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Sleeman et al.

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(54) **METHODS FOR TREATING
HYPERCHOLESTEROLEMIA USING
ANTIBODIES TO PCSK9**

(58) **Field of Classification Search** None
See application file for complete search history.

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15, 2008, provisional application No. 61/210,566,
filed on Mar. 18, 2009, provisional application No.
61/168,753, filed on Apr. 13, 2009, provisional
application No. 61/218,136, filed on Jun. 18, 2009,
provisional application No. 61/249,135, filed on Oct.
6, 2009, provisional application No. 61/261,776, filed
on Nov. 17, 2009.

(51) **Int. Cl.**
A61K 39/395 (2006.01)
C07K 16/00 (2006.01)
C12P 21/08 (2006.01)

(52) **U.S. Cl.** **424/158.1; 530/387.1; 530/387.9**

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,029,895	B2	4/2006	Glucksmann et al.
7,129,338	B1	10/2006	Ota et al.
7,300,754	B2	11/2007	Abi Fadel et al.
7,482,147	B2	1/2009	Glucksmann et al.
2006/0147945	A1	7/2006	Edmonds et al.
2007/0082345	A1	4/2007	Ota et al.
2007/0224663	A1	9/2007	Rosen et al.
2008/0008697	A1	1/2008	Mintier et al.
2009/0142352	A1	6/2009	Jackson et al.
2009/0232795	A1	9/2009	Condra et al.
2009/0246192	A1	10/2009	Condra et al.
2009/0269350	A1	10/2009	Glucksmann et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP 1 067 182 A2 1/2001

(Continued)

OTHER PUBLICATIONS

Benjannet et al. (2006) "The Proprotein Convertase (PC) PCSK9 is
Inactivated by Furin and/or PC5/6A" J. Biol. Chem. 281(41):30561-
30572.

(Continued)

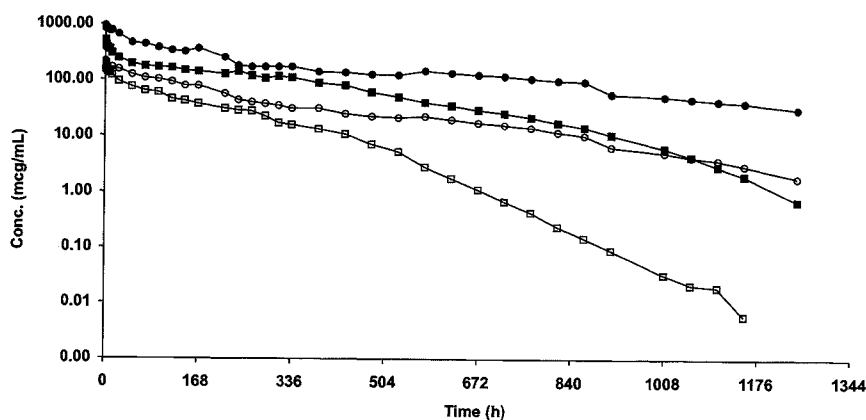
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(57) **ABSTRACT**

The present invention provides methods for treating hypercholesterolemia. The methods of the present invention comprise administering to a subject in need thereof a therapeutic composition comprising an anti-PCSK9 antibody or antigen-binding fragment thereof.

16 Claims, 14 Drawing Sheets



U.S. PATENT DOCUMENTS

2009/0326202 A1 12/2009 Jackson et al.
2010/0040610 A1 2/2010 Sitlani et al.
2010/0040611 A1 2/2010 Sparrow et al.
2010/0041102 A1 2/2010 Sitlani et al.
2010/0068199 A1 3/2010 Liang et al.

FOREIGN PATENT DOCUMENTS

EP 1 514 933 A1 3/2005
EP 1 618 212 B1 11/2007
WO WO 01/57081 A2 8/2001
WO WO 2008/057457 A2 5/2008
WO WO 2008/057458 A2 5/2008
WO WO 2008/057459 A2 5/2008
WO WO 2008/063382 A2 5/2008
WO WO 2008/125623 A2 10/2008
WO WO 2008/133647 A2 11/2008
WO WO 2009/026558 A1 2/2009

WO WO 2009/055783 A2 4/2009
WO WO 2009/100297 A1 8/2009
WO WO 2009/100318 A1 8/2009

OTHER PUBLICATIONS

Grozdanov et al. (2006) "Expression and Localization of PCSK9 in Rat Hepatic Cells," *Biochem. Cell Biol.* 84:80-92.
Maxwell et al. (2004) "Adenoviral-Mediated Expression of Pcsk9 in Mice Results in a Low-Density Lipoprotein Receptor Knockout . . .," *Proc Natl Acad Sci USA* 101(18):7100-7105.
Rashid et al. (2005) "Decreased Plasma Cholesterol and Hypersensitivity to Statins in Mice Lacking PCSK9," *Proc Natl Acad Sci USA* 102(15):5374-5379.
Lagace et al. (2006) "Secreted PCSK9 Decreases the Number of LDL Receptors in Hepatocytes and in Livers of Parabiotic Mice," *J. Clin. Invest.* 116(11):2995-3005.
Chan et al. (2009) "A Proprotein Convertase Subtilisin/Kexin Type 9 Neutralizing Antibody Reduced Serum Cholesterol in Mice and . . .," *Proc Natl Acad Sci USA* 106(24):9820-9825.

