagta cggcccaccg tgcccgcctt gtcccgcgcc ggagttcctc 720

ggcggtccct cggtctttct gttcccaccg aagcccaagg acactttgat gatttcccgc 780

acccctgaag tgacatgcgt ggtcgtggac gtgtcacagg aagatccgga ggtgcagttc 840

aattggtacg tggatggcgt cgaggtgcac aacgccaaaa ccaagccgag ggaggagcag 900

ttcaactcca cttaccgcgt cgtgtccgtg ctgacggtgc tgcatcagga ctggctgaac 960

gggaaggagt acaagtgcaa agtgtccaac aagggacttc ctagctcaat cgaaaagacc 1020

atctcgaaag ccaagggaca gccccgggaa ccccaagtgt ataccctgcc accgagccag 1080

gaagaaatga ctaagaacca agtctcattg acttgccttg tgaagggctt ctacccatcg 1140

gatatcgccg tggaatggga gtccaacggc cagccggaaa acaactacaa gaccacccct 1200

ccggtgctgg actcagacgg atccttcttc ctctactcgc ggctgaccgt ggataagagc 1260

agatggcagg agggaaatgt gttcagctgt tctgtgatgc atgaagccct gcacaaccac 1320

tacactcaga agtccctgtc cctctccctg gga 1353

<210> 729
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 729
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ctggcgcctc cgtgaaggtg 60

tcctgcaagg cctctggctt caccctgacc aactacggca tgaactgggt gcgacaggcc 120

cctggacagg gcctggaatg gatgggctgg atcaacaccg acaccggcga gcctacctac 180

gccgacgact tcaagggcag attcgtgttc tccctggaca cctccgtgtc caccgcctac 240

ctgcagatct ccagcctgaa ggccgaggat accgccgtgt actactgcgc ccggaacccc 300

ccttactact acggcaccaa caacgccgag gccatggact attggggcca gggcaccacc 360

gtgaccgtgt cctctgcttc taccaagggg cccagcgtgt tccccctggc cccctgctcc 420

agaagcacca gcgagagcac agccgccctg ggctgcctgg tgaaggacta cttccccgag 480

cccgtgaccg tgtcctggaa cagcggagcc ctgaccagcg gcgtgcacac cttccccgcc 540

gtgctgcaga gcagcggcct gtacagcctg agcagcgtgg tgaccgtgcc cagcagcagc 600

ctgggcacca agacctacac ctgtaacgtg gaccacaagc ccagcaacac caaggtggac 660

aagagggtgg agagcaagta cggcccaccc tgcccccct gcccagcccc cgagttcctg 720

ggcggaccca gcgtgttcct gttcccccc aagcccaagg acaccctgat gatcagcaga 780

acccccgagg tgacctgtgt ggtggtggac gtgtcccagg aggaccccga ggtccagttc 840

aactggtacg tggacggcgt ggaggtgcac aacgccaaga ccaagcccag agaggagcag 900

tttaacagca cctaccgggt ggtgtccgtg ctgaccgtgc tgcaccagga ctggctgaac 960

ggcaaagagt acaagtgtaa ggtctccaac aagggcctgc caagcagcat cgaaaagacc 1020

atcagcaagg ccaagggcca gcctagagag ccccaggtct acaccctgcc acccagccaa 1080

gaggagatga ccaagaacca ggtgtccctg acctgtctgg tgaagggctt ctacccaagc 1140

gacatcgccg tggagtggga gagcaacggc cagcccgaga acaactacaa gaccaccccc 1200

ccagtgctgg acagcgacgg cagcttcttc ctgtacagca ggctgaccgt ggacaagtcc 1260

agatggcagg agggcaacgt ctttagctgc tccgtgatgc acgaggccct gcacaaccac 1320

tacacccaga agagcctgag cctgtccctg ggc 1353

<210> 730
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 730
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Leu Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Asn Asn Ile Glu Ser
65 70 75 80

Glu Asp Ala Ala Tyr Tyr Phe Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 731
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 731
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gctctagtca ggatatctct aactacctga actggtatca gcagaagccc 120

ggtaaagccc ctaagctgct gatctactac actagcaccc tgcacctggg aatcccccct 180

aggtttagcg gtagcggcta cggcaccgac ttcaccctga ctattaacaa tatcgagtca 240

gaggacgccg cctactactt ctgtcagcag tactataacc tgccctggac cttcggtcaa 300

ggcactaagg tcgagattaa g 321

<210> 732
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 732
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatca gcagaagccc 120

ggcaaggccc ccaagctgct gatctactac acctccaccc tgcacctggg catccccct 180

agattctccg gctctggcta cggcaccgac ttcaccctga ccatcaacaa catcgagtcc 240

gaggacgccg cctactactt ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa g 321

<210> 733
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 733

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15


Asp Arg Val Thr Ile Thr Cys Ser Ser Ser Gln Asp Ile Ser Asn Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Tyr Thr Ser Thr Leu His Leu Gly Ile Pro Pro Arg Phe Ser Gly
    50                  55                  60


Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Asn Asn Ile Glu Ser
65                  70                  75                  80


Glu Asp Ala Ala Tyr Tyr Phe Cys Gln Gln Tyr Tyr Asn Leu Pro Trp
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
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Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160


Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175


Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190


Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205


Phe Asn Arg Gly Glu Cys
    210


<210> 734
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 734
gatattcaga tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact       60

atcacctgta gctctagtca ggatatctct aactacctga actggtatca gcagaagccc      120

ggtaaagccc ctaagctgct gatctactac actagcaccc tgcacctggg aatcccccct      180

aggtttagcg gtagcggcta cggcaccgac ttcaccctga ctattaacaa tatcgagtca      240

gaggacgccg cctactactt ctgtcagcag tactataacc tgccctggac cttcggtcaa      300

ggcactaagg tcgagattaa gcgtacggtg gccgctccca gcgtgttcat cttccccccc      360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac      420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag      480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc      540
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ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 735
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 735
gacatccaga tgacccagtc cccctccagc ctgtctgctt ccgtgggcga cagagtgacc 60

atcacctgtt cctccagcca ggacatctcc aactacctga actggtatca gcagaagccc 120

ggcaaggccc ccaagctgct gatctactac acctccaccc tgcacctggg catcccccct 180

agattctccg gctctggcta cggcaccgac ttcaccctga ccatcaacaa catcgagtcc 240

gaggacgccg cctactactt ctgccagcag tactacaacc tgccctggac cttcggccag 300

ggcaccaagg tggaaatcaa gcgtacggtg gccgctccca gcgtgttcat cttcccccca 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gtctgctgaa caacttctac 420

cccagggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gtgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 736
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

oligonucleotide"

<400> 736
aattacggga tgaac 15

<210> 737
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 737
aactacggca tgaac 15

<210> 738
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 738
tggattaaca ccgacaccgg ggagcctacc tacgcggacg atttcaaggg a 51

<210> 739
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 739
tggatcaaca ccgacaccgg cgagcctacc tacgccgacg acttcaaggg c 51

<210> 740
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 740
aacccgccct actactacgg aaccaacaac gccgaagcca tggactac 48

<210> 741
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 741
aacccccctt actactacgg caccaacaac gccgaggcca tggactat 48

<210> 742
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 742
ggattcaccc tcaccaatta c 21

<210> 743
<211> 21
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 743
ggcttcaccc tgaccaacta c 21

<210> 744
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 744
aacaccgaca ccggggag 18

<210> 745
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 745
aacaccgaca ccggcgag 18

<210> 746
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 746
agctctagtc aggatatctc taactacctg aac 33

<210> 747
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 747
tcctccagcc aggacatctc caactacctg aac 33

<210> 748
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 748
tacactagca ccctgcacct g 21

<210> 749
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 749
tacacctcca ccctgcacct g 21

<210> 750
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 750
cagcagtact ataacctgcc ctggacc 27

<210> 751
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 751
cagcagtact acaacctgcc ctggacc 27

<210> 752
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 752
agtcaggata tctctaacta c 21

<210> 753
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 753
agccaggaca tctccaacta c 21

<210> 754
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 754
tacactagc 9

<210> 755
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 755
tacacctcc 9

<210> 756
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 756
tactataacc tgccctgg 18

<210> 757
<211> 18

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 757
tactacaacc tgccctgg 18

<210> 758
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 758
aactacggga tgaac 15

<210> 759
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 759
tggattaaca ccgacaccgg cgagcctacc tacgccgacg actttaaggg c 51

<210> 760
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

oligonucleotide"

<400> 760
aacccccccct actactacgg cactaacaac gccgaggcta tggactac 48

<210> 761
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 761
ggcttcaccc tgactaacta c 21

<210> 762
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 762
Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

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

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

Gly Glu Ile Asn His Arg Gly Ser Thr Asn Ser Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Leu Ser Leu Asp Thr Ser Lys Asn Gln Phe Ser Leu

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65                  70                  75                  80

Lys Leu Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Phe Gly Tyr Ser Asp Tyr Glu Tyr Asn Trp Phe Asp Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
```

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            260                 265                 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440                 445
```

<210> 763

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

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 763

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Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45


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


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu
                85                  90                  95


Thr Phe Gly Gln Gly Thr Asn Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
```

```
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175


Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190


Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205


Phe Asn Arg Gly Glu Cys
    210


<210> 764
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 764
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1               5                   10                  15


Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ala Tyr
            20                  25                  30


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


Gly Met Ile Trp Asp Asp Gly Ser Thr Asp Tyr Asn Ser Ala Leu Lys
    50                  55                  60


Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65                  70                  75                  80
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Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Arg Tyr Tyr Cys Ala
                85                  90                  95

Arg Glu Gly Asp Val Ala Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270
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Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285


Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300


Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320


Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335


Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350


Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365


Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380


Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400


Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415


Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430


Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> 765
<211> 220
<212> PRT
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<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 765
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Val Gly
1 5 10 15

Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Gly
20 25 30

Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

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

Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr Phe Cys Leu Gln
85 90 95

His Phe Gly Thr Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

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

```
Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175


Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190


Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205


Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220


<210> 766
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 766
Gly Phe Thr Leu Thr Asn Tyr Gly Met Asn
1               5                   10


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<210> 801
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 801
Ser Tyr Asn Met His
1 5

<210> 802
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 802
Asp Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 803
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 803
Val Gly Gly Ala Phe Pro Met Asp Tyr
1 5

<210> 804
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 804
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 805
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 805
Tyr Pro Gly Asn Gly Asp
1 5

<210> 806
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 806
Gln Val 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 Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 807
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 807
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggctctag cgtgaaagtt 60

tcttgtaaag ctagtggcta caccttcact agctataata tgcactgggt tcgccaggcc 120

ccagggcaag gcctcgagtg gatgggcgat atctaccccg ggaacggcga cactagttat 180

aatcagaagt ttaagggtag agtcactatc accgccgata agtctactag caccgtctat 240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc ctatggacta ctggggtcaa ggcactaccg tgaccgtgtc tagc 354

<210> 808
<211> 444
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 808
Gln Val 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 Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser 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 Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350
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```
Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365


Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380


Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400


Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415


Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430


His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440


<210> 809
<211> 1332
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 809
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggctctag cgtgaaagtt       60

tcttgtaaag ctagtggcta caccttcact agctataata tgcactgggt tcgccaggcc      120

ccagggcaag gcctcgagtg gatgggcgat atctaccccg ggaacggcga cactagttat      180

aatcagaagt ttaagggtag agtcactatc accgccgata agtctactag caccgtctat      240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc      300

ggagccttcc ctatggacta ctggggtcaa ggcactaccg tgaccgtgtc tagcgctagc      360

actaagggcc cgtccgtgtt ccccctggca ccttgtagcc ggagcactag cgaatccacc      420
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gctgccctcg gctgcctggt caaggattac ttcccggagc ccgtgaccgt gtcctggaac 480

agcggagccc tgacctccgg agtgcacacc ttccccgctg tgctgcagag ctccgggctg 540

tactcgctgt cgtcggtggt cacggtgcct tcatctagcc tgggtaccaa gacctacact 600

tgcaacgtgg accacaagcc ttccaacact aaggtggaca agcgcgtcga atcgaagtac 660

ggcccaccgt gcccgccttg tcccgcgccg gagttcctcg gcggtccctc ggtctttctg 720

ttcccaccga agcccaagga cactttgatg atttcccgca cccctgaagt gacatgcgtg 780

gtcgtggacg tgtcacagga agatccggag gtgcagttca attggtacgt ggatggcgtc 840

gaggtgcaca acgccaaaac caagccgagg gaggagcagt tcaactccac ttaccgcgtc 900

gtgtccgtgc tgacggtgct gcatcaggac tggctgaacg ggaaggagta caagtgcaaa 960

gtgtccaaca agggacttcc tagctcaatc gaaaagacca tctcgaaagc caagggacag 1020

ccccgggaac cccaagtgta taccctgcca ccgagccagg aagaaatgac taagaaccaa 1080

gtctcattga cttgccttgt gaagggcttc tacccatcgg atatcgccgt ggaatgggag 1140

tccaacggcc agccggaaaa caactacaag accacccctc cggtgctgga ctcagacgga 1200

tccttcttcc tctactcgcg gctgaccgtg gataagagca gatggcagga gggaaatgtg 1260

ttcagctgtt ctgtgatgca tgaagccctg cacaaccact acactcagaa gtccctgtcc 1320

ctctccctgg ga 1332

<210> 810
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 810
Arg Ala Ser Glu Ser Val Glu Tyr Tyr Gly Thr Ser Leu Met Gln
1 5 10 15

<210> 811
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 811
Ala Ala Ser Asn Val Glu Ser
1 5

<210> 812
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 812
Gln Gln Ser Arg Lys Asp Pro Ser Thr
1 5

<210> 813
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 813
Ser Glu Ser Val Glu Tyr Tyr Gly Thr Ser Leu
1 5 10

<210> 814
<211> 3

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 814
Ala Ala Ser
1

<210> 815
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 815
Ser Arg Lys Asp Pro Ser
1 5

<210> 816
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 816
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
20 25 30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro

35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Ser
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Ser Arg
85 90 95

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 817
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 817
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat 120

cagcagaagc ccgggaaagc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca 180

ggcgtgccct ctaggtttag cggtagcggt agtggcaccg acttcaccct gactatctct 240

agcctgcagc ccgaggactt cgctacctac ttctgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aag 333

<210> 818
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 818

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Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
            20                  25                  30


Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
        35                  40                  45


Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Ser
    50                  55                  60


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80


Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Ser Arg
                85                  90                  95


Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110


Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125


Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140


Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175
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Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 819
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 819
gctattcagc tgactcagtc acctagtagc ctgagcgcta gtgtgggcga tagagtgact 60

atcacctgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat 120

cagcagaagc ccgggaaagc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca 180

ggcgtgccct ctaggtttag cggtagcggt agtggcaccg acttcaccct gactatctct 240

agcctgcagc ccgaggactt cgctacctac ttctgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aagcgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgtccag ccccgtgacc aagagcttca acaggggcga gtgc 654

<210> 820
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 820
Asp Ile Tyr Pro Gly Gln Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 821
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 821
Tyr Pro Gly Gln Gly Asp
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<210> 822
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 822
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


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


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


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


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210> 823
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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<400> 823
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtt       60

agctgtaaag ctagtggcta tactttcact tcttataata tgcactgggt ccgccaggcc      120

ccaggtcaag gcctcgagtg gatcggcgat atctaccccg gtcaaggcga cacttcctat      180

aatcagaagt ttaagggtag agctactatg accgccgata agtctacttc taccgtctat      240
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atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc caatggacta ctggggtcaa ggcaccctgg tcaccgtgtc tagc 354