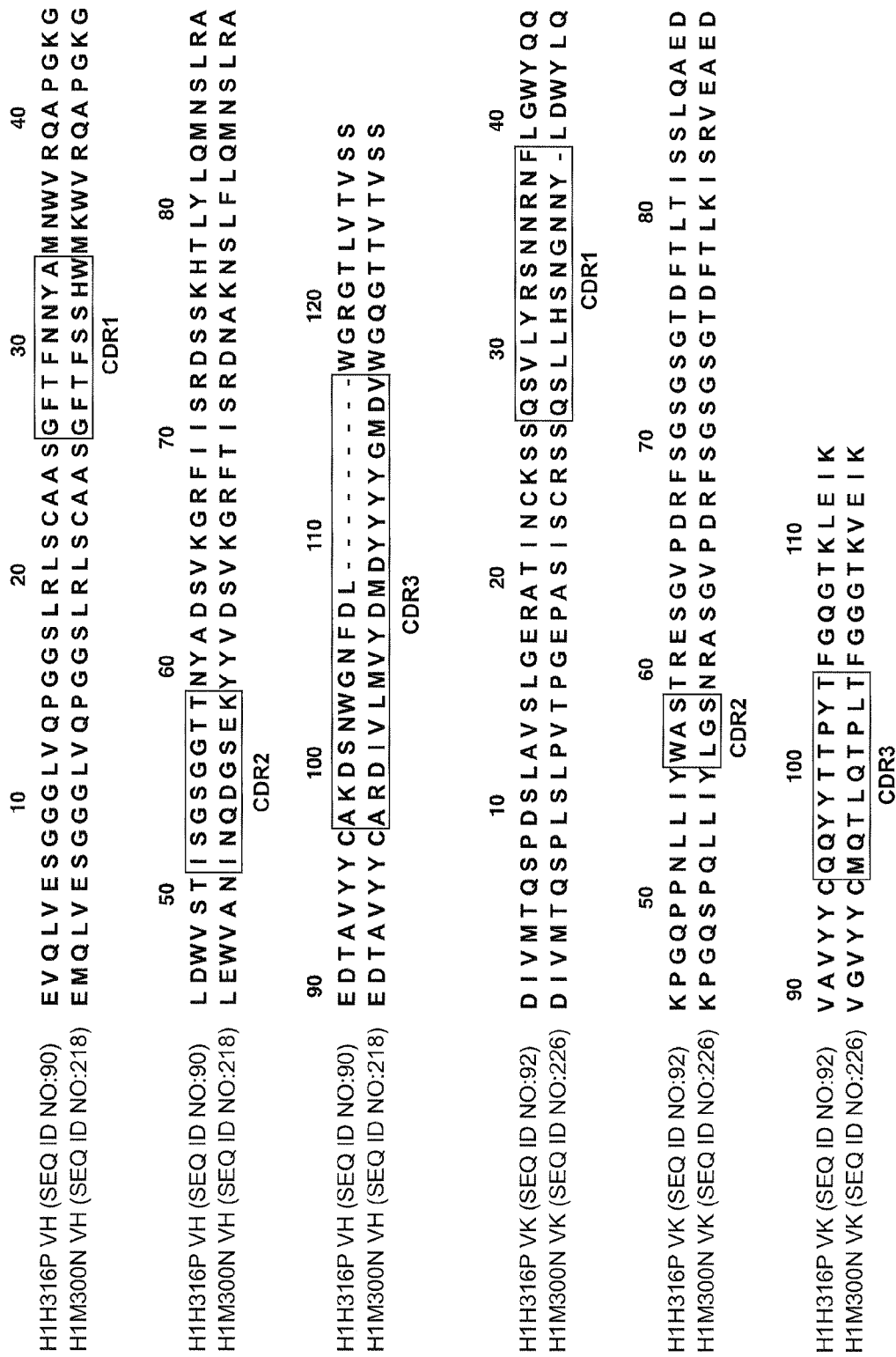


Fig. 1

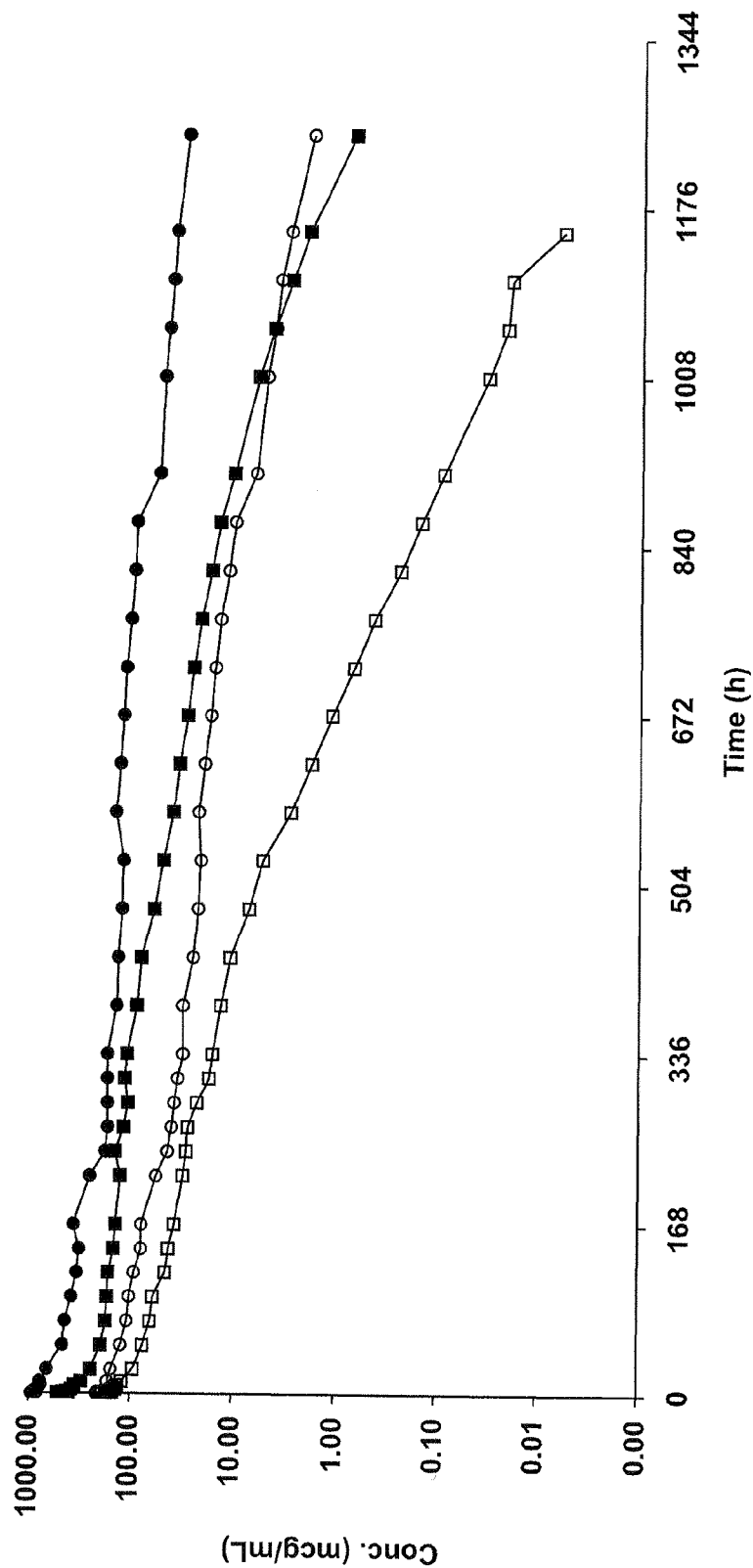


Fig. 2

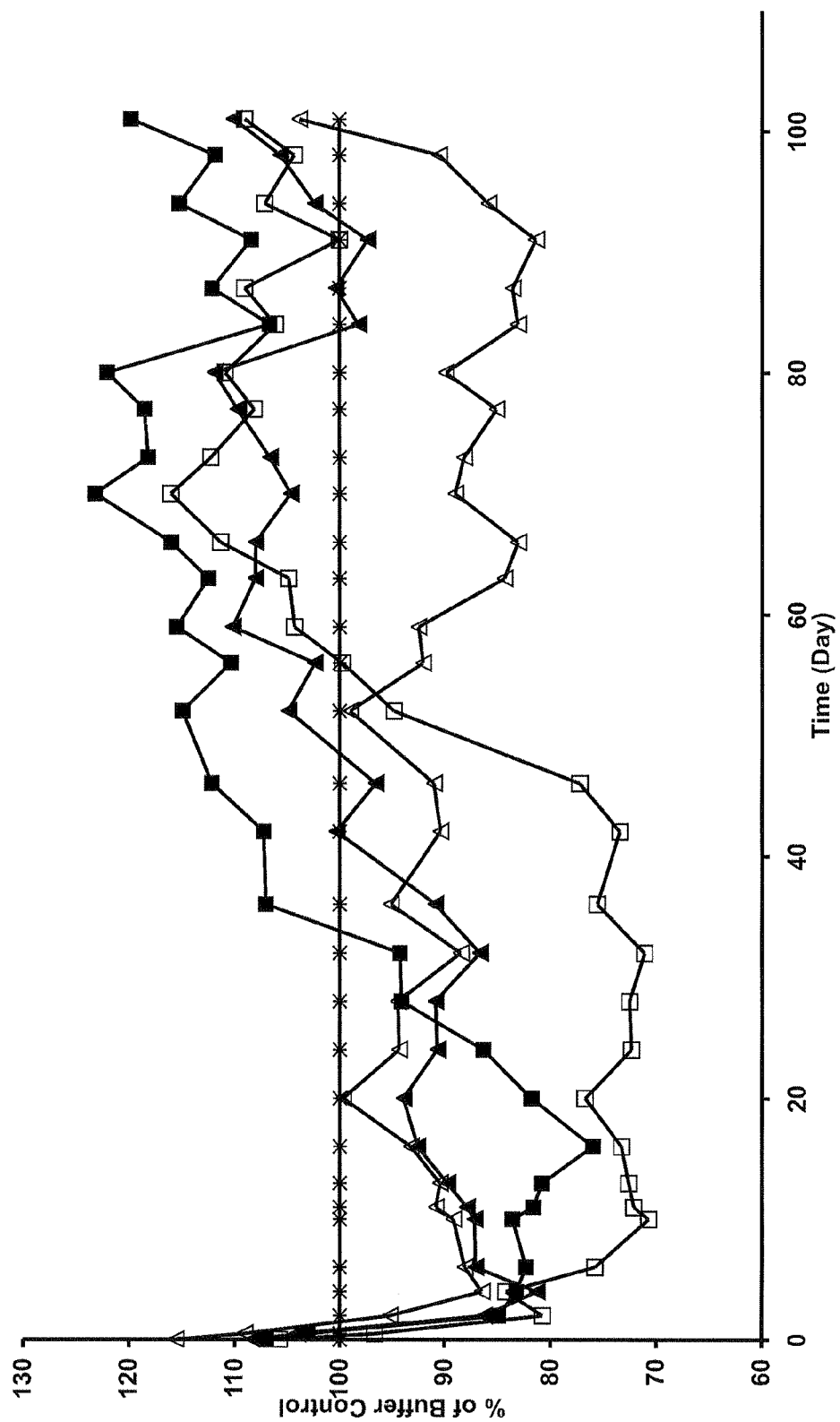


Fig. 3

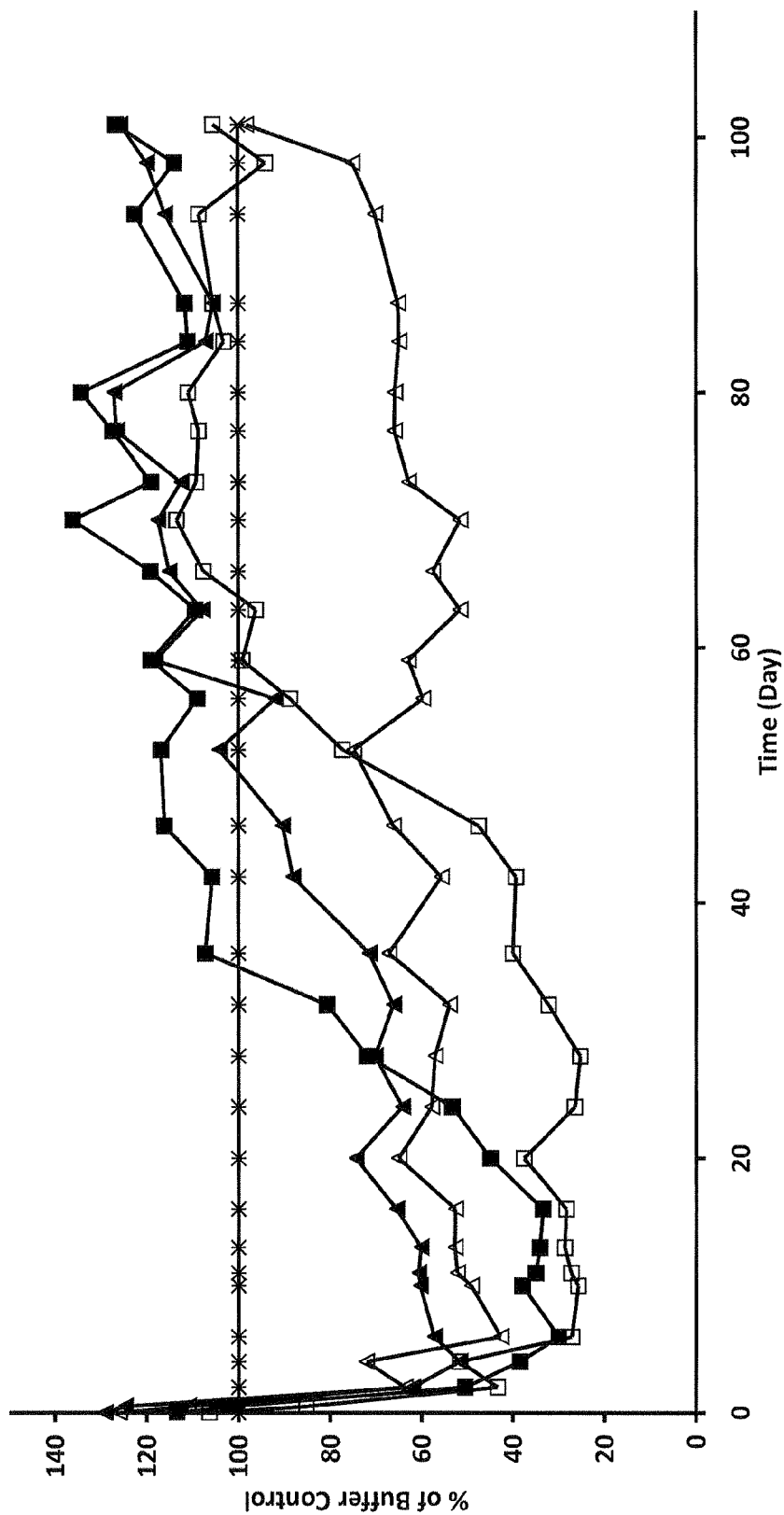


Fig. 4

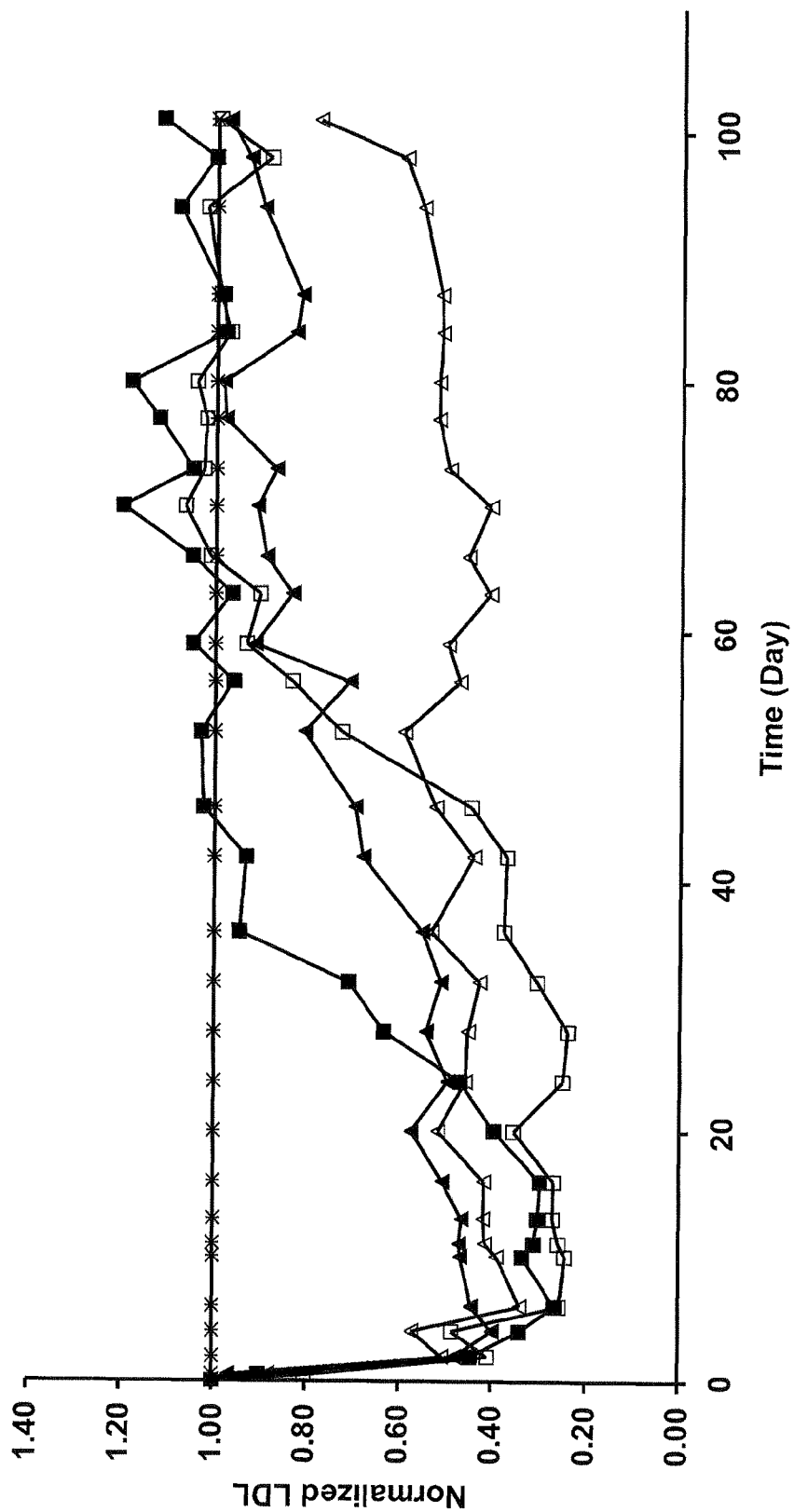


Fig. 5

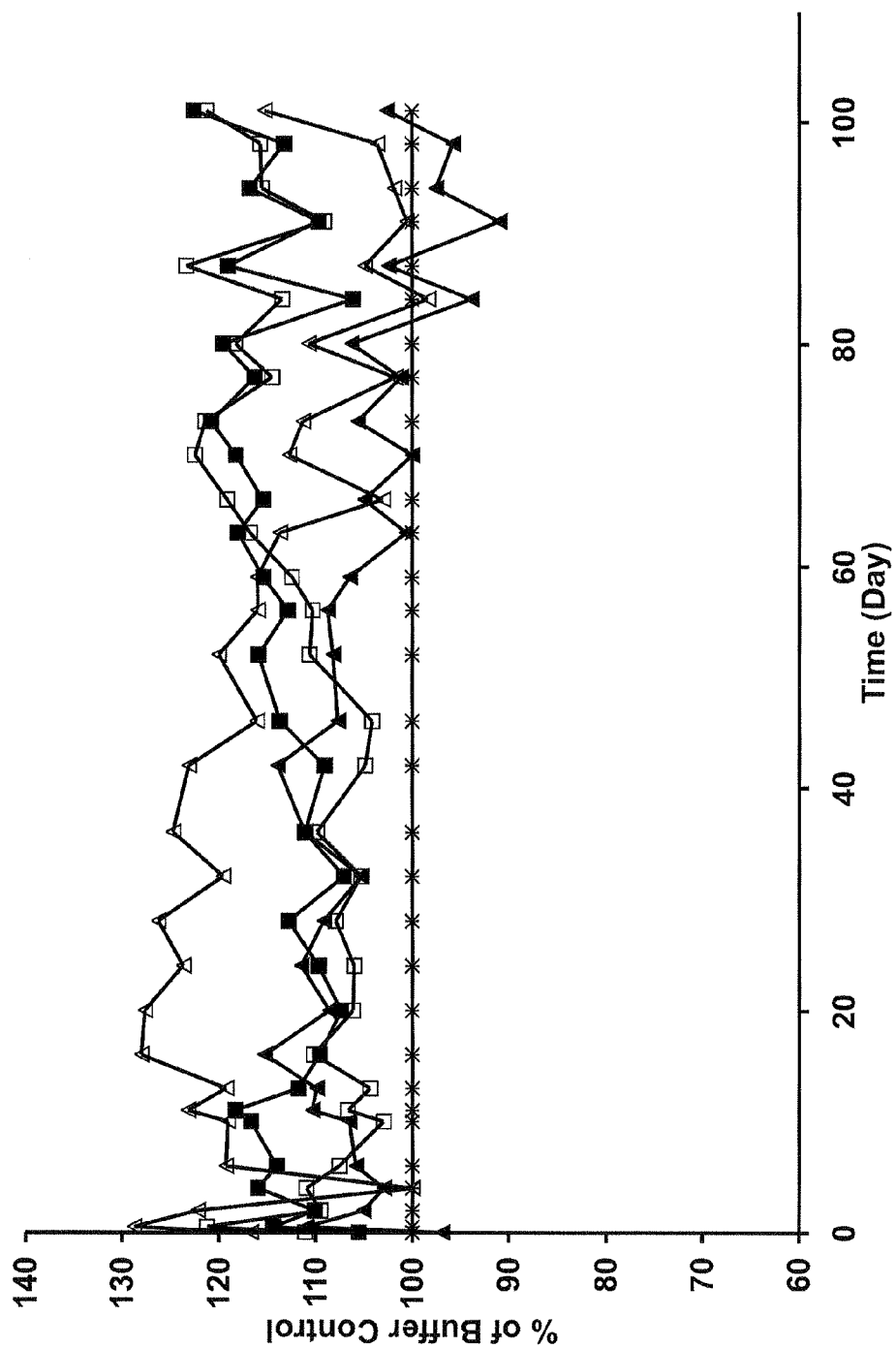


Fig. 6

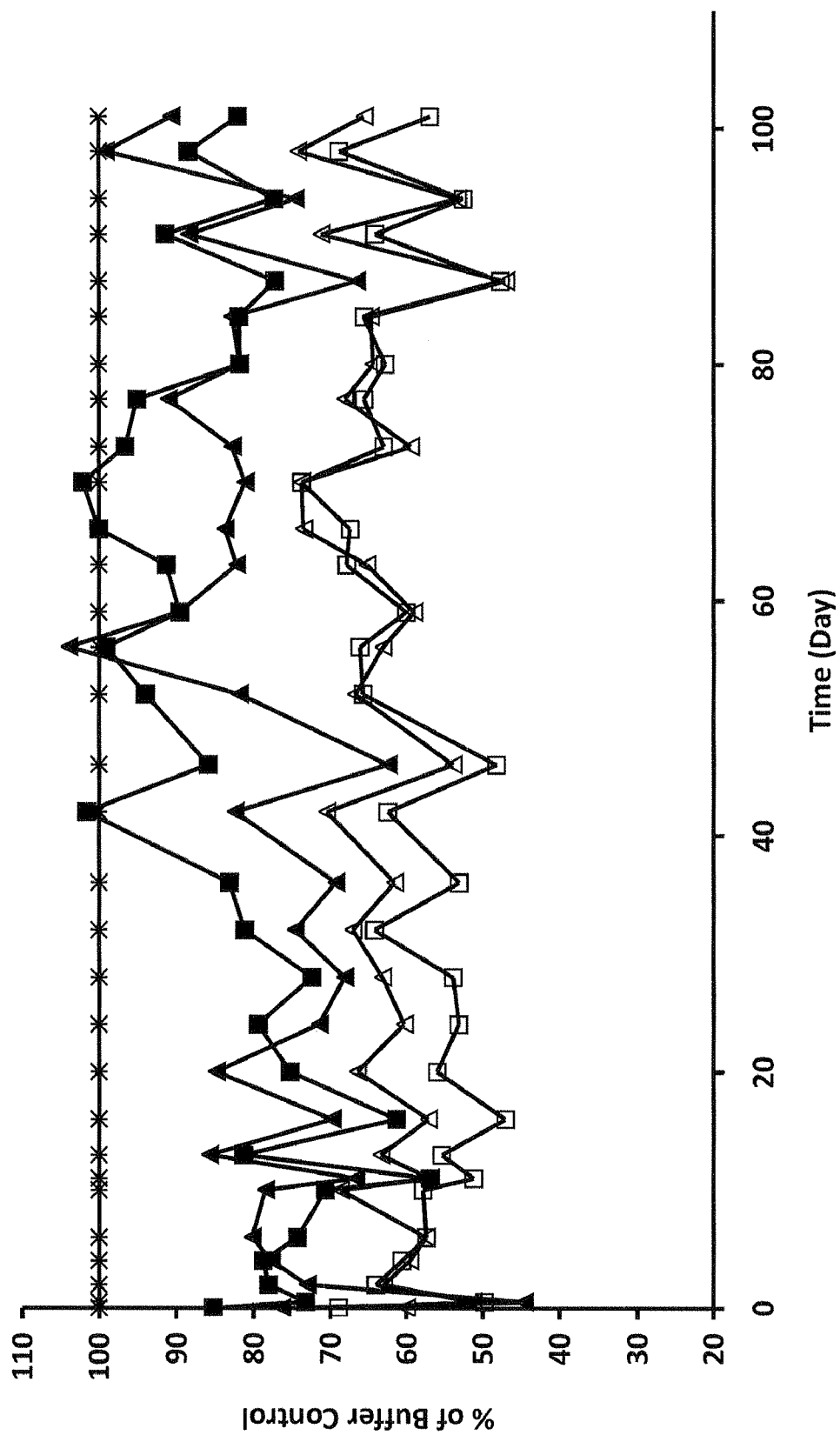


Fig. 7

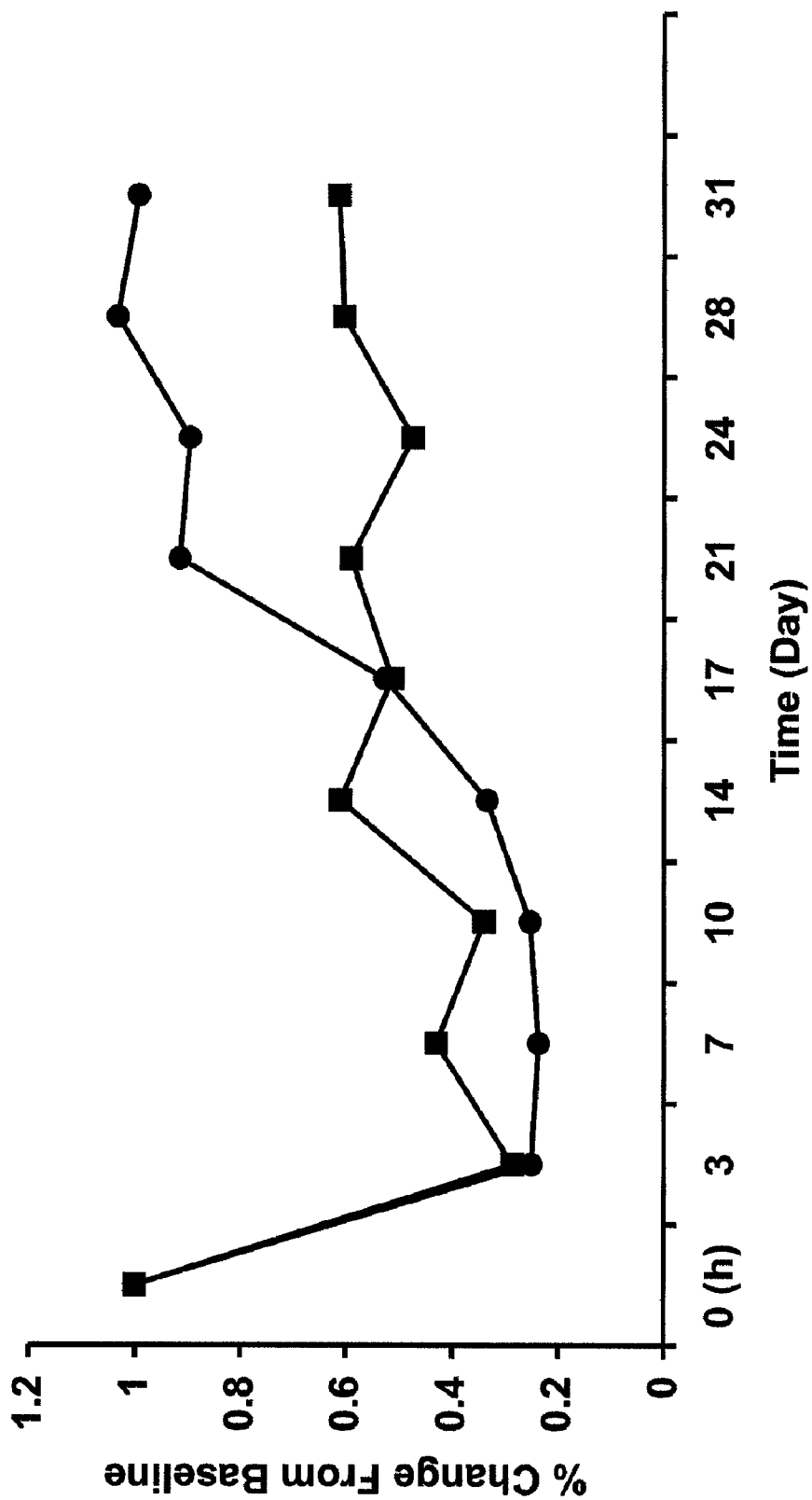


Fig. 8

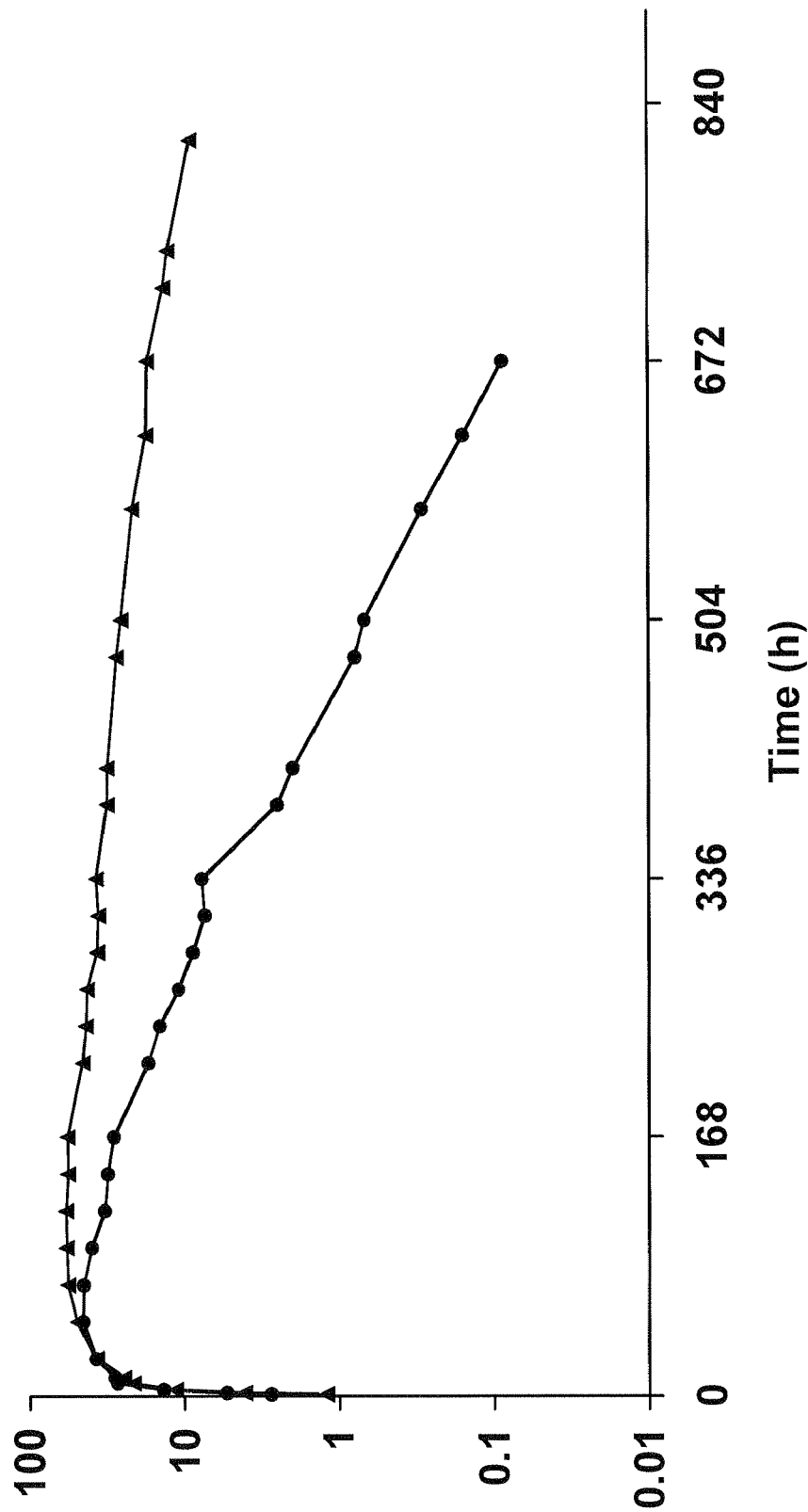


Fig. 9

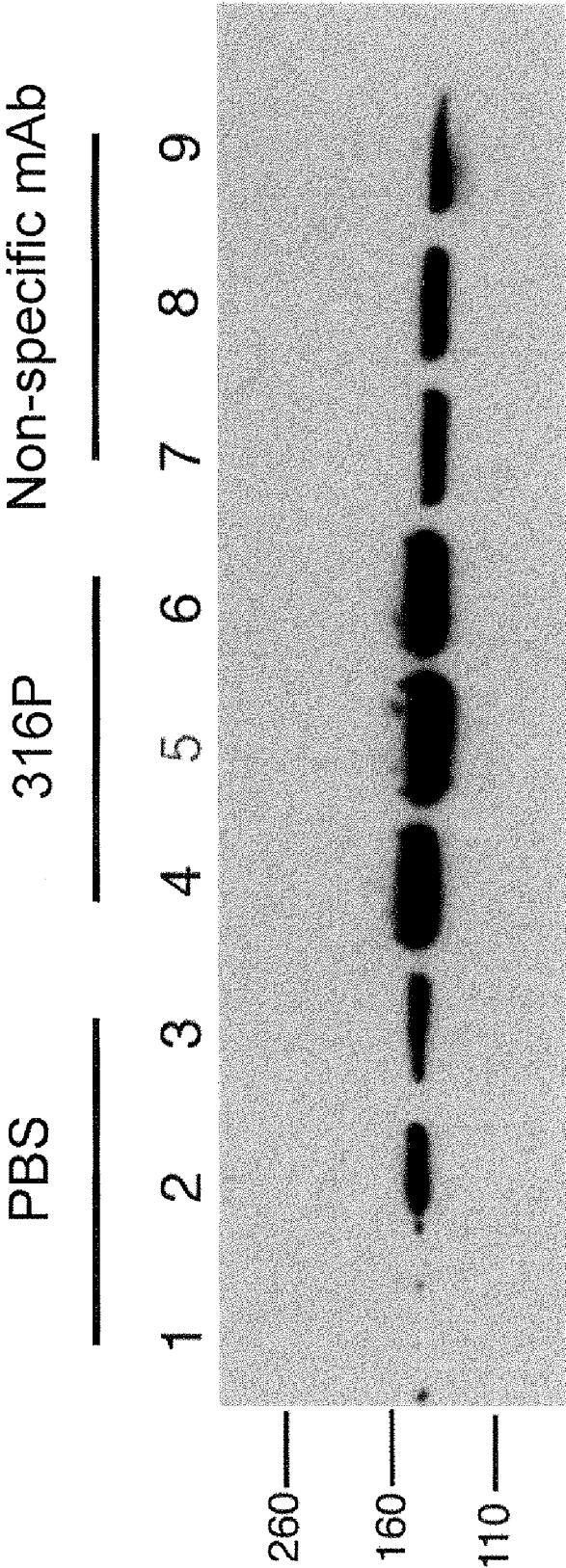


Fig. 10

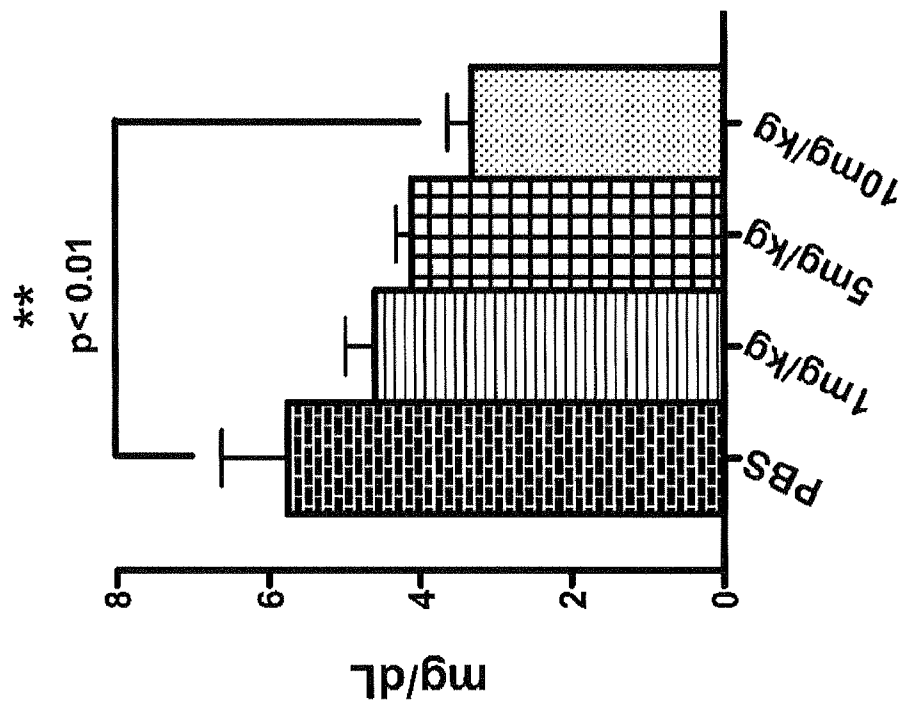


Fig. 11

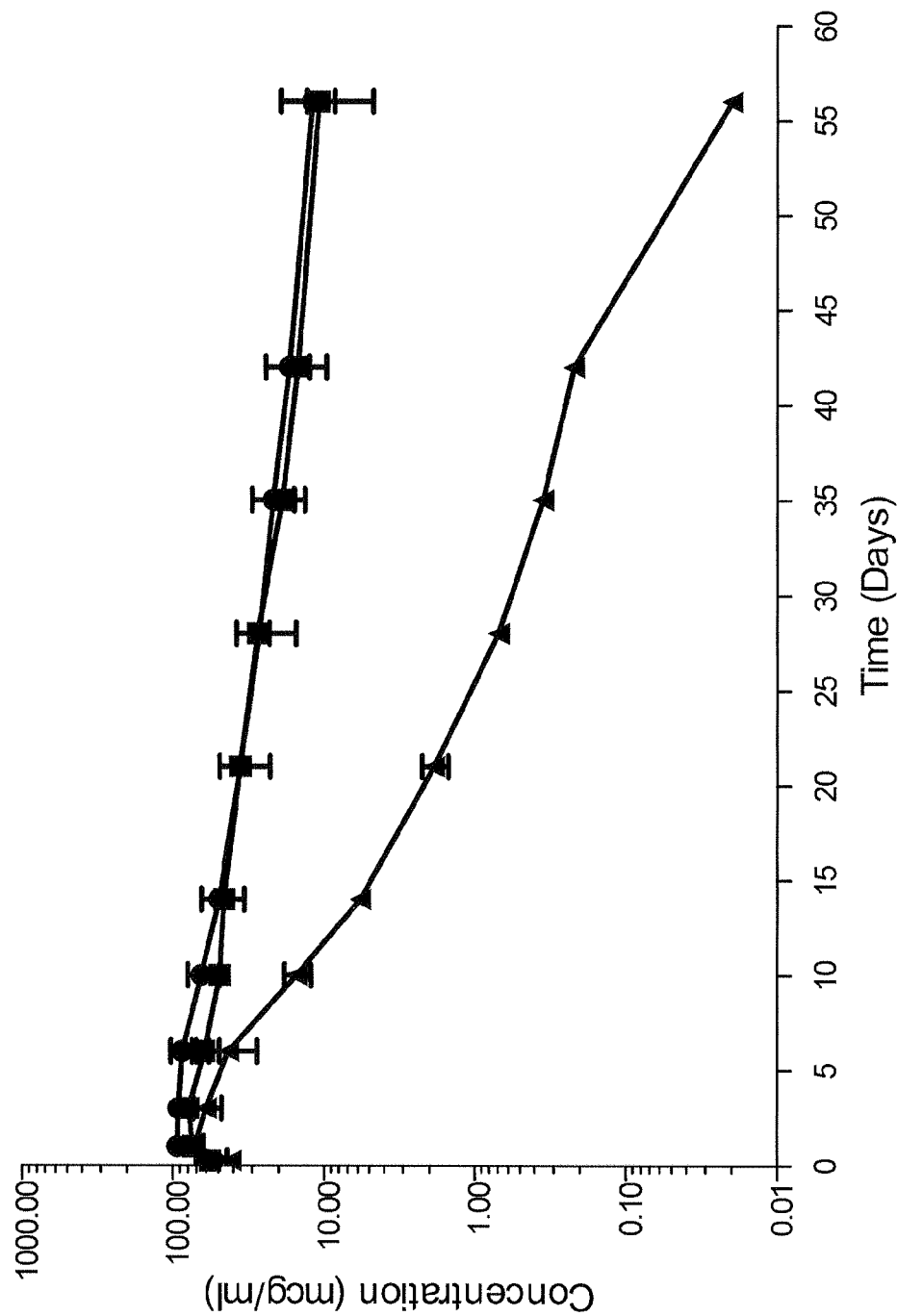


Fig. 12

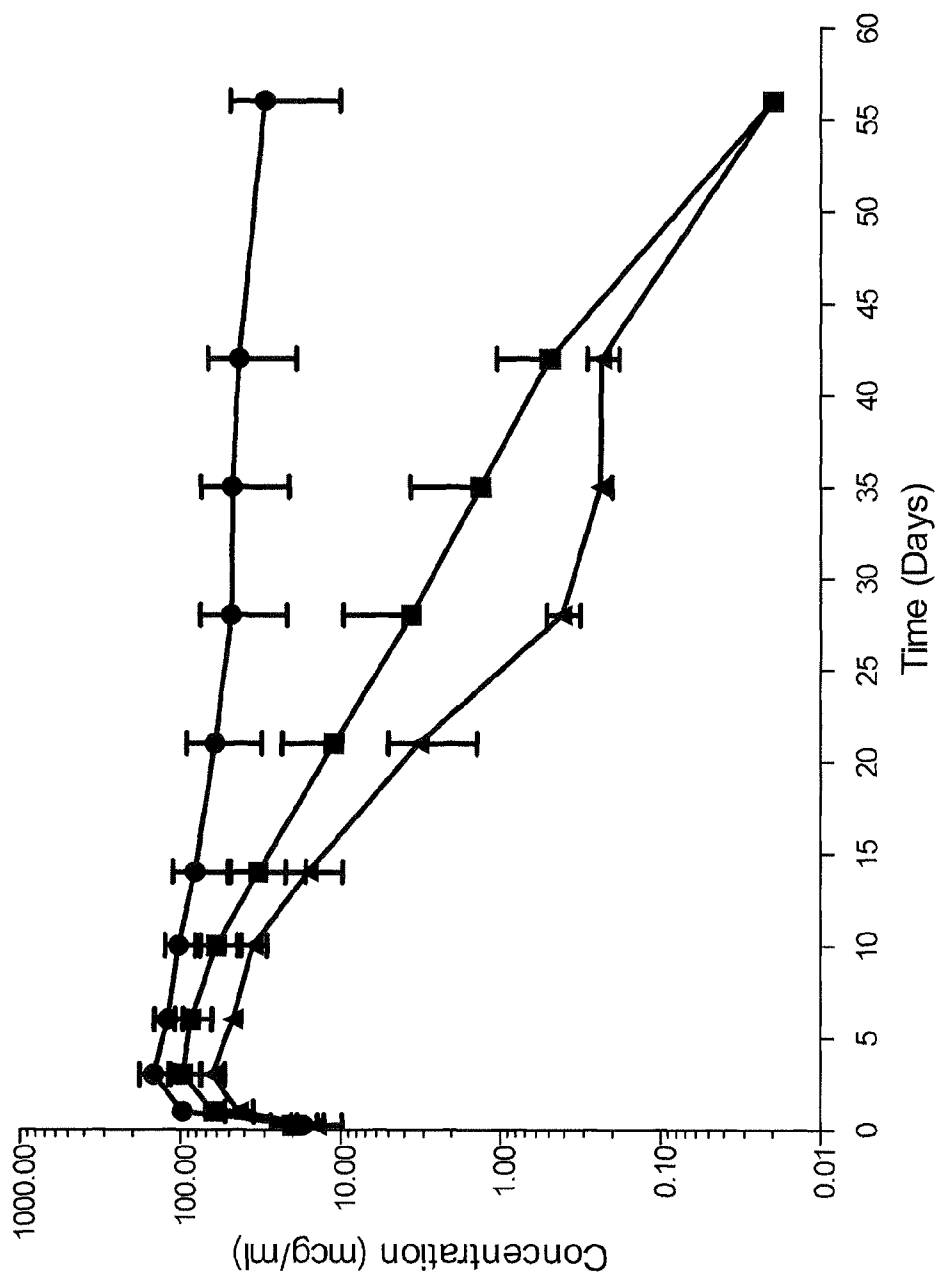


Fig. 13

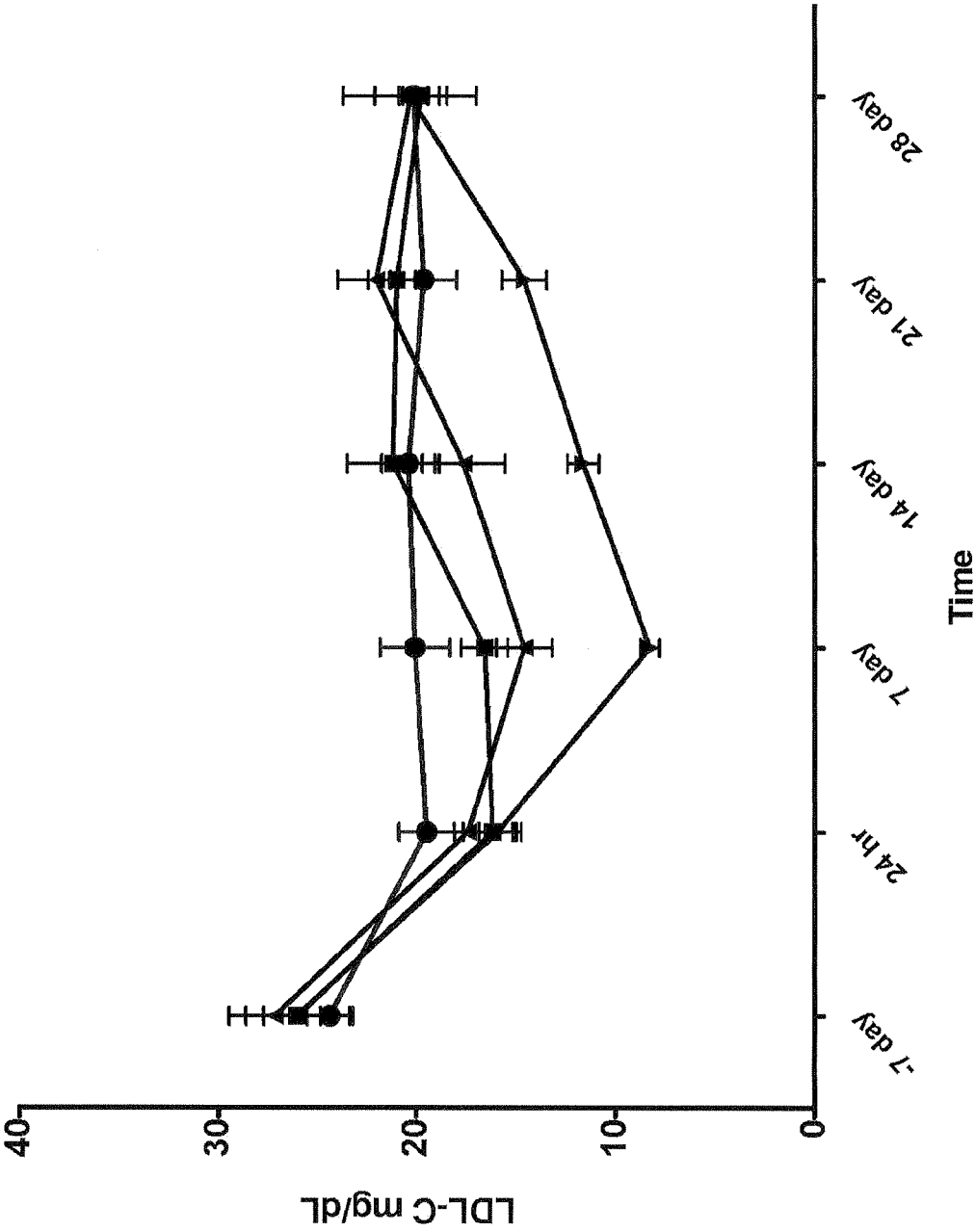


Fig. 14

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METHODS FOR TREATING HYPERCHOLESTEROLEMIA USING ANTIBODIES TO PCSK9

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. application Ser.No. 12/637,942, filed on 15 Dec. 2009, now U.S. Pat. No. 8,062,640, which claims the benefit under 35 USC §119(e) of U.S. Provisional Nos. 61/261,776 filed 17 Nov. 2009, 61/249,135 filed 06 Oct. 2009, 61/218,136 filed 18 Jun. 2009, 61/168,753 filed 13 Apr. 2009, 61/210,566 filed 18 Mar. 2009 and 61/122,482 filed 15 Dec. 2008, which applications are herein specifically incorporated by reference in their entirety.

FIELD OF THE INVENTION

The present invention is related to human antibodies and antigen-binding fragments of human antibodies that specifically bind human proprotein convertase subtilisin/kexin type 9 (PCSK9), and therapeutic methods of using those antibodies.

STATEMENT OF RELATED ART

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a proprotein convertase belonging to the proteinase K subfamily of the secretory subtilase family. The encoded protein is synthesized as a soluble zymogen that undergoes autocatalytic intramolecular processing in the endoplasmic reticulum. Evidence suggest that PCSK9 increases plasma LDL cholesterol by promoting degradation of the LDL receptor, which mediates LDL endocytosis in the liver, the major route of LDL clearance from circulation. The structure of PCSK9 protein shows that it has a signal sequence, followed by a prodomain, a catalytic domain that contains a conserved triad of residues (D186, H226 and S386), and a C-terminal domain. It is synthesized as a soluble 74-kDa precursor that undergoes autocatalytic cleavage in the ER, generating a 14-kDa prodomain and 60-kDa catalytic fragment. The autocatalytic activity has been shown to be required for secretion. After cleavage the prodomain remains tightly associated with the catalytic domain.

Antibodies to PCSK9 are described in, for example, WO 2008/057457, WO 2008/057458, WO 2008/057459, WO 2008/063382, WO 2008/125623, and US 2008/0008697.

BRIEF SUMMARY OF THE INVENTION

In a first aspect, the invention provides fully human monoclonal antibodies (mAbs) and antigen-binding fragments thereof that specifically bind and neutralize human PCSK9 (hPCSK9) activity.

In one embodiment, the invention comprises an antibody or antigen-binding fragment of an antibody that specifically binds hPCSK9 and is characterized by at least one of:

(i) capable of reducing serum total cholesterol at least about 25-35% and sustaining the reduction over at least a 24 day period relative to a predose level, preferably the reduction in serum total cholesterol is at least about 30-40%;

(ii) capable of reducing serum LDL cholesterol at least about 65-80% and sustaining the reduction over at least a 24 day period relative to a predose level;

(iii) capable of reducing serum triglyceride at least about 25-40% relative to predose level;

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(iv) does not reduce serum HDL cholesterol or reduces serum HDL cholesterol no more than 5% relative to predose level.

In one embodiment, the invention comprises an antibody or antigen-binding fragment of an antibody that specifically binds hPCSK9 and is characterized by at least one of:

(i) capable of reducing serum LDL cholesterol at least about 40-70% and sustaining the reduction over at least a 60 or 90 day period relative to a predose level;

(ii) capable of reducing serum triglyceride at least about 25-40% relative to predose level;

(iii) does not reduce serum HDL cholesterol or reduces serum HDL cholesterol no more than 5% relative to predose level.

In one embodiment, the antibody or antigen-binding fragment is characterized as binding an epitope comprising amino acid residue 238 of hPCSK9 (SEQ ID NO:755). In a more specific embodiment, the antibody or antigen-binding fragment binds an epitope comprising one or more of amino acid residue 238, 153, 159 and 343 of hPCSK9 (SEQ ID NO:755). In a more specific embodiment, the antibody or fragment thereof is characterized as binding an epitope which does not comprise an amino acid residue at position 192, 194, 197 and/or 237 of SEQ ID NO:755.

In one embodiment, the antibody or antigen-binding fragment is characterized as binding an epitope comprising amino acid residue 366 of hPCSK9 (SEQ ID NO:755). In a more specific embodiment, the antibody or antigen-binding fragment binds an epitope comprising one or more of amino acid residue at position 147, 366 and 380 of SEQ ID NO:755. In a more specific embodiment, the antibody or antigen-binding fragment of an antibody is characterized as binding an epitope which does not comprise an amino acid residue at position 215 or 238 of SEQ ID NO:755.

In one embodiment, the antibody or antigen-binding fragment is characterized as exhibiting an enhanced binding affinity (K_D) for hPCSK9 at pH 5.5 relative to the K_D at pH 7.4, as measured by plasmon surface resonance. In a specific embodiment, the antibody or fragment thereof exhibits at least a 20-fold, at least a 40-fold or at least a 50-fold enhanced affinity for PCSK9 at an acidic pH relative to a neutral pH, as measured by surface plasmon resonance.

In one embodiment, the antibody or antigen-binding fragment is characterized as not exhibiting an enhanced binding affinity for PCSK9 at an acidic pH relative to a neutral pH, as measured by surface plasmon resonance. In a specific embodiment, the antibody or fragment thereof exhibits a decreased binding affinity at an acidic pH.

In another embodiment, the antibody or antigen-binding fragment binds human, human GOF mutation D374Y, cynomolgus monkey, rhesus monkey, mouse, rat and hamster PCSK9.

In one embodiment, the antibody or antigen-binding fragment binds human and monkey PCSK9, but does not bind mouse, rat or hamster PCSK9.

The mAbs can be full-length (, an IgG1 or IgG4 antibody) or may comprise only an antigen-binding portion (, a Fab, F(ab')₂ or scFv fragment), and may be modified to affect functionality, e.g., to eliminate residual effector functions (Reddy et al. (2000) J. Immunol. 164:1925-1933).

In one embodiment, the invention comprises an antibody or antigen-binding fragment of an antibody comprising a heavy chain variable region (HCVR) selected from the group consisting of SEQ ID NO:2, 18, 22, 26, 42, 46, 50, 66, 70, 74, 90, 94, 98, 114, 118, 122, 138, 142, 146, 162, 166, 170, 186, 190, 194, 210, 214, 218, 234, 238, 242, 258, 262, 266, 282, 286, 290, 306, 310, 314, 330, 334, 338, 354, 358, 362, 378, 382,