<210> 824
<211> 444
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 824
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

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

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

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

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Gly Ala Phe Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

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Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser 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 Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320
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Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440


<210> 825
<211> 1332
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 825
caggtgcagc tggtgcagtc aggcgccgaa gtgaagaaac ccggcgctag tgtgaaagtt       60

agctgtaaag ctagtggcta tactttcact tcttataata tgcactgggt ccgccaggcc      120

ccaggtcaag gcctcgagtg gatcggcgat atctaccccg gtcaaggcga cacttcctat      180
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aatcagaagt ttaagggtag agctactatg accgccgata agtctacttc taccgtctat 240

atggaactga gttccctgag gtctgaggac accgccgtct actactgcgc tagagtgggc 300

ggagccttcc caatggacta ctggggtcaa ggcaccctgg tcaccgtgtc tagcgctagc 360

actaagggcc cgtccgtgtt ccccctggca ccttgtagcc ggagcactag cgaatccacc 420

gctgccctcg gctgcctggt caaggattac ttcccggagc ccgtgaccgt gtcctggaac 480

agcggagccc tgacctccgg agtgcacacc ttccccgctg tgctgcagag ctccgggctg 540

tactcgctgt cgtcggtggt cacggtgcct tcatctagcc tgggtaccaa gacctacact 600

tgcaacgtgg accacaagcc ttccaacact aaggtggaca agcgcgtcga atcgaagtac 660

ggcccaccgt gcccgccttg tcccgcgccg gagttcctcg gcggtccctc ggtctttctg 720

ttcccaccga agcccaagga cactttgatg atttcccgca cccctgaagt gacatgcgtg 780

gtcgtggacg tgtcacagga agatccggag gtgcagttca attggtacgt ggatggcgtc 840

gaggtgcaca acgccaaaac caagccgagg gaggagcagt tcaactccac ttaccgcgtc 900

gtgtccgtgc tgacggtgct gcatcaggac tggctgaacg ggaaggagta caagtgcaaa 960

gtgtccaaca agggacttcc tagctcaatc gaaaagacca tctcgaaagc caagggacag 1020

ccccgggaac cccaagtgta taccctgcca ccgagccagg aagaaatgac taagaaccaa 1080

gtctcattga cttgccttgt gaagggcttc tacccatcgg atatcgccgt ggaatgggag 1140

tccaacggcc agccggaaaa caactacaag accacccctc cggtgctgga ctcagacgga 1200

tccttcttcc tctactcgcg gctgaccgtg gataagagca gatggcagga gggaaatgtg 1260

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ctctccctgg ga 1332

<210> 826
<211> 111
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 826

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

<210> 827
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 827
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cagcagaagc ccggtcaacc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca 180

ggcgtgcccg ataggtttag cggtagcggt agtggcaccg acttcaccct gactattagt 240

agcctgcagg ccgaggacgt ggccgtctac tactgtcagc agtctaggaa ggaccctagc 300

accttcggcg gaggcactaa ggtcgagatt aag 333

<210> 828
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 828
Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Glu Tyr Tyr
20 25 30

Gly Thr Ser Leu Met Gln Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Val Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

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

Lys Asp Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

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Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125


Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140


Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160


Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175


Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190


His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 829
<211> 654
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 829
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attaactgta gagctagtga atcagtcgag tactacggca ctagcctgat gcagtggtat      120

cagcagaagc ccggtcaacc ccctaagctg ctgatctacg ccgcctctaa cgtggaatca      180

ggcgtgcccg ataggtttag cggtagcggt agtggcaccg acttcaccct gactattagt      240

agcctgcagg ccgaggacgt ggccgtctac tactgtcagc agtctaggaa ggaccctagc      300
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accttcggcg gaggcactaa ggtcgagatt aagcgtacgg tggccgctcc cagcgtgttc 360

atcttccccc ccagcgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt caccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctga ccctgagcaa ggccgactac gagaagcata aggtgtacgc ctgcgaggtg 600

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<210> 830
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 830
Glu Val 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 Ala Ala Ser Gly Phe Thr Phe Ser Ser
20 25 30

Tyr Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp
35 40 45

Val Ser Thr Ile Ser Gly Gly Gly Thr Tyr Thr Tyr Tyr Gln Asp Ser
50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
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 Ser Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser
100 105 110

Ser Ala

<210> 831
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 831
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Arg Tyr
20 25 30

Leu Asn Trp Tyr His Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser His Ser Ala Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 832
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<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 832
Glu Val Gln Val Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
35 40 45

Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser
50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
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 Lys Lys Tyr Tyr Val Gly Pro Ala Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly
115 120

<210> 833
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 833
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

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

Tyr Tyr Ser Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Ile Glu Val
100 105 110

Lys

<210> 834

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<210> 901
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 901
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Ser Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Ser Ser Tyr
20 25 30

Gly Val Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Val Ile Trp Gly Gly Gly Gly Thr Tyr Tyr Ala Ser Ser Leu Met
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

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

Arg His Ala Tyr Gly His Asp Gly Gly Phe Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 902
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 902
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Ser Ser Asn
20 25 30

Val Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gly Gln Ser Tyr Ser Tyr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 903
<211> 451
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 903

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Ser Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Ser Ser Tyr
            20                  25                  30

Gly Val Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Gly Val Ile Trp Gly Gly Gly Gly Thr Tyr Tyr Ala Ser Ser Leu Met
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

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

Arg His Ala Tyr Gly His Asp Gly Gly Phe Ala Met Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175
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Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

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

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365
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Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380


Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400


Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415


Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430


His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445


Pro Gly Lys
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<210> 904
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

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Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Ser Ser Asn
            20                  25                  30


Val Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45
```