386, 402, 406, 410, 426, 430, 434, 450, 454, 458, 474, 478, 482, 498, 502, 506, 522, 526, 530, 546, 550, 554, 570, 574, 578, 594, 598, 602, 618, 622, 626, 642, 646, 650, 666, 670, 674, 690, 694, 698, 714, 718, 722, 738 and 742, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the HCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NO:50, 66, 70, 74, 90, 94, 122, 138, 142, 218, 234, 238, 242, 258, 262, 314, 330 and 334. In a more specific embodiment, the HCVR comprises SEQ ID NO:90 or 218.

In one embodiment, the antibody or fragment thereof further comprises a light chain variable region (LCVR) selected from the group consisting of SEQ ID NO:10, 20, 24, 34, 44, 48, 58, 68, 72, 82, 92, 96, 106, 116, 120, 130, 140, 144, 154, 164, 168, 178, 188, 192, 202, 212, 216, 226, 236, 240, 250, 260, 264, 274, 284, 288, 298, 308, 312, 322, 332, 336, 346, 356, 360, 370, 380, 384, 394, 404, 408, 418, 428, 432, 442, 452, 456, 466, 476, 480, 490, 500, 504, 514, 524, 528, 538, 548, 552, 562, 572, 576, 586, 596, 600, 610, 620, 624, 634, 644, 648, 658, 668, 672, 682, 692, 696, 706, 716, 720, 730, 740 and 744, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the LCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 58, 68, 72, 82, 92, 96, 130, 140, 144, 226, 236, 240, 250, 260, 264, 322, 332 and 336. In a more specific embodiment, the LCVR comprises SEQ ID NO:92 or 226.

In specific embodiments, the antibody or fragment thereof comprises a HCVR and LCVR (HCVR/LCVR) sequence pair selected from the group consisting of SEQ ID NO: 2/10, 18/20, 22/24, 26/34, 42/44, 46/48, 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 98/106, 114/116, 118/120, 122/130, 138/140, 142/144, 146/154, 162/164, 166/168, 170/178, 186/188, 190/192, 194/202, 210/212, 214/216, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 266/274, 282/284, 286/288, 290/298, 306/308, 310/312, 314/322, 330/332, 334/336, 338/346, 354/356, 358/360, 362/370, 378/380, 382/384, 386/394, 402/404, 406/408, 410/418, 426/428, 430/432, 434/442, 450/452, 454/456, 458/466, 474/476, 478/480, 482/490, 498/500, 502/504, 506/514, 522/524, 526/528, 530/538, 546/548, 550/552, 554/562, 570/572, 574/576, 578/586, 594/596, 598/600, 602/610, 618/620, 622/624, 626/634, 642/644, 646/648, 650/658, 666/668, 670/672, 674/682, 690/692, 694/696, 698/706, 714/716, 718/720, 722/730, 738/740 and 742/744. In one embodiment, the HCVR and LCVR sequence pair comprises one of SEQ ID NO: 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 122/130, 138/140, 142/144, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 314/322, 330/332 and 334/336. In a more specific embodiment, the HCVR/LCVR pair comprises SEQ ID NO:90/92 or 218/226.

In a second aspect, the invention features an antibody or antigen-binding fragment of an antibody comprising a heavy chain CDR3 (HCDR3) domain selected from the group consisting of SEQ ID NO:8, 32, 56, 80, 104, 128, 152, 176, 200, 224, 248, 272, 296, 320, 344, 368, 392, 416, 440, 464, 488, 512, 536, 560, 584, 608, 632, 656, 680, 704 and 728, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; and a light chain CDR3 (LCDR3) domain selected from the group consisting of SEQ ID NO:16, 40, 64, 88, 112, 136, 160, 184, 208, 232, 256, 280, 304, 328, 352, 376, 400, 424, 448, 472, 496, 520, 544, 568, 592, 616, 640, 664, 688, 712 and 736, or substantially similar sequences thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the HCDR3/LCDR3 sequence pair is selected from the group consisting of SEQ ID NO:56/64,

80/88, 128/136, 224/232, 248/256 and 320/328. In a more specific embodiment, the HCDR3/LCDR3 sequence pair comprises SEQ ID NO:80/88 or 224/232.

In a further embodiment, the invention comprising an antibody or fragment thereof further comprising a heavy chain CDR1 (HCDR1) domain selected from the group consisting of SEQ ID NO:4, 28, 52, 76, 100, 124, 148, 172, 196, 220, 244, 268, 292, 316, 340, 364, 388, 412, 436, 460, 484, 508, 532, 556, 580, 604, 628, 652, 676, 700 and 724, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; a heavy chain CDR2 (HCDR2) domain selected from the group consisting of SEQ ID NO:6, 30, 54, 78, 102, 126, 150, 174, 198, 222, 246, 270, 294, 318, 342, 366, 390, 414, 438, 462, 486, 510, 534, 558, 582, 606, 630, 654, 678, 702 and 726, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; a light chain CDR1 (LCDR1) domain selected from the group consisting of SEQ ID NO:12, 36, 60, 84, 108, 132, 156, 180, 204, 228, 252, 276, 300, 324, 348, 372, 396, 420, 444, 468, 492, 516, 540, 564, 588, 612, 636, 660, 684, 708 and 732, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity; and a light chain CDR2 (LCDR2) domain selected from the group consisting of SEQ ID NO:14, 38, 62, 86, 110, 134, 158, 182, 206, 230, 254, 278, 302, 326, 350, 374, 398, 422, 446, 470, 494, 518, 542, 566, 590, 614, 638, 662, 686, 710 and 734, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the heavy and light chain CDR sequences comprise a sequence selected from the group consisting of SEQ ID NO:52, 54, 56, 60, 62, 64; 76, 78, 80, 84, 86, 88; 124, 126, 128, 132, 134, 136; 220, 222, 224, 228, 230, 232; 244, 246, 248, 252, 254, 256; and 316, 318, 320, 324, 326, 328. In more specific embodiments, the CDR sequences comprise SEQ ID NO: 76, 78, 80, 84, 86, 88; or 220, 222, 224, 228, 230, 232.

In a related embodiment, the invention comprises an antibody or antigen-binding fragment of an antibody which specifically binds hPCK9, wherein the antibody or fragment comprises heavy and light chain CDR domains contained within heavy and light chain sequence pairs selected from the group consisting of SEQ ID NO: 2/10, 18/20, 22/24, 26/34, 42/44, 46/48, 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 98/106, 114/116, 118/120, 122/130, 138/140, 142/144, 146/154, 162/164, 166/168, 170/178, 186/188, 190/192, 194/202, 210/212, 214/216, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 266/274, 282/284, 286/288, 290/298, 306/308, 310/312, 314/322, 330/332, 334/336, 338/346, 354/356, 358/360, 362/370, 378/380, 382/384, 386/394, 402/404, 406/408, 410/418, 426/428, 430/432, 434/442, 450/452, 454/456, 458/466, 474/476, 478/480, 482/490, 498/500, 502/504, 506/514, 522/524, 526/528, 530/538, 546/548, 550/552, 554/562, 570/572, 574/576, 578/586, 594/596, 598/600, 602/610, 618/620, 622/624, 626/634, 642/644, 646/648, 650/658, 666/668, 670/672, 674/682, 690/692, 694/696, 698/706, 714/716, 718/720, 722/730, 738/740 and 742/744. In one embodiment, the CDR sequences are contained within HCVR and LCVR selected from the amino acid sequence pairs of SEQ ID NO: 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 122/130, 138/140, 142/144, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 314/322, 330/332 and 334/336. In more specific embodiments, the CDR sequences are comprised within HCVR/LCVR sequences selected from SEQ ID NO: 90/92 or 218/226.

In one embodiment, the invention provides fully human monoclonal antibody or antigen-binding fragment thereof

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that specifically bind hPCSK9 and neutralize PCSK9 activity, wherein the antibody or fragment thereof exhibits one or more of the following characteristics: (i) capable of reducing serum total cholesterol at least about 25-35% and sustaining the reduction over at least a 24 day period relative to a predose level, preferably the reduction in serum total cholesterol is at least about 30-40%; (ii) capable of reducing serum LDL cholesterol at least about 65-80% and sustaining the reduction over at least a 24 day period relative to a predose level; (iii) capable of reducing serum triglyceride at least about 25-40% relative to predose level; (iv) does not reduce serum HDL cholesterol or reduces serum HDL cholesterol no more than 5% relative to predose level; (v) binds an epitope comprising amino acid residue 238 of hPCSK9 (SEQ ID NO:755); (vi) exhibits an enhanced binding affinity (K_D) for hPCSK9 at pH 5.5 relative to the K_D at pH 7.4, as measured by plasmon surface resonance, wherein the enhanced affinity is at least about a 20- to 50-fold increase in affinity; (vii) binds human, human GOF mutation D374Y, cynomolgus monkey, rhesus monkey, mouse, rat and hamster PCSK9; (viii) comprises heavy and light chain CDR3 sequences comprising SEQ ID NO:80 and 88; and (ix) comprises CDR sequences from SEQ ID NO:90 and 92.

In one embodiment, the invention provides fully human monoclonal antibody or antigen-binding fragment thereof that specifically bind human PCSK9 (hPCSK9) and neutralize PCSK9 activity, wherein the antibody or fragment thereof exhibits one or more of the following characteristics: (i) capable of reducing serum LDL cholesterol at least about 40-70% and sustaining the reduction over at least a 60 or 90 day period relative to a predose level; (ii) capable of reducing serum triglyceride at least about 25-40% relative to predose level; (iii) does not reduce serum HDL cholesterol or reduces serum HDL cholesterol no more than 5% relative to predose level; (iv) binds an epitope comprising amino acid residue 366 of hPCSK9 (SEQ ID NO:755); (v) does not exhibit an enhanced binding affinity for PCSK9 at an acidic pH relative to a neutral pH, as measured by surface plasmon resonance; (vi) binds human and monkey PCSK9, but does not bind mouse, rat or hamster PCSK9; (vii) comprises heavy and light chain CDR3 sequences comprising SEQ ID NO:224 and 232; and (viii) comprises CDR sequences from SEQ ID NO:218 and 226.

In a third aspect, the invention provides nucleic acid molecules encoding anti-PCSK9 antibodies or fragments thereof. Recombinant expression vectors carrying the nucleic acids of the invention, and host cells into which such vectors have been introduced, are also encompassed by the invention, as are methods of producing the antibodies by culturing the host cells under conditions permitting production of the antibodies, and recovering the antibodies produced.

In one embodiment, the invention provides an antibody or fragment thereof comprising a HCVR encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, 17, 21, 25, 41, 45, 49, 65, 69, 73, 89, 93, 97, 113, 117, 121, 137, 141, 145, 161, 165, 169, 185, 189, 193, 209, 213, 217, 233, 237, 241, 257, 261, 265, 281, 285, 289, 305, 309, 313, 329, 333, 337, 353, 357, 361, 377, 381, 385, 401, 405, 409, 425, 429, 433, 449, 453, 457, 473, 477, 481, 497, 501, 505, 521, 525, 529, 545, 549, 553, 569, 573, 577, 593, 597, 601, 617, 621, 625, 641, 645, 649, 665, 669, 673, 689, 693, 697, 713, 717, 721, 737 and 741, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. In one embodiment, the HCVR is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 49, 65, 69, 73, 89, 93, 121, 137, 141, 217, 233, 237, 241, 257, 261, 313, 329 and 333. In more

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specific embodiments, the HCVR is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 89 and 217.

In one embodiment, the antibody or fragment thereof further comprises a LCVR encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 9, 19, 23, 33, 43, 47, 57, 67, 71, 81, 91, 95, 105, 115, 119, 129, 139, 143, 153, 163, 167, 177, 187, 191, 201, 211, 215, 225, 235, 239, 249, 259, 263, 273, 283, 287, 297, 307, 311, 321, 331, 335, 345, 355, 359, 369, 379, 383, 393, 403, 407, 417, 427, 431, 441, 451, 455, 465, 475, 479, 489, 499, 503, 513, 523, 527, 537, 547, 551, 561, 571, 575, 585, 595, 599, 609, 619, 623, 633, 643, 647, 657, 667, 671, 681, 691, 695, 705, 715, 719, 729, 739 and 743, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. In one embodiment, the LCVR is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 57, 67, 71, 81, 91, 95, 129, 139, 143, 225, 235, 239, 249, 259, 263, 321, 331 and 335. In more specific embodiments, the LCVR is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 91 and 225.

In one embodiment, the invention features an antibody or antigen-binding fragment of an antibody comprising a HCDR3 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 7, 31, 55, 79, 103, 127, 151, 175, 199, 223, 247, 271, 295, 319, 343, 367, 391, 415, 439, 463, 487, 511, 535, 559, 583, 607, 631, 655, 679, 703 and 727, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; and a LCDR3 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 15, 39, 63, 87, 111, 135, 159, 183, 207, 231, 255, 279, 303, 327, 351, 375, 399, 423, 447, 471, 495, 519, 543, 567, 591, 615, 639, 663, 687, 711 and 735, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. In one embodiment, the HCDR3 and LCDR3 comprise a sequence pair encoded by the nucleic acid sequence of SEQ ID NO: 55/63, 79/87, 127/135, 223/231, 247/255 and 319/327, respectively. In more specific embodiments, the HCDR3 and LCDR3 comprise a sequence pair encoded by the nucleic acid sequence of SEQ ID NO: 79/87 and 223/231.

In a further embodiment, the antibody or fragment thereof further comprises, a HCDR1 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 3, 27, 51, 75, 99, 123, 147, 171, 195, 219, 243, 267, 291, 315, 339, 363, 387, 411, 435, 459, 483, 507, 531, 555, 579, 603, 627, 651, 675, 699 and 723, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; a HCDR2 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 5, 29, 53, 77, 101, 125, 149, 173, 197, 221, 245, 269, 293, 317, 341, 365, 389, 413, 437, 461, 485, 509, 533, 557, 581, 605, 629, 653, 677, 701 and 725, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; a LCDR1 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 11, 35, 59, 83, 107, 131, 155, 179, 203, 227, 251, 275, 299, 323, 347, 371, 395, 419, 443, 467, 491, 515, 539, 563, 587, 611, 635, 659, 683, 707 and 731, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; and a LCDR2 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, 205, 229, 253, 277, 301, 325, 349, 373, 397, 421, 445, 469, 493, 517, 541, 565, 589, 613, 637, 661, 685,

709 and 733, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. In one embodiment, the heavy and light chain CDR sequences are encoded by the nucleic acid sequences of SEQ ID NO: 51, 53, 55, 59, 61, 63; 75, 77, 79, 83, 85, 87; 123, 125, 127, 131, 133, 135; 219, 221, 223, 227, 229, 231; 243, 245, 247, 251, 253, 255; and 315, 317, 319, 323, 325, 327. In more specific embodiments, the heavy and light chain CDR sequences are encoded by the nucleic acid sequences of SEQ ID NO: 75, 77, 79, 83, 85, 87; and 219, 221, 223, 227, 229, 231.

In a fourth aspect, the invention features an isolated antibody or antigen-binding fragment thereof that specifically binds hPCSK9, comprising a HCDR3 and a LCDR3, wherein HCDR3 comprises an amino acid sequence of the formula $X^1-X^2-X^3-X^4-X^5-X^6-X^7-X^8-X^9-X^{10}-X^{11}-X^{12}-X^{13}-X^{14}-X^{15}-X^{16}-X^{17}-X^{18}-X^{19}-X^{20}$ (SEQ ID NO:747), wherein X^1 is Ala, X^2 is Arg or Lys, X^3 is Asp, X^4 is Ser or Ile, X^5 is Asn or Val, X^6 is Leu or Trp, X^7 is Gly or Met, X^8 is Asn or Val, X^9 is Phe or Tyr, X^{10} is Asp, X^{11} is Leu or Met, X^{12} is Asp or absent, X^{13} is Tyr or absent, X^{14} is Tyr or absent, X^{15} is Tyr or absent, X^{16} is Tyr or absent, X^{17} is Gly or absent, X^{18} is Met or absent, X^{19} is Asp or absent, and X^{20} is Val or absent; and LCDR3 comprises an amino acid sequence of the formula $X^1-X^2-X^3-X^4-X^5-X^6-X^7-X^8-X^9$ (SEQ ID NO:750), wherein X^1 is Gln or Met, X^2 is Gln, X^3 is Tyr or Thr, X^4 is Tyr or Leu, X^5 is Thr or Gln, X^6 is Thr, X^7 is Pro, X^8 is Tyr or Leu, and X^9 is Thr.

In a further embodiment, the antibody or fragment thereof further comprise a HCDR1 sequence of the formula $X^1-X^2-X^3-X^4-X^5-X^6-X^7-X^8$ (SEQ ID NO:745), wherein X^1 is Gly, X^2 is Phe, X^3 is Thr, X^4 is Phe, X^5 is Ser or Asn, X^6 is Ser or Asn, X^7 is Tyr or His, and X^8 is Ala or Trp; a HCDR2 sequence of the formula $X^1-X^2-X^3-X^4-X^5-X^6-X^7-X^8$ (SEQ ID NO:746), wherein X^1 is Ile, X^2 is Ser or Asn, X^3 is Gly or Gln, X^4 is Asp or Ser, X^5 is Gly, X^6 is Ser or Gly, X^7 is Thr or Glu, and X^8 is Thr or Lys; a LCDR1 sequence of the formula $X^1-X^2-X^3-X^4-X^5-X^6-X^7-X^8-X^9-X^{10}-X^{11}-X^{12}$ (SEQ ID NO:748) wherein X^1 is Gln, X^2 is Ser, X^3 is Val or Leu, X^4 is Leu, X^5 is His or Tyr, X^6 is Arg or Ser, X^7 is Ser or Asn, X^8 is Asn or Gly, X^9 is Asn, X^{10} is Arg or Asn, X^{11} is Asn or Tyr, and X^{12} is Phe or absent; a LCDR2 sequence of the formula $X^1-X^2-X^3$ (SEQ ID NO:749) wherein X^1 is Trp or Leu, X^2 is Ala or Gly, and X^3 is Ser. FIG. 1 shows the sequence alignment of heavy and light chain variable regions for 316P and 300N mAbs.

In a fifth aspect, the invention features a human anti-PCSK9 antibody or antigen-binding fragment of an antibody comprising a heavy chain variable region (HCVR) encoded by nucleotide sequence segments derived from V_H , D_H and J_H germ-line sequences, and a light chain variable region (LCVR) encoded by nucleotide sequence segments derived from V_K and J_K germ-line sequences, wherein the germ-line sequences are (a) V_H gene segment 3-23, D_H gene segment 7-27, J_H gene segment 2, V_K gene segment 4-1 and J_K gene segment 2; or (b) V_H gene segment 3-7, D_H gene segment 2-8, J_H gene segment 6, V_K gene segment 2-28 and J_K gene segment 4.

In a sixth aspect, the invention features an antibody or antigen-binding fragment thereof that binds to a PCSK9 protein of SEQ ID NO:755, wherein the binding of the antibody or fragment thereof to a variant PCSK9 protein is less than 50% of the binding between the antibody or fragment thereof and the PCSK9 protein of SEQ ID NO:755. In specific embodiment, the antibody or fragment thereof binds to the variant PCSK9 protein with a binding affinity (K_D) which is less than about 50%, less than about 60%, less than about

70%, less than about 80%, less than about 90% or less than about 95% compared to the binding to PCSK9 (SEQ ID NO:755).

In one embodiment, the variant PCSK9 protein comprises at least one mutation at position 238 of SEQ ID NO:755. In a more specific embodiment, the mutation is D238R. In one embodiment, the antibody or antibody fragment binding affinity for the variant PCSK9 protein is at least 90% less relative to the wildtype protein of SEQ ID NO:755, wherein the variant protein comprises a mutation at residue 238. In one embodiment, the antibody or antibody fragment binding affinity for the variant PCSK9 protein is at least 80% less relative to the wildtype protein of SEQ ID NO:755, wherein the variant protein comprises a mutation at one or more of residue 153, 159, 238 and 343. In a more specific embodiment, the mutation is one of S153R, E159R, D238R and D343R.

In one embodiment, the variant PCSK9 protein comprises at least one mutation at position 366 of SEQ ID NO:755. In a more specific embodiment, the mutation is E366K. In one embodiment, the antibody or antibody fragment binding affinity for the variant PCSK9 protein is at least 95% less relative to the wildtype protein of SEQ ID NO:755, wherein the variant protein comprises a mutation at residue 366. In one embodiment, the antibody or antibody fragment binding affinity for the variant PCSK9 protein is at least 90% less relative to the wildtype protein of SEQ ID NO:755, wherein the variant protein comprises a mutation at one or more of residue 147, 366 and 380. In a more specific embodiment, the mutation is one of S147F, E366K and V380M. In one embodiment, the antibody or antibody fragment binding affinity for the variant PCSK9 protein is at least 80% less relative to the wildtype protein of SEQ ID NO:755, wherein the variant protein comprises a mutation at one or more of residue 147, 366 and 380. In a more specific embodiment, the mutation is one of S147F, E366K and V380M.

The invention encompasses anti-PCSK9 antibodies having a modified glycosylation pattern. In some applications, modification to remove undesirable glycosylation sites may be useful, or, removal of a fucose moiety to increase antibody dependent cellular cytotoxicity (ADCC) function (see Shield et al. (2002) JBC 277:26733). In other applications, modification of galactosylation can be made in order to modify complement dependent cytotoxicity (CDC).