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Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gly Gln Ser Tyr Ser Tyr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
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<210> 905
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
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polynucleotide"

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cctggcaagg gcctggaatg ggtgggagtg atctggggcg gaggcggcac ctactacgcc 180

tcttccctga tgggccggtt caccatctcc cgggacaact ccaagaacac cctgtacctg 240

cagatgaact ccctgcgggc cgaggacacc gccgtgtact actgcgccag acacgcctac 300

ggccacgacg gcggcttcgc catggattat tggggccagg gcaccctggt gacagtgtcc 360

tcc 363

<210> 906
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 906
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ggtcaggccc ctcggctgct gatctacggc gcctctaacc gggccaccgg catccctgcc 180

agattctccg gctccggcag cggcaccgac ttcaccctga ccatctcccg gctggaaccc 240

gaggacttcg ccgtgtacta ctgcggccag tcctactcat acccccttcac cttcggccag 300

ggcaccaagc tggaaatcaa g 321

<210> 907
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<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 907
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tcttgcgctg cctccggctt ctccctgtcc tcttacggcg tggactgggt gcgacaggcc 120

cctggcaagg gcctggaatg ggtgggagtg atctggggcg gaggcggcac ctactacgcc 180

tcttccctga tgggccggtt caccatctcc cgggacaact ccaagaacac cctgtacctg 240

cagatgaact ccctgcgggc cgaggacacc gccgtgtact actgcgccag acacgcctac 300

ggccacgacg gcggcttcgc catggattat tggggccagg gcaccctggt gacagtgtcc 360

tccgctagca ccaagggccc aagtgtgttt cccctggccc ccagcagcaa gtctacttcc 420

ggcggaactg ctgccctggg ttgcctggtg aaggactact tccccgagcc cgtgacagtg 480

tcctggaact ctggggctct gacttccggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg acagtgccct ccagctctct gggaacccag 600

acctatatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gagagtggag 660

cccaagagct gcgacaagac ccacacctgc ccccctgcc cagctccaga actgctggga 720

gggccttccg tgttcctgtt ccccccaag cccaaggaca ccctgatgat cagcaggacc 780

cccgaggtga cctgcgtggt ggtggacgtg tcccacgagg acccagaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agcccagaga ggagcagtac 900

aacagcacct acagggtggt gtccgtgctg accgtgctgc accaggactg gctgaacggc 960

aaagaataca agtgcaaagt ctccaacaag gccctgccag ccccaatcga aaagacaatc 1020

agcaaggcca agggccagcc acgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctgacc tgtctggtga agggcttcta ccccagcgat 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccca 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tgaccgtgga caagtccagg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaagt ccctgagcct gagccccggc aag 1353

<210> 908
<211> 642
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 908
gagatcgtga tgacccagtc ccccgccacc ctgtctgtgt ctcccggcga gagagccacc 60

ctgagctgca gagcctccga gtccgtgtcc tccaacgtgg cctggtatca gcagagacct 120

ggtcaggccc ctcggctgct gatctacggc gcctctaacc gggccaccgg catccctgcc 180

agattctccg gctccggcag cggcaccgac ttcaccctga ccatctcccg gctggaaccc 240

gaggacttcg ccgtgtacta ctgcggccag tcctactcat acccccttcac cttcggccag 300

ggcaccaagc tggaaatcaa gcgtacggtg gccgctccca gcgtgttcat cttcccccccc 360

agcgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtca ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctgacc 540

ctgagcaagg ccgactacga gaagcataag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgtccagcc ccgtgaccaa gagcttcaac aggggcgagt gc 642

<210> 909
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<212> PRT
<213> Artificial Sequence

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<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 909
Ser Tyr Gly Val Asp
1 5

<210> 910
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 910
Gly Phe Ser Leu Ser Ser Tyr
1 5

<210> 911
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 911
Val Ile Trp Gly Gly Gly Gly Thr Tyr Tyr Ala Ser Ser Leu Met Gly
1 5 10 15

<210> 912
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 912
Trp Gly Gly Gly Gly
1   5

<210> 913
<211> 13
<212> PRT
<213> Artificial Sequence

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<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 913
His Ala Tyr Gly His Asp Gly Gly Phe Ala Met Asp Tyr
1   5   10

<210> 914
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
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<400> 914
Arg Ala Ser Glu Ser Val Ser Ser Asn Val Ala
1   5   10

<210> 915
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 915
Ser Glu Ser Val Ser Ser Asn

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<210> 916
<211> 7
<212> PRT
<213> Artificial Sequence

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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 916
Gly Ala Ser Asn Arg Ala Thr
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<210> 917
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<220>
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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 917
Gly Ala Ser
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<210> 918
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<213> Artificial Sequence

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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 918
Gly Gln Ser Tyr Ser Tyr Pro Phe Thr
1 5

<210> 919
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<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 919
Ser Tyr Ser Tyr Pro Phe
1 5

<210> 920
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 920
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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

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Ala Arg Gly Gly Ser Met Val Arg Gly Asp Tyr Tyr Tyr Gly Met Asp
            100                 105                 110


Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 921
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 921
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Tyr
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
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<210> 1001
<211> 114
<212> PRT
<213> Homo sapiens

<400> 1001
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
1   5   10   15

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
            20   25   30

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

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
    50   55   60

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
65   70   75   80

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
                85   90   95

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
            100   105   110

Thr Ser

<210> 1002
<211> 170
<212> PRT
<213> Homo sapiens

<400> 1002
Ile Thr Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val
1   5   10   15

Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly
            20   25   30

Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn

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        35                  40                  45

Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile
    50                  55                  60