In a seventh aspect, the invention features a pharmaceutical composition comprising a recombinant human antibody or fragment thereof which specifically binds hPCSK9 and a pharmaceutically acceptable carrier. In one embodiment, the invention features a composition which is a combination of an antibody or antigen-binding fragment of an antibody of the invention, and a second therapeutic agent. The second therapeutic agent may be any agent that is advantageously combined with the antibody or fragment thereof of the invention, for example, an agent capable of inducing a cellular depletion of cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl (HMG)-coenzyme A (CoA) reductase, such as, for example, cerivastatin, atorvastatin, simvastatin, pitavastatin, rosuvastatin, fluvastatin, lovastatin, pravastatin, etc.; capable of inhibiting cholesterol uptake and or bile acid re-absorption; capable of increasing lipoprotein catabolism (such as niacin); and/or activators of the LXR transcription factor that plays a role in cholesterol elimination such as 22-hydroxycholesterol.

In an eighth aspect, the invention features methods for inhibiting hPCSK9 activity using the anti-PCSK9 antibody or antigen-binding portion of the antibody of the invention, wherein the therapeutic methods comprise administering a

therapeutically effective amount of a pharmaceutical composition comprising an antibody or antigen-binding fragment of an antibody of the invention. The disorder treated is any disease or condition which is improved, ameliorated, inhibited or prevented by removal, inhibition or reduction of PCSK9 activity. Specific populations treatable by the therapeutic methods of the invention include subjects indicated for LDL apheresis, subjects with PCSK9-activating mutations (gain of function mutations, "GOF"), subjects with heterozygous Familial Hypercholesterolemia (heFH); subjects with primary hypercholesterolemia who are statin intolerant or statin uncontrolled; and subjects at risk for developing hypercholesterolemia who may be preventably treated. Other indications include dyslipidemia associated with secondary causes such as Type 2 diabetes mellitus, cholestatic liver diseases (primary biliary cirrhosis), nephrotic syndrome, hypothyroidism, obesity; and the prevention and treatment of atherosclerosis and cardiovascular diseases.

In specific embodiments of the method of the invention, the anti-hPCSK9 antibody or antibody fragment of the invention is useful to reduce elevated total cholesterol, non-HDL cholesterol, LDL cholesterol, and/or apolipoprotein B (apolipoprotein B100).

The antibody or antigen-binding fragment of the invention may be used alone or in combination with a second agent, for example, an HMG-CoA reductase inhibitor and/or other lipid lowering drugs.

Other embodiments will become apparent from a review of the ensuing detailed description.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1. Sequence comparison tables of heavy chain (A) and light chain (B) variable regions and CDRs of antibodies H1H316P and H1M300N.

FIG. 2. Antibody concentrations in serum over time. 316P 5 mg/kg (□); 300N 5 mg/kg (○); 316P 15 mg/kg (v); 300N 15 mg/kg (●).

FIG. 3. Serum total cholesterol level as a percentage of change over buffer control. Buffer control (T); 316P 5 mg/kg (v); 300N 5 mg/kg (σ); 316P 15 mg/kg (□); 300N 15 mg/kg (Δ).

FIG. 4. Serum LDL cholesterol level as a percentage of change over buffer control: Buffer Control (T); 316P 5 mg/kg (v); 300N 5 mg/kg (σ); 316P 15 mg/kg (□); 300N 15 mg/kg (Δ).

FIG. 5. Serum LDL cholesterol level normalized to buffer control. Buffer control (T); 316P 5 mg/kg (v); 300N 5 mg/kg (σ); 316P 15 mg/kg (□); 300N 15 mg/kg (Δ).

FIG. 6. Serum HDL cholesterol level as a percentage of change over buffer control. Buffer control (T); 316P 5 mg/kg (v); 300N 5 mg/kg (σ); 316P 15 mg/kg (□); 300N 15 mg/kg (Δ).

FIG. 7. Serum triglyceride level expressed as a percentage of change over buffer control. Buffer control (T); 316P 5 mg/kg (v); 300N 5 mg/kg (σ); 316P 15 mg/kg (□); 300N 15 mg/kg (Δ).

FIG. 8. Serum LDL cholesterol level expressed as a percentage of change over baseline following a single dose subcutaneous administration. 316P 5 mg/kg (v); 300N 5 mg/kg (●).

FIG. 9. Antibody concentrations in serum over time following a single dose subcutaneous administration. 316P 5 mg/kg (●); 300N 5 mg/kg (σ).

FIG. 10. Western blot for mouse LDL receptor of total liver homogenates. Samples were taken 24 hours after PBS (lanes 1-3), 5 mg/kg 316P (lanes 4-6), or 5 mg/kg of non-hPCSK9

specific mAb (lanes 7-8) administration and 4 hours after 1.2 mg/kg hPCSK9-mmh (all lanes).

FIG. 11. Effects of 316P on serum LDL cholesterol level in PCSK9^{hu/hu} mice. Buffer control (■) 316P 1 mg/kg (.) 316P 5 mg/kg (.) 316P 10 mg/kg (.)

FIG. 12. Anti-hPCSK9 mAb serum pharmacokinetic profile in C57BL/6 mice. Single dose of Control I mAb (λ) at 10 mg/kg; 316P (σ) at 10 mg/kg and 300N (v) at 10 mg/kg.

FIG. 13. Anti-hPCSK9 mAb serum pharmacokinetic profile in hPCSK9 heterozygous mice. Single dose of Control I mAb (λ) at 10 mg/kg; 316P (σ) at 10 mg/kg and 300N (v) at 10 mg/kg.

FIG. 14. Effect of 316P on serum LDL cholesterol levels in Syrian Hamster fed a normal diet. Buffer control (●); 316P 1 mg/kg (v); 316P 3 mg/kg (σ); 316P 5 mg/kg (τ).

DETAILED DESCRIPTION

Before the present methods are described, it is to be understood that this invention is not limited to particular methods, and experimental conditions described, as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference in their entirety.

Definitions

The term "human proprotein convertase subtilisin/kexin type 9" or "hPCSK9", as used herein, refers to hPCSK9 having the nucleic acid sequence shown in SEQ ID NO:754 and the amino acid sequence of SEQ ID NO:755, or a biologically active fragment thereof.

The term "antibody", as used herein, is intended to refer to immunoglobulin molecules comprised of four polypeptide chains, two heavy (H) chains and two light (L) chains interconnected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region ("HCVR" or "VH") and a heavy chain constant region (comprised of domains CH1, CH2 and CH3). Each light chain is comprised of a light chain variable region ("LCVR" or "VL") and a light chain constant region (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 carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

Substitution of one or more CDR residues or omission of one or more CDRs is also possible. Antibodies have been described in the scientific literature in which one or two CDRs can be dispensed with for binding. Padlan et al. (1995 FASEB J. 9:133-139) analyzed the contact regions between antibodies and their antigens, based on published crystal structures, and concluded that only about one fifth to one third of CDR residues actually contact the antigen. Padlan also found many

antibodies in which one or two CDRs had no amino acids in contact with an antigen (see also, Vajdos et al. 2002 J Mol Biol 320:415-428).

CDR residues not contacting antigen can be identified based on previous studies (for example residues H60-H65 in CDRH2 are often not required), from regions of Kabat CDRs lying outside Chothia CDRs, by molecular modeling and/or empirically. If a CDR or residue(s) thereof is omitted, it is usually substituted with an amino acid occupying the corresponding position in another human antibody sequence or a consensus of such sequences. Positions for substitution within CDRs and amino acids to substitute can also be selected empirically. Empirical substitutions can be conservative or non-conservative substitutions.

The term "human antibody", as used herein, is intended to include antibodies having variable and constant regions derived from human germline immunoglobulin sequences. The human mAbs of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (, mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo), for example in the CDRs and in particular CDR3. However, the term "human antibody", as used herein, is not intended to include mAbs in which CDR sequences derived from the germline of another mammalian species (, mouse), have been grafted onto human FR sequences.

The term "specifically binds," or the like, means that an antibody or antigen-binding fragment thereof forms a complex with an antigen that is relatively stable under physiologic conditions. Specific binding can be characterized by an equilibrium dissociation constant of at least about 1×10^{-6} M or less (, a smaller K_D denotes a tighter binding). Methods for determining whether two molecules specifically bind are well known in the art and include, for example, equilibrium dialysis, surface plasmon resonance, and the like. An isolated antibody that specifically binds hPCSK9 may, however, exhibit cross-reactivity to other antigens such as PCSK9 molecules from other species. Moreover, multi-specific antibodies (, bispecifics) that bind to hPCSK9 and one or more additional antigens are nonetheless considered antibodies that "specifically bind" hPCSK9, as used herein.

The term "high affinity" antibody refers to those mAbs having a binding affinity to hPCSK9 of at least 10^{-10} M; preferably 10^{-11} M; even more preferably 10^{-12} M, as measured by surface plasmon resonance, e.g., BIACORE™ or solution-affinity ELISA.

By the term "slow off rate", "K_{off}" or "kd" is meant an antibody that dissociates from hPCSK9 with a rate constant of 1×10^{-3} s⁻¹ or less, preferably 1×10^{-4} s⁻¹ or less, as determined by surface plasmon resonance, e.g., BIACORE™.

The term "antigen-binding portion" of an antibody (or simply "antibody fragment"), as used herein, refers to one or more fragments of an antibody that retain the ability to specifically bind to hPCSK9. An antibody fragment may include a Fab fragment, a F(ab')₂ fragment, a Fv fragment, a dAb fragment, a fragment containing a CDR, or an isolated CDR.

The specific embodiments, antibody or antibody fragments of the invention may be conjugated to a therapeutic moiety ("immunoconjugate"), such as a cytotoxin, a chemotherapeutic drug, an immunosuppressant or a radioisotope.

An "isolated antibody", as used herein, is intended to refer to an antibody that is substantially free of other mAbs having different antigenic specificities (, an isolated antibody that specifically binds hPCSK9 is substantially free of mAbs that specifically bind antigens other than hPCSK9). An isolated

antibody that specifically binds hPCSK9 may, however, have cross-reactivity to other antigens, such as PCSK9 molecules from other species.

A "neutralizing antibody", as used herein (or an "antibody that neutralizes PCSK9 activity"), is intended to refer to an antibody whose binding to hPCSK9 results in inhibition of at least one biological activity of PCSK9. This inhibition of the biological activity of PCSK9 can be assessed by measuring one or more indicators of PCSK9 biological activity by one or more of several standard in vitro or in vivo assays known in the art (see examples below).

The term "surface plasmon resonance", as used herein, refers to an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix, for example using the BIACORE™ system (Pharmacia Biosensor AB, Uppsala, Sweden and Piscataway, N.J.).

The term " K_D ", as used herein, is intended to refer to the equilibrium dissociation constant of a particular antibody-antigen interaction.

The term "epitope" is a region of an antigen that is bound by an antibody. Epitopes may be defined as structural or functional. Functional epitopes are generally a subset of the structural epitopes and have those residues that directly contribute to the affinity of the interaction. Epitopes may also be conformational, that is, composed of non-linear amino acids. In certain embodiments, epitopes may include determinants that are chemically active surface groupings of molecules such as amino acids, sugar side chains, phosphoryl groups, or sulfonyl groups, and, in certain embodiments, may have specific three-dimensional structural characteristics, and/or specific charge characteristics.

The term "substantial identity" or "substantially identical," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 90%, and more preferably at least about 95%, 96%, 97%, 98% or 99% of the nucleotide bases, as measured by any well-known algorithm of sequence identity, such as FASTA, BLAST or GAP, as discussed below.

As applied to polypeptides, the term "substantial similarity" or "substantially similar" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 90% sequence identity, even more preferably at least 95%, 98% or 99% sequence identity. Preferably, residue positions which are not identical differ by conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (, charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well known to those of skill in the art. See, e.g., Pearson (1994) Methods Mol. Biol. 24: 307-331, which is herein incorporated by reference. Examples of groups of amino acids that have side chains with similar chemical properties include 1) aliphatic side chains: glycine, alanine, valine, leucine and isoleucine; 2) aliphatic-hydroxyl side chains: serine and threonine; 3) amide-containing side chains: asparagine and glutamine; 4) aromatic side chains: phenylalanine, tyrosine, and tryptophan; 5) basic side chains: lysine, argin-

ine, and histidine; 6) acidic side chains: aspartate and glutamate, and 7) sulfur-containing side chains: cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamate-aspartate, and asparagine-glutamine. Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet et al. (1992) *Science* 256: 1443-45, herein incorporated by reference. A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

Sequence similarity for polypeptides is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG software contains programs such as GAP and BESTFIT which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild type protein and a mutein thereof. See, e.g., GCG Version 6.1. Polypeptide sequences also can be compared using FASTA with default or recommended parameters; a program in GCG Version 6.1. FASTA (, FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (2000) *supra*). Another preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially BLASTP or TBLASTN, using default parameters. See, e.g., Altschul et al. (1990) *J. Mol. Biol.* 215: 403-410 and (1997) *Nucleic Acids Res.* 25:3389-402, each of which is herein incorporated by reference.

In specific embodiments, the antibody or antibody fragment for use in the method of the invention may be monospecific, bispecific, or multispecific. Multispecific antibodies may be specific for different epitopes of one target polypeptide or may contain antigen-binding domains specific for epitopes of more than one target polypeptide. An exemplary bi-specific antibody format that can be used in the context of the present invention involves the use of a first immunoglobulin (Ig) CH3 domain and a second Ig CH3 domain, wherein the first and second Ig CH3 domains differ from one another by at least one amino acid, and wherein at least one amino acid difference reduces binding of the bispecific antibody to Protein A as compared to a bi-specific antibody lacking the amino acid difference. In one embodiment, the first Ig CH3 domain binds Protein A and the second Ig CH3 domain contains a mutation that reduces or abolishes Protein A binding such as an H95R modification (by IMGT exon numbering; H435R by EU numbering). The second CH3 may further comprise an Y96F modification (by IMGT; Y436F by EU). Further modifications that may be found within the second CH3 include: D16E, L18M, N44S, K52N, V57M, and V82I (by IMGT; D356E, L358M, N384S, K392N, V397M, and V422I by EU) in the case of IgG1 mAbs; N44S, K52N, and V82I (IMGT; N384S, K392N, and V422I by EU) in the case of IgG2 mAbs; and Q15R, N44S, K52N, V57M, R69K, E79Q, and V82I (by IMGT; Q355R, N384S, K392N, V397M, R409K, E419Q, and V422I by EU) in the case of IgG4 mAbs. Variations on the bi-specific antibody format described above are contemplated within the scope of the present invention.

By the phrase "therapeutically effective amount" is meant an amount that produces the desired effect for which it is administered. The exact amount will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (see, for example, Lloyd (1999) *The Art, Science and Technology of Pharmaceutical Compounding*).

Preparation of Human Antibodies

Methods for generating human antibodies in transgenic mice are known (see for example, U.S. Pat. No. 6,596,541, Regeneron Pharmaceuticals, VELOCIMMUNE™). The VELOCIMMUNE™ technology involves generation of a transgenic mouse having a genome comprising human heavy and light chain variable regions operably linked to endogenous mouse constant region loci such that the mouse produces an antibody comprising a human variable region and a mouse constant region in response to antigenic stimulation. The DNA encoding the variable regions of the heavy and light chains of the antibody are isolated and operably linked to DNA encoding the human heavy and light chain constant regions. The DNA is then expressed in a cell capable of expressing the fully human antibody. In specific embodiment, the cell is a CHO cell.

Antibodies may be therapeutically useful in blocking a ligand-receptor interaction or inhibiting receptor component interaction, rather than by killing cells through fixation of complement and participation in complement-dependent cytotoxicity (CDC), or killing cells through antibody-dependent cell-mediated cytotoxicity (ADCC). The constant region of an antibody is thus important in the ability of an antibody to fix complement and mediate cell-dependent cytotoxicity. Thus, the isotype of an antibody may be selected on the basis of whether it is desirable for the antibody to mediate cytotoxicity.

Human antibodies can exist in two forms that are associated with hinge heterogeneity. In one form, an antibody molecule comprises a stable four-chain construct of approximately 150-160 kDa in which the dimers are held together by an interchain heavy chain disulfide bond. In a second form, the dimers are not linked via inter-chain disulfide bonds and a molecule of about 75-80 kDa is formed composed of a covalently coupled light and heavy chain (half-antibody). These forms have been extremely difficult to separate, even after affinity purification.

The frequency of appearance of the second form in various intact IgG isotypes is due to, but not limited to, structural differences associated with the hinge region isotype of the antibody. A single amino acid substitution in the hinge region of the human IgG4 hinge can significantly reduce the appearance of the second form (Angal et al. (1993) *Molecular Immunology* 30:105) to levels typically observed using a human IgG1 hinge. The instant invention encompasses antibodies having one or more mutations in the hinge, CH2 or CH3 region which may be desirable, for example, in production, to improve the yield of the desired antibody form.

Generally, a VELOCIMMUNE™ mouse is challenged with the antigen of interest, and lymphatic cells (such as B-cells) are recovered from the mice that express antibodies. The lymphatic cells may be fused with a myeloma cell line to prepare immortal hybridoma cell lines, and such hybridoma cell lines are screened and selected to identify hybridoma cell lines that produce antibodies specific to the antigen of interest. DNA encoding the variable regions of the heavy chain and light chain may be isolated and linked to desirable isotypic constant regions of the heavy chain and light chain. Such an antibody protein may be produced in a cell, such as a CHO cell. Alternatively, DNA encoding the antigen-specific

chimeric antibodies or the variable domains of the light and heavy chains may be isolated directly from antigen-specific lymphocytes.

Initially, high affinity chimeric antibodies are isolated having a human variable region and a mouse constant region. As described below, the antibodies are characterized and selected for desirable characteristics, including affinity, selectivity, epitope, etc. The mouse constant regions are replaced with a desired human constant region to generate the fully human antibody of the invention, for example wild-type or modified IgG1 or IgG4 (for example, SEQ ID NO:751, 752, 753). While the constant region selected may vary according to specific use, high affinity antigen-binding and target specificity characteristics reside in the variable region. Epitope Mapping and Related Technologies

To screen for antibodies that bind to a particular epitope (, those which block binding of IgE to its high affinity receptor), a routine cross-blocking assay such as that described *Antibodies*, Harlow and Lane (Cold Spring Harbor Press, Cold Spring Harb., N.Y.) can be performed. Other methods include alanine scanning mutants, peptide blots (Reineke (2004) *Methods Mol Biol* 248:443-63) (herein specifically incorporated by reference in its entirety), or peptide cleavage analysis. In addition, methods such as epitope excision, epitope extraction and chemical modification of antigens can be employed (Tomer (2000) *Protein Science* 9: 487-496) (herein specifically incorporated by reference in its entirety).

The term "epitope" refers to a site on an antigen to which B and/or T cells respond. B-cell epitopes can be formed both from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents, whereas epitopes formed by tertiary folding are typically lost on treatment with denaturing solvents. An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation.

Modification-Assisted Profiling (MAP), also known as Antigen Structure-based Antibody Profiling (ASAP) is a method that categorizes large numbers of monoclonal antibodies (mAbs) directed against the same antigen according to the similarities of the binding profile of each antibody to chemically or enzymatically modified antigen surfaces (US 2004/0101920, herein specifically incorporated by reference in its entirety). Each category may reflect a unique epitope either distinctly different from or partially overlapping with epitope represented by another category. This technology allows rapid filtering of genetically identical mAbs, such that characterization can be focused on genetically distinct mAbs. When applied to hybridoma screening, MAP may facilitate identification of rare hybridoma clones that produce mAbs having the desired characteristics. MAP may be used to sort the anti-PCSK9 mAbs of the invention into groups of mAbs binding different epitopes.

In various embodiments, the anti-hPCSK9 antibody or antigen-binding fragment of an antibody binds an epitope within the catalytic domain, which is about 153 to 425 of SEQ ID NO:755; more specifically, an epitope from about 153 to about 250 or from about 250 to about 425; more specifically, the antibody or antibody fragment of the invention binds an epitope within the fragment from about 153 to about 208, from about 200 to about 260, from about 250 to about 300, from about 275 to about 325, from about 300 to about 360, from about 350 to about 400, and/or from about 375 to about 425.

In various embodiments, the anti-hPCSK9 antibody or antigen-binding fragment of an antibody binds an epitope

within the propeptide domain (residues 31 to 152 of SEQ ID NO:755); more specifically, an epitope from about residue 31 to about residue 90 or from about residue 90 to about residue 152; more specifically, the antibody or antibody fragment of the invention binds an epitope within the fragment from about residue 31 to about residue 60, from about residue 60 to about residue 90, from about residue 85 to about residue 110, from about residue 100 to about residue 130, from about residue 125 to about residue 150, from about residue 135 to about residue 152, and/or from about residue 140 to about residue 152.

In some embodiments, the anti-hPCSK9 antibody or antigen-binding fragment of an antibody binds an epitope within the C-terminal domain, (residues 426 to 692 of SEQ ID NO:755); more specifically, an epitope from about residue 426 to about residue 570 or from about residue 570 to about residue 692; more specifically, the antibody or antibody fragment of the invention binds an epitope within the fragment from about residue 450 to about residue 500, from about residue 500 to about residue 550, from about residue 550 to about residue 600, and/or from about residue 600 to about residue 692.

In some embodiments, the antibody or antibody fragment binds an epitope which includes more than one of the enumerated epitopes within the catalytic, propeptide or C-terminal domain, and/or within two or three different domains (for example, epitopes within the catalytic and C-terminal domains, or within the propeptide and catalytic domains, or within the propeptide, catalytic and C-terminal domains).

In some embodiments, the antibody or antigen-binding fragment binds an epitope on hPCSK9 comprising amino acid residue 238 of hPCSK9 (SEQ ID NO:755). Experimental results (Table 27) show that when D238 was mutated, the K_D of mAb 316P exhibited >400-fold reduction in binding affinity ($\sim 1 \times 10^{-9}$ M to $\sim 410 \times 10^{-9}$ M) and $T_{1/2}$ decreased >30-fold (from ~ 37 to ~ 1 min). In a specific embodiment, the mutation was D238R. In specific embodiments, the antibody or antigen-binding fragment of the invention binds an epitope of hPCSK9 comprising two or more of amino acid residues at positions 153, 159, 238 and 343.

As shown below, a mutation in amino acid residue 153, 159 or 343 resulted in about a 5- to 10-fold decrease in affinity or similar shortening in $T_{1/2}$. In specific embodiments, the mutation was S153R, E159R and/or D343R.

In some embodiments, the antibody or antigen-binding fragment binds an epitope on hPCSK9 comprising amino acid residue 366 of hPCSK9 (SEQ ID NO:755). Experimental results (Table 27) show that when E366 was mutated, the affinity of mAb 300N exhibited about 50-fold decrease ($\sim 0.7 \times 10^{-9}$ M to $\sim 36 \times 10^{-9}$ M) and a similar shortening in $T_{1/2}$ (from ~ 120 to ~ 2 min). In a specific embodiment, the mutation is E366K.

The present invention includes anti-PCSK9 antibodies that bind to the same epitope as any of the specific exemplary antibodies described herein. Likewise, the present invention also includes anti-PCSK9 antibodies that compete for binding to PCSK9 or a PCSK9 fragment with any of the specific exemplary antibodies described herein.

One can easily determine whether an antibody binds to the same epitope as, or competes for binding with, a reference anti-PCSK9 antibody by using routine methods known in the art. For example, to determine if a test antibody binds to the same epitope as a reference anti-PCSK9 antibody of the invention, the reference antibody is allowed to bind to a PCSK9 protein or peptide under saturating conditions. Next, the ability of a test antibody to bind to the PCSK9 molecule is assessed. If the test antibody is able to bind to PCSK9 fol-

lowing saturation binding with the reference anti-PCSK9 antibody, it can be concluded that the test antibody binds to a different epitope than the reference anti-PCSK9 antibody. On the other hand, if the test antibody is not able to bind to the PCSK9 molecule following saturation binding with the reference anti-PCSK9 antibody, then the test antibody may bind to the same epitope as the epitope bound by the reference anti-PCSK9 antibody of the invention.

To determine if an antibody competes for binding with a reference anti-PCSK9 antibody, the above-described binding methodology is performed in two orientations: In a first orientation, the reference antibody is allowed to bind to a PCSK9 molecule under saturating conditions followed by assessment of binding of the test antibody to the PCSK9 molecule. In a second orientation, the test antibody is allowed to bind to a PCSK9 molecule under saturating conditions followed by assessment of binding of the reference antibody to the PCSK9 molecule. If, in both orientations, only the first (saturating) antibody is capable of binding to the PCSK9 molecule, then it is concluded that the test antibody and the reference antibody compete for binding to PCSK9. As will be appreciated by a person of ordinary skill in the art, an antibody that competes for binding with a reference antibody may not necessarily bind to the identical epitope as the reference antibody, but may sterically block binding of the reference antibody by binding an overlapping or adjacent epitope.

Two antibodies bind to the same or overlapping epitope if each competitively inhibits (blocks) binding of the other to the antigen. That is, a 1-, 5-, 10-, 20- or 100-fold excess of one antibody inhibits binding of the other by at least 50% but preferably 75%, 90% or even 99% as measured in a competitive binding assay (see, e.g., Junghans et al., *Cancer Res.* 1990 50:1495-1502). Alternatively, two antibodies have the same epitope if essentially all amino acid mutations in the antigen that reduce or eliminate binding of one antibody reduce or eliminate binding of the other. Two antibodies have overlapping epitopes if some amino acid mutations that reduce or eliminate binding of one antibody reduce or eliminate binding of the other.

Additional routine experimentation (, peptide mutation and binding analyses) can then be carried out to confirm whether the observed lack of binding of the test antibody is in fact due to binding to the same epitope as the reference antibody or if steric blocking (or another phenomenon) is responsible for the lack of observed binding. Experiments of this sort can be performed using ELISA, RIA, surface plasmon resonance, flow cytometry or any other quantitative or qualitative antibody-binding assay available in the art.

In a specific embodiment, the invention comprises an anti-PCSK9 antibody or antigen binding fragment of an antibody that binds an PCSK9 protein of SEQ ID NO:755, wherein the binding between the antibody or fragment thereof to PCSK9 and a variant PCSK9 protein is less than 50% of the binding between the antibody or fragment and the PCSK9 protein of SEQ ID NO:755. In one specific embodiment, the variant PCSK9 protein comprises at least one mutation of a residue at a position selected from the group consisting of 153, 159, 238 and 343. In a more specific embodiment, the at least one mutation is S153R, E159R, D238R, and/or D343R. In another specific embodiment, the variant PCSK9 protein comprises at least one mutation of a residue at a position selected from the group consisting of 366. In one specific embodiment, the variant PCSK9 protein comprises at least one mutation of a residue at a position selected from the group consisting of 147, 366 and 380. In a more specific embodiment, the mutation is S147F, E366K and V380M.

Immunoconjugates

The invention encompasses a human anti-PCSK9 monoclonal antibody conjugated to a therapeutic moiety ("immunoconjugate"), such as a cytotoxin, a chemotherapeutic drug, an immunosuppressant or a radioisotope. Cytotoxin agents include any agent that is detrimental to cells. Examples of suitable cytotoxin agents and chemotherapeutic agents for forming immunoconjugates are known in the art, see for example, WO 05/103081.

Bispecifics

The antibodies of the present invention may be monospecific, bispecific, or multispecific. Multispecific mAbs may be specific for different epitopes of one target polypeptide or may contain antigen-binding domains specific for more than one target polypeptide. See, e.g., Tutt et al. (1991) *J. Immunol.* 147:60-69. The human anti-PCSK9 mAbs can be linked to or co-expressed with another functional molecule, e.g., another peptide or protein. For example, an antibody or fragment thereof can be functionally linked (, by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody or antibody fragment, to produce a bispecific or a multispecific antibody with a second binding specificity.

An exemplary bi-specific antibody format that can be used in the context of the present invention involves the use of a first immunoglobulin (Ig) CH3 domain and a second Ig CH3 domain, wherein the first and second Ig CH3 domains differ from one another by at least one amino acid, and wherein at least one amino acid difference reduces binding of the bispecific antibody to Protein A as compared to a bi-specific antibody lacking the amino acid difference. In one embodiment, the first Ig CH3 domain binds Protein A and the second Ig CH3 domain contains a mutation that reduces or abolishes Protein A binding such as an H95R modification (by IMGT exon numbering; H435R by EU numbering). The second CH3 may further comprise a Y96F modification (by IMGT; Y436F by EU). Further modifications that may be found within the second CH3 include: D16E, L18M, N44S, K52N, V57M, and V82I (by IMGT; D356E, L358M, N384S, K392N, V397M, and V422I by EU) in the case of IgG1 antibodies; N44S, K52N, and V82I (IMGT; N384S, K392N, and V422I by EU) in the case of IgG2 antibodies; and Q15R, N44S, K52N, V57M, R69K, E79Q, and V82I (by IMGT; Q355R, N384S, K392N, V397M, R409K, E419Q, and V422I by EU) in the case of IgG4 antibodies. Variations on the bi-specific antibody format described above are contemplated within the scope of the present invention.

Bioequivalents

The anti-PCSK9 antibodies and antibody fragments of the present invention encompass proteins having amino acid sequences that vary from those of the described mAbs, but that retain the ability to bind human PCSK9. Such variant mAbs and antibody fragments comprise one or more additions, deletions, or substitutions of amino acids when compared to parent sequence, but exhibit biological activity that is essentially equivalent to that of the described mAbs. Likewise, the anti-PCSK9 antibody-encoding DNA sequences of the present invention encompass sequences that comprise one or more additions, deletions, or substitutions of nucleotides when compared to the disclosed sequence, but that encode an anti-PCSK9 antibody or antibody fragment that is essentially bioequivalent to an anti-PCSK9 antibody or antibody fragment of the invention. Examples of such variant amino acid and DNA sequences are discussed above.

Two antigen-binding proteins, or antibodies, are considered bioequivalent if, for example, they are pharmaceutical equivalents or pharmaceutical alternatives whose rate and

extent of absorption do not show a significant difference when administered at the same molar dose under similar experimental conditions, either single dose or multiple dose. Some antibodies will be considered equivalents or pharmaceutical alternatives if they are equivalent in the extent of their absorption but not in their rate of absorption and yet may be considered bioequivalent because such differences in the rate of absorption are intentional and are reflected in the labeling, are not essential to the attainment of effective body drug concentrations on, e.g., chronic use, and are considered medically insignificant for the particular drug product studied. In one embodiment, two antigen-binding proteins are bioequivalent if there are no clinically meaningful differences in their safety, purity, and potency.

In one embodiment, two antigen-binding proteins are bioequivalent if a patient can be switched one or more times between the reference product and the biological product without an expected increase in the risk of adverse effects, including a clinically significant change in immunogenicity, or diminished effectiveness, as compared to continued therapy without such switching.

In one embodiment, two antigen-binding proteins are bioequivalent if they both act by a common mechanism or mechanisms of action for the condition or conditions of use, to the extent that such mechanisms are known.

Bioequivalence may be demonstrated by in vivo and in vitro methods. Bioequivalence measures include, e.g., (a) an in vivo test in humans or other mammals, in which the concentration of the antibody or its metabolites is measured in blood, plasma, serum, or other biological fluid as a function of time; (b) an in vitro test that has been correlated with and is reasonably predictive of human in vivo bioavailability data; (c) an in vivo test in humans or other mammals in which the appropriate acute pharmacological effect of the antibody (or its target) is measured as a function of time; and (d) in a well-controlled clinical trial that establishes safety, efficacy, or bioavailability or bioequivalence of an antibody.

Bioequivalent variants of anti-PCSK9 antibodies of the invention may be constructed by, for example, making various substitutions of residues or sequences or deleting terminal or internal residues or sequences not needed for biological activity. For example, cysteine residues not essential for biological activity can be deleted or replaced with other amino acids to prevent formation of unnecessary or incorrect intramolecular disulfide bridges upon renaturation.

Treatment Population

The methods of the present invention comprise administering to a subject in need thereof a therapeutic composition comprising an anti-PCSK9 antibody. The therapeutic composition can comprise any of the anti-PCSK9 antibodies, or fragments thereof, as disclosed herein. As used herein, the expression "a subject in need thereof" means a human or non-human animal that exhibits one or more symptoms or indicia of hypercholesterolemia or who has been diagnosed with hypercholesterolemia. Specific exemplary populations treatable by the therapeutic methods of the invention include patients indicated for LDL apheresis, subjects with PCSK9-activating (GOF) mutations, patients with heterozygous Familial Hypercholesterolemia (heFH); subjects with primary hypercholesterolemia who are statin intolerant or statin uncontrolled; and subjects at risk for developing hypercholesterolemia who may be preventably treated.