Arg Asp Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro Ser Thr Val
65                  70                  75                  80

Thr Thr Ala Gly Val Thr Pro Gln Pro Glu Ser Leu Ser Pro Ser Gly
                85                  90                  95

Lys Glu Pro Ala Ala Ser Ser Pro Ser Ser Asn Asn Thr Ala Ala Thr
            100                 105                 110

Thr Ala Ala Ile Val Pro Gly Ser Gln Leu Met Pro Ser Lys Ser Pro
        115                 120                 125

Ser Thr Gly Thr Thr Glu Ile Ser Ser His Glu Ser Ser His Gly Thr
    130                 135                 140

Pro Ser Gln Thr Thr Ala Lys Asn Trp Glu Leu Thr Ala Ser Ala Ser
145                 150                 155                 160

His Gln Pro Pro Gly Val Tyr Pro Gln Gly
                165                 170


<210> 1003
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1003
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
1               5                   10                  15
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```
Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
            20                  25                  30


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


Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
    50                  55                  60


Asn Leu Ile Ile Leu Ala Asn Asp Ser Leu Ser Ser Asn Gly Asn Val
65                  70                  75                  80


Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
                85                  90                  95


Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
            100                 105                 110


Thr Ser



<210> 1004
<211> 297
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1004
Ile Thr Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val
1               5                   10                  15


Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly
            20                  25                  30
```

```
Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn
        35                  40                  45

Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile
    50                  55                  60

Arg Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
65                  70                  75                  80

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
                85                  90                  95

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            100                 105                 110

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        115                 120                 125

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    130                 135                 140

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
145                 150                 155                 160

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                165                 170                 175

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            180                 185                 190

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        195                 200                 205

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    210                 215                 220
```

```
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
225                 230                 235                 240


Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                245                 250                 255


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            260                 265                 270


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        275                 280                 285


Lys Ser Leu Ser Leu Ser Pro Gly Lys
    290                 295


<210> 1005
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"


<220>
<221> VARIANT
<222> (93)..(93)
<223> /replace="Lys"

<220>
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<222> (1)..(114)
<223> /note="Variant residues given in the sequence have no
      preference with respect to those in the annotations
      for variant positions"

<400> 1005
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
1               5                   10                  15
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```
Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
            20                  25                  30


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


Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
    50                  55                  60


Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
65                  70                  75                  80


Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
                85                  90                  95


Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
            100                 105                 110


Thr Ser



<210> 1006
<211> 77
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1006
Ile Thr Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val
1               5                   10                  15


Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly
            20                  25                  30
```

```
Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn
        35                  40                  45


Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile
    50                  55                  60


Arg Asp Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro
65                  70                  75


<210> 1007
<211> 422
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1007
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                   10                  15


His Ser Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp
            20                  25                  30


Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp
        35                  40                  45


Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu
    50                  55                  60


Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr
65                  70                  75                  80


Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly
                85                  90                  95


Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys
```

```
            100                 105                 110

Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe
        115                 120                 125

Ile Asn Thr Ser Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Leu Gln Ile Thr
145                 150                 155                 160

Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val Lys Ser
                165                 170                 175

Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly Phe Lys
            180                 185                 190

Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn Lys Ala
        195                 200                 205

Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile Arg Asp
    210                 215                 220

Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro Ser Thr Val Thr Thr
225                 230                 235                 240

Ala Gly Val Thr Pro Gln Pro Glu Ser Leu Ser Pro Ser Gly Lys Glu
                245                 250                 255

Pro Ala Ala Ser Ser Pro Ser Ser Asn Asn Thr Ala Ala Thr Thr Ala
            260                 265                 270

Ala Ile Val Pro Gly Ser Gln Leu Met Pro Ser Lys Ser Pro Ser Thr
        275                 280                 285

Gly Thr Thr Glu Ile Ser Ser His Glu Ser Ser His Gly Thr Pro Ser
```

290 295 300

Gln Thr Thr Ala Lys Asn Trp Glu Leu Thr Ala Ser Ala Ser His Gln
305 310 315 320

Pro Pro Gly Val Tyr Pro Gln Gly His Ser Asp Thr Thr Val Ala Ile
325 330 335

Ser Thr Ser Thr Val Leu Leu Cys Gly Leu Ser Ala Val Ser Leu Leu
340 345 350

Ala Cys Tyr Leu Lys Ser Arg Gln Thr Pro Pro Leu Ala Ser Val Glu
355 360 365

Met Glu Ala Met Glu Ala Leu Pro Val Thr Trp Gly Thr Ser Ser Arg
370 375 380

Asp Glu Asp Leu Glu Asn Cys Ser His His Leu Ser Arg Met Asp Tyr
385 390 395 400

Lys Asp Asp Asp Asp Lys Asp Tyr Lys Asp Asp Asp Asp Lys Asp Tyr
405 410 415

Lys Asp Asp Asp Asp Lys
420

<210> 1008
<211> 209
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1008
Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val Lys Ser
1 5 10 15

```
Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly Phe Lys
            20                  25                  30

Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn Lys Ala
        35                  40                  45

Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile Arg Asp
    50                  55                  60

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

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu Gln Asn
                85                  90                  95

Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile Gln
            100                 105                 110

Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His Pro
        115                 120                 125

Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln Val
    130                 135                 140

Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu Asn
145                 150                 155                 160

Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val Thr
                165                 170                 175

Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile Lys
            180                 185                 190

Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn Thr
        195                 200                 205
```

Ser

<210> 1009
<211> 459
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1009
Ala Cys Asp Cys Arg Gly Asp Cys Phe Cys Gly Gly Gly Gly Gly Ser
1 5 10 15

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
20 25 30

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
35 40 45

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
50 55 60

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
65 70 75 80

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
85 90 95

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

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
115 120 125

```
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
    130                 135                 140

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
145                 150                 155                 160

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
                165                 170                 175

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
            180                 185                 190

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
        195                 200                 205

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
    210                 215                 220

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
225                 230                 235                 240

Pro Gly Lys Gly Gly Gly Gly Ser Pro Pro Pro Met Ser Val Glu His
                245                 250                 255

Ala Asp Ile Trp Val Lys Ser Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr
            260                 265                 270

Ile Cys Asn Ser Gly Phe Lys Arg Lys Ala Gly Thr Ser Ser Leu Thr
        275                 280                 285

Glu Cys Val Leu Asn Lys Ala Thr Asn Val Ala His Trp Thr Thr Pro
    290                 295                 300

Ser Leu Lys Cys Ile Arg Asp Pro Ala Leu Val His Gln Arg Pro Ala
305                 310                 315                 320
```

```
Pro Pro Ser Thr Val Ser Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
                325                 330                 335


Gly Ser Gly Gly Gly Gly Ser Leu Gln Asn Trp Val Asn Val Ile Ser
            340                 345                 350


Asp Leu Lys Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala
        355                 360                 365


Thr Leu Tyr Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala
    370                 375                 380


Met Lys Cys Phe Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly
385                 390                 395                 400


Asp Ala Ser Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn
                405                 410                 415


Asn Ser Leu Ser Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu
            420                 425                 430


Cys Glu Glu Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe
        435                 440                 445


Val His Ile Val Gln Met Phe Ile Asn Thr Ser
    450                 455


<210> 1010
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      6xHis tag"

<400> 1010
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His His His His His His
1   5

<210> 1011
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1011
Arg Gly Asp Ser
1

<210> 1012
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1012
Gln Val 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 Ala Ser Gly Tyr Thr Phe Ser Ser Asn
            20   25   30

Val Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Gly Val Ile Pro Ile Val Asp Ile Ala Asn Tyr Ala Gln Arg Phe
    50   55   60

Lys Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Thr Tyr
65   70   75   80

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Thr Leu Gly Leu Val Leu Asp Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
    210                 215                 220

Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
            260                 265                 270
```

```
Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
        435                 440                 445
```

<210> 1013
<211> 215

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1013

```
Glu Thr Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Gly Ser Ser
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Tyr Gly Ala Ser Ser Arg Ala Pro Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Asp Ser Pro
                85                  90                  95


Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala
            100                 105                 110


Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125


Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140


Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160
```

```
Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175


Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190


Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205


Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 1014
<211> 478
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1014
Met Leu Leu Val Asn Gln Ser His Gln Gly Phe Asn Lys Glu His Thr
1               5                   10                  15


Ser Lys Met Val Ser Ala Ile Val Leu Tyr Val Leu Leu Ala Ala Ala
            20                  25                  30


Ala His Ser Ala Phe Ala Thr Arg Asp Val Arg Glu Pro Pro Ala Leu
        35                  40                  45


Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser Ser His Thr Ser Met Phe
    50                  55                  60


Ile Tyr Lys Trp Pro Ala Asp Lys Glu Asn Asp Thr Gly Ile Val Gly
65                  70                  75                  80
```

```
Gln His Ser Ser Cys Asp Val Pro Gly Gly Gly Ile Ser Ser Tyr Ala
                85                  90                  95

Asp Asn Pro Ser Gly Ala Ser Gln Ser Leu Val Gly Cys Leu Glu Gln
            100                 105                 110

Ala Leu Gln Asp Val Pro Lys Glu Arg His Ala Gly Thr Pro Leu Tyr
        115                 120                 125

Leu Gly Ala Thr Ala Gly Met Arg Leu Leu Asn Leu Thr Asn Pro Glu
    130                 135                 140

Ala Ser Thr Ser Val Leu Met Ala Val Thr His Thr Leu Thr Gln Tyr
145                 150                 155                 160

Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu Ser Gly Gln Glu Glu Gly
                165                 170                 175

Val Phe Gly Trp Val Thr Ala Asn Tyr Leu Leu Glu Asn Phe Ile Lys
            180                 185                 190

Tyr Gly Trp Val Gly Arg Trp Phe Arg Pro Arg Lys Gly Thr Leu Gly
        195                 200                 205

Ala Met Asp Leu Gly Gly Ala Ser Thr Gln Ile Thr Phe Glu Thr Thr
    210                 215                 220

Ser Pro Ala Glu Asp Arg Ala Ser Glu Val Gln Leu His Leu Tyr Gly
225                 230                 235                 240

Gln His Tyr Arg Val Tyr Thr His Ser Phe Leu Cys Tyr Gly Arg Asp
                245                 250                 255

Gln Val Leu Gln Arg Leu Leu Ala Ser Ala Leu Gln Thr His Gly Phe
            260                 265                 270
```

```
His Pro Cys Trp Pro Arg Gly Phe Ser Thr Gln Val Leu Leu Gly Asp
        275                 280                 285

Val Tyr Gln Ser Pro Cys Thr Met Ala Gln Arg Pro Gln Asn Phe Asn
    290                 295                 300

Ser Ser Ala Arg Val Ser Leu Ser Gly Ser Ser Asp Pro His Leu Cys
305                 310                 315                 320

Arg Asp Leu Val Ser Gly Leu Phe Ser Phe Ser Ser Cys Pro Phe Ser
                325                 330                 335

Arg Cys Ser Phe Asn Gly Val Phe Gln Pro Pro Val Ala Gly Asn Phe
            340                 345                 350

Val Ala Phe Ser Ala Phe Phe Ala Thr Val Asp Phe Leu Arg Thr Ser
        355                 360                 365

Met Gly Leu Pro Val Ala Thr Leu Gln Gln Leu Glu Ala Ala Ala Val
    370                 375                 380

Asn Val Cys Asn Gln Thr Trp Ala Gln Leu Gln Ala Arg Val Pro Gly
385                 390                 395                 400

Gln Arg Ala Arg Leu Ala Asp Tyr Cys Ala Gly Ala Met Phe Val Gln
                405                 410                 415

Gln Leu Leu Ser Arg Gly Tyr Gly Phe Asp Glu Arg Ala Phe Gly Gly
            420                 425                 430

Val Ile Phe Gln Lys Lys Ala Ala Asp Thr Ala Val Gly Trp Ala Leu
        435                 440                 445

Gly Tyr Met Leu Asn Leu Thr Asn Leu Ile Pro Ala Asp Pro Pro Gly
    450                 455                 460
```

Leu Arg Lys Gly Thr Asp Phe Ser His His His His His His
465 470 475

<210> 1015
<211> 478
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1015
Met Leu Leu Val Asn Gln Ser His Gln Gly Phe Asn Lys Glu His Thr
1 5 10 15

Ser Lys Met Val Ser Ala Ile Val Leu Tyr Val Leu Leu Ala Ala Ala
20 25 30

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

Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser Ser His Thr Ser Met Phe
50 55 60

Val Tyr Lys Trp Pro Ala Asp Lys Glu Asn Asp Thr Gly Ile Val Gly
65 70 75 80

Gln His Ser Ser Cys Asp Val Arg Gly Gly Gly Ile Ser Ser Tyr Ala
85 90 95

Asn Asp Pro Ser Arg Ala Gly Gln Ser Leu Val Glu Cys Leu Glu Gln
100 105 110

Ala Leu Arg Asp Val Pro Lys Asp Arg Tyr Ala Ser Thr Pro Leu Tyr
115 120 125

Leu Gly Ala Thr Ala Gly Met Arg Leu Leu Asn Leu Thr Ser Pro Glu

```
    130                 135                 140

Ala Thr Ala Lys Val Leu Glu Ala Val Thr Gln Thr Leu Thr Arg Tyr
145                 150                 155                 160

Pro Phe Asp Phe Arg Gly Ala Arg Ile Leu Ser Gly Gln Asp Glu Gly
                165                 170                 175

Val Phe Gly Trp Val Thr Ala Asn Tyr Leu Leu Glu Asn Phe Ile Lys
            180                 185                 190

Tyr Gly Trp Val Gly Arg Trp Ile Arg Pro Arg Lys Gly Thr Leu Gly
        195                 200                 205

Ala Met Asp Leu Gly Gly Ala Ser Thr Gln Ile Thr Phe Glu Thr Thr
    210                 215                 220

Ser Pro Ser Glu Asp Pro Asp Asn Glu Val His Leu Arg Leu Tyr Gly
225                 230                 235                 240

Gln His Tyr Arg Val Tyr Thr His Ser Phe Leu Cys Tyr Gly Arg Asp
                245                 250                 255

Gln Val Leu Gln Arg Leu Leu Ala Ser Ala Leu Gln Ile His Arg Phe
            260                 265                 270

His Pro Cys Trp Pro Lys Gly Tyr Ser Thr Gln Val Leu Leu Arg Glu
        275                 280                 285

Val Tyr Gln Ser Pro Cys Thr Met Gly Gln Arg Pro Gln Thr Phe Asn
    290                 295                 300

Ser Ser Ala Thr Val Ser Leu Ser Gly Thr Ser Asn Ala Ala Leu Cys
305                 310                 315                 320

Arg Asp Leu Val Ser Gly Leu Phe Asn Ile Ser Ser Cys Pro Phe Ser
```

```
                325                 330                 335

Gln Cys Ser Phe Asn Gly Val Phe Gln Pro Pro Val Ala Gly Asn Phe
            340                 345                 350

Ile Ala Phe Ser Ala Phe Tyr Tyr Thr Val Asp Phe Leu Lys Thr Val
        355                 360                 365

Met Gly Leu Pro Val Gly Thr Leu Lys Gln Leu Glu Asp Ala Thr Glu
    370                 375                 380

Thr Thr Cys Asn Gln Thr Trp Ala Glu Leu Gln Ala Arg Val Pro Gly
385                 390                 395                 400

Gln Gln Thr Arg Leu Pro Asp Tyr Cys Ala Val Ala Met Phe Ile His
                405                 410                 415

Gln Leu Leu Ser Arg Gly Tyr Arg Phe Asp Glu Arg Ser Phe Arg Gly
            420                 425                 430

Val Val Phe Glu Lys Lys Ala Ala Asp Thr Ala Val Gly Trp Ala Leu
        435                 440                 445

Gly Tyr Met Leu Asn Leu Thr Asn Leu Ile Pro Ala Asp Leu Pro Gly
    450                 455                 460

Leu Arg Lys Gly Thr His Phe Ser His His His His His His
465                 470                 475
```