While modifications in lifestyle and conventional drug treatment are often successful in reducing cholesterol levels, not all patients are able to achieve the recommended target cholesterol levels with such approaches. Various conditions, such as familial hypercholesterolemia (FH), appear to be

resistant to lowering of LDL-C levels in spite of aggressive use of conventional therapy. Homozygous and heterozygous familial hypercholesterolemia (hoFH, heFH) are conditions associated with premature atherosclerotic vascular disease. However, patients diagnosed with hoFH are largely unresponsive to conventional drug therapy and have limited treatment options. Specifically, treatment with statins, which reduce LDL-C by inhibiting cholesterol synthesis and upregulating the hepatic LDL receptor, may have little effect in patients whose LDL receptors are non-existent or defective. A mean LDL-C reduction of only less than about 20% has been recently reported in patients with genotype-confirmed hoFH treated with the maximal dose of statins. The addition of ezetimibe 10 mg/day to this regimen resulted in a total reduction of LDL-C levels of 27%, which is still far from optimal. Likewise, many patients are statin non-responsive, poorly controlled with statin therapy, or cannot tolerate statin therapy; in general, these patients are unable to achieve cholesterol control with alternative treatments. There is a large unmet medical need for new treatments that can address the short-comings of current treatment options.

Thus, the invention includes therapeutic methods in which the antibody or antibody fragment of the invention is administered to a patient to treat hypercholesterolemia. Specific non-limiting examples of types of hypercholesterolemia which are treatable in accordance with the methods of the present invention include, e.g., heterozygous Familial Hypercholesterolemia (heFH), homozygous Familial Hypercholesterolemia (hoFH), as well as incidences of hypercholesterolemia that are distinct from Familial Hypercholesterolemia (nonFH).

Therapeutic Administration and Formulations

The invention provides therapeutic compositions comprising the anti-PCSK9 antibodies or antigen-binding fragments thereof of the present invention. The administration of therapeutic compositions in accordance with the invention will be administered with suitable carriers, excipients, and other agents that are incorporated into formulations to provide improved transfer, delivery, tolerance, and the like. A multitude of appropriate formulations can be found in the formulary known to all pharmaceutical chemists: Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pa. These formulations include, for example, powders, pastes, ointments, jellies, waxes, oils, lipids, lipid (cationic or anionic) containing vesicles (such as LIPOFECTIN™), DNA conjugates, anhydrous absorption pastes, oil-in-water and water-in-oil emulsions, emulsions carbowax (polyethylene glycols of various molecular weights), semi-solid gels, and semi-solid mixtures containing carbowax. See also Powell et al. "Compendium of excipients for parenteral formulations" PDA (1998) J Pharm Sci Technol 52:238-311.

The dose may vary depending upon the age and the size of a subject to be administered, target disease, conditions, route of administration, and the like. When the antibody of the present invention is used for treating various conditions and diseases associated with PCSK9, including hypercholesterolemia, disorders associated with LDL and apolipoprotein B, and lipid metabolism disorders, and the like, in an adult patient, it is advantageous to intravenously administer the antibody of the present invention normally at a single dose of about 0.01 to about 20 mg/kg body weight, more preferably about 0.02 to about 7, about 0.03 to about 5, or about 0.05 to about 3 mg/kg body weight. Depending on the severity of the condition, the frequency and the duration of the treatment can be adjusted.

Various delivery systems are known and can be used to administer the pharmaceutical composition of the invention,

e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the mutant viruses, receptor mediated endocytosis (see, e.g., Wu et al. (1987) *J. Biol. Chem.* 262:4429-4432). Methods of introduction include, but are not limited to, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The composition may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (, oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local.

The pharmaceutical composition can be also delivered in a vesicle, in particular a liposome (see Langer (1990) *Science* 249:1527-1533; Treat et al. (1989) in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez Berestein and Fidler (eds.), Liss, New York, pp. 353-365; Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*).

In certain situations, the pharmaceutical composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton (1987) *CRC Crit. Ref. Biomed. Eng.* 14:201). In another embodiment, polymeric materials can be used; see, *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974). In yet another embodiment, a controlled release system can be placed in proximity of the composition's target, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138, 1984).

The injectable preparations may include dosage forms for intravenous, subcutaneous, intracutaneous and intramuscular injections, drip infusions, etc. These injectable preparations may be prepared by methods publicly known. For example, the injectable preparations may be prepared, e.g., by dissolving, suspending or emulsifying the antibody or its salt described above in a sterile aqueous medium or an oily medium conventionally used for injections. As the aqueous medium for injections, there are, for example, physiological saline, an isotonic solution containing glucose and other auxiliary agents, etc., which may be used in combination with an appropriate solubilizing agent such as an alcohol (e.g., ethanol), a polyalcohol (, propylene glycol, polyethylene glycol), a nonionic surfactant [, polysorbate 80, HCO-50 (polyoxyethylene (50 mol) adduct of hydrogenated castor oil)], etc. As the oily medium, there are employed, e.g., sesame oil, soybean oil, etc., which may be used in combination with a solubilizing agent such as benzyl benzoate, benzyl alcohol, etc. The injection thus prepared is preferably filled in an appropriate ampoule. A pharmaceutical composition of the present invention can be delivered subcutaneously or intravenously with a standard needle and syringe. In addition, with respect to subcutaneous delivery, a pen delivery device readily has applications in delivering a pharmaceutical composition of the present invention. Such a pen delivery device can be reusable or disposable. A reusable pen delivery device generally utilizes a replaceable cartridge that contains a pharmaceutical composition. Once all of the pharmaceutical composition within the cartridge has been administered and the cartridge is empty, the empty cartridge can readily be discarded and replaced with a new cartridge that contains the pharmaceutical composition. The pen delivery device can then be reused. In a disposable pen delivery device, there is no replaceable cartridge. Rather, the disposable pen delivery device comes prefilled with the pharmaceutical composition held in a reservoir within the device. Once the reservoir is emptied of the pharmaceutical composition, the entire device is discarded.

Numerous reusable pen and autoinjector delivery devices have applications in the subcutaneous delivery of a pharmaceutical composition of the present invention. Examples include, but certainly are not limited to AUTOPEN™ (Owen Mumford, Inc., Woodstock, UK), DISETRONIC™ pen (Disetronic Medical Systems, Burghdorf, Switzerland), HUMALOG MIX 75/25™ pen, HUMALOG™ pen, HUMALIN 70/30™ pen (Eli Lilly and Co., Indianapolis, Ind.), NOVOPEN™ I; II and III (Novo Nordisk, Copenhagen, Denmark), NOVOPEN JUNIOR™ (Novo Nordisk, Copenhagen, Denmark), BD™ pen (Becton Dickinson, Franklin Lakes,), OPTIPEN™, OPTIPEN PRO™, OPTIPEN STARLET™, and OPTICLIK™ (sanofi-aventis, Frankfurt, Germany), to name only a few. Examples of disposable pen delivery devices having applications in subcutaneous delivery of a pharmaceutical composition of the present invention include, but certainly are not limited to the SOLOSTAR™ pen (sanofi-aventis), the FLEXPEN™ (Novo Nordisk), and the KWIKPEN™ (Eli Lilly).

Advantageously, the pharmaceutical compositions for oral or parenteral use described above are prepared into dosage forms in a unit dose suited to fit a dose of the active ingredients. Such dosage forms in a unit dose include, for example, tablets, pills, capsules, injections (ampoules), suppositories, etc.

Dosage

The amount of anti-PCSK9 antibody administered to a subject according to the methods of the present invention is, generally, a therapeutically effective amount. As used herein, the phrase "therapeutically effective amount" means a dose of anti-PCSK9 antibody that results in a detectable improvement in one or more symptoms or indicia of hypercholesterolemia, or a dose of anti-PCSK9 antibody that inhibits, prevents, lessens, or delays the progression of hypercholesterolemia in a patient. In the case of an anti-PCSK9 antibody, a therapeutically effective amount can be from about 0.05 mg, to about 600 mg, e.g., about 0.05 mg, about 0.1 mg, about 1.0 mg, about 1.5 mg, about 2.0 mg, about 10 mg, about 20 mg, 25 mg about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg about 310 mg, about 320 mg, about 330 mg, about 340 mg, about 350 mg, about 360 mg, about 370 mg, about 380 mg, about 390 mg, about 400 mg, about 410 mg, about 420 mg, about 430 mg, about 440 mg, about 450 mg, about 460 mg, about 470 mg, about 480 mg, about 490 mg, about 500 mg, about 510 mg, about 520 mg, about 530 mg, about 540 mg, about 550 mg, about 560 mg, about 570 mg, about 580 mg, about 590 mg, or about 600 mg, of the anti-PCSK9 antibody.

The amount of anti-PCSK9 antibody contained within the individual doses may be expressed in terms of milligrams of antibody per kilogram of patient body weight (i.e., mg/kg). For example, the anti-PCSK9 antibody may be administered to a patient at a dose of about 0.0001 to about 10 mg/kg of patient body weight.

Combination and Adjunct Therapies

The methods of the present invention, according to certain embodiments, may comprise administering a pharmaceutical composition comprising an anti-PCSK9 antibody to a patient who is on a therapeutic regimen for the treatment of hypercholesterolemia at the time of, or just prior to, administration of the pharmaceutical composition of the invention. For

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example, a patient who has previously been diagnosed with hypercholesterolemia may have been prescribed and is taking a stable therapeutic regimen of another drug prior to and/or concurrent with administration of a pharmaceutical composition comprising an anti-PCSK9 antibody. The prior or concurrent therapeutic regimen may comprise, e.g., (1) an agent which induces a cellular depletion of cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl (HMG)-coenzyme A (CoA) reductase, such as a statin (e.g., cerivastatin, atorvastatin, simvastatin, pitavastatin, rosuvastatin, fluvastatin, lovastatin, pravastatin, etc.); (2) an agent which inhibits cholesterol uptake and or bile acid re-absorption; (3) an agent which increase lipoprotein catabolism (such as niacin); and/or (4) activators of the LXR transcription factor that plays a role in cholesterol elimination such as 22-hydroxycholesterol. In certain embodiments, the patient, prior to or concurrent with administration of an anti-PCSK9 antibody is on a fixed combination of therapeutic agents such as ezetimibe plus simvastatin; a statin with a bile resin (, cholestyramine, colestipol, colesvelam); niacin plus a statin (, niacin with lovastatin); or with other lipid lowering agents such as omega-3-fatty acid ethyl esters (for example, omacor).

EXAMPLES

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the methods and compositions of the invention, and are not intended to limit the scope of what the inventors regard as their invention. Efforts have been made to ensure accuracy with respect to numbers used but some experimental errors and deviations should be accounted for. Unless indicated otherwise, molecular weight is average molecular weight, temperature is in degrees Centigrade, and pressure is at or near atmospheric.

Example 1

Generation of Human Antibodies to Human PCSK9

VELOCIMMUNE™ mice were immunized with human PCSK9, and the antibody immune response monitored by antigen-specific immunoassay using serum obtained from these mice. Anti-hPCSK9 expressing B cells were harvested from the spleens of immunized mice shown to have elevated anti-hPCSK9 antibody titers were fused with mouse myeloma cells to form hybridomas. The hybridomas were screened and selected to identify cell lines expressing hPCSK9-specific antibodies using assays as described below. The assays identified several cell lines that produced chimeric anti-hPCSK9 antibodies designated as H1M300, H1M504, H1M505, H1M500, H1M497, H1M498, H1M494, H1M309, H1M312, H1M499, H1M493, H1M496, H1M503, H1M502, H1M508, H1M495 and H1M492.

Human PCSK9-specific antibodies were also isolated directly from antigen-immunized B cells without fusion to myeloma cells, as described in 2007/0280945A1, hereby incorporated by reference in its entirety. Heavy and light chain variable regions were cloned to generate fully human anti-hPCSK9 antibodies designated as H1H313, H1H314, H1H315, H1H316, H1H317, H1H318, H1H320, H1H321 and H1H334. Stable recombinant antibody-expressing CHO cell lines expressing these antibodies were established.

Example 2

Gene Utilization Analysis

To analyze the structure of the mAbs produced, the nucleic acids encoding antibody variable regions were cloned and

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sequenced. The predicted amino acid sequences of the variable regions were confirmed by N-terminal amino acid sequencing. From the nucleic acid sequence and predicted amino acid sequence of the mAbs, gene usage was identified for each antibody chain.

TABLE 1

		Heavy Chain Variable Region			Light Chain Variable Region	
10	Antibody	VH	D	JH	VK	JK
	H1H313	3-13	1-26	4	3-15	3
	H1H314	3-33	3-3	4	1-5	2
	H1H315	3-33	3-3	4	4-1	1
	H1H316	3-23	7-27	2	4-1	2
15	H1H317	3-13	1-26	4	1-6	1
	H1H318	4-59	3-10	6	1-9	1
	H1H320	1-18	2-2	6	2-30	1
	H1H321	2-5	1-7	6	2-28	4
	H1H334	2-5	6-6	6	2-28	4
	H1M300	3-7	2-8	6	2-28	4
20	H1M504	3-30	2-8	6	2-28	4
	H1M505	3-30	2-8	6	2-28	4
	H1M500	2-5	5-5	6	2-28	4
	H1M497	1-18	2-2	6	2-30	2
	H1M498	3-21	2-2	4	1-5	2
	H1M494	3-11	5-12	6	3-20	4
25	H1M309	3-21	6-13	4	1-5	1
	H1M312	3-21	6-13	4	1-5	1
	H1M499	3-21	6-13	4	1-5	1
	H1M493	3-21	6-13	4	1-5	1
	H1M496	3-13	6-19	4	3-15	3
	H1M503	1-18	2-2	6	2-28	1
30	H1M502	3-13	6-13	4	3-15	3
	H1M508	3-13	6-13	4	3-15	3
	H1M495	3-9	4-17	6	1-9	3
	H1M492	3-23	3-3	2	3-20	4

Example 3

Antigen Binding Affinity Determination

Equilibrium dissociation constants (K_D) for hPCSK9 binding to mAbs generated by hybridoma cell lines described above were determined by surface kinetics in a real-time biosensor surface plasmon resonance assay (BIAcore™ T100). Each antibody was captured at a flow rate of 4 μ l/min for 90 sec on a goat anti-mouse IgG polyclonal antibody surface created through direct chemical coupling to a BIAcore™ chip to form a captured antibody surface. Human PCSK9-myc-myc-his (hPCSK9-mmh) at a concentration of 50 nM or 12.5 nM was injected over the captured antibody surfaces at a flowrate of 50 μ l/min for 300 sec, and antigen-antibody dissociation was monitored for 15 min at either 25° C. or 37° C. (K_D =pM; $T_{1/2}$ =min).

TABLE 2

Antibody	25° C.		37° C.	
	K_D	$T_{1/2}$	K_D	$T_{1/2}$
H1M300	399	170	1510	32
H1M309	29.9	7461	537	326
H1M312	0.225	15568	432	392
H1M493	46.5	4921	522	341
H1M494	870	114	2350	30
H1M495	440	222	7500	19
H1M496	254	257	421	118
H1M497	20.1	5801	480	290
H1M498	6400	30	7500	14
H1M499	106	2253	582	316
H1M500	1400	91	6010	15

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TABLE 2-continued

Antibody	25° C.		37° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
H1M502	78.3	958	411	151
H1M503	510	118	1880	30
H1M504	3470	35	11200	6
H1M505	2740	42	9200	6
H1M508	138	572	442	139
H1M510	1070	68	3960	10

Equilibrium dissociation constants (K_D) for hPCSK9 binding to mAbs generated via direct isolation of splenocytes were determined by surface kinetics in a real-time biosensor surface plasmon resonance assay (BIAcore™ T100). Each selected antibody was captured at a flowrate of 2 µl/min for 6 min on a goat anti-human IgG polyclonal antibody surface created through direct chemical coupling to a BIAcore™ chip to form a captured antibody surface. Human PCSK9-mmh at a concentration of 50 nM or 12.5 nM was injected over the captured antibody surface at a flowrate of 70 µl/min for 5 min, and antigen-antibody dissociation was monitored for 15 min at either 25° C. or 37° C. (K_D=pM; T_{1/2}=min).

TABLE 3

Antibody	25° C.		37° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
H1H313P	244	230	780	60
H1H314P	3990	65	3560	43
H1H315P	129	151	413	35
H1H316P	377	42	1080	11
H1H317P	30400	137	18600	70
H1H318P	972	59	1690	28
H1H320P	771	28	1930	8
H1H321P	865	106	3360	23
H1H334P	3750	46	15900	8

Dissociation rate (kd) of selected mAbs for tagged rhesus monkey (*Macaca mulata*) PCSK9 (mmPCSK9; SEQ ID NO:756) (mmPCSK9-mmh) at 25° C. was determined as described above.

TABLE 4

Antibody	kd (1/s)	T _{1/2} (min)
H1H313P	2.92 × 10 ⁻⁵	396
H1H318P	3.69 × 10 ⁻³	3
H1H334P	8.06 × 10 ⁻³	1
H1H315P	2.29 × 10 ⁻⁴	51
H1H316P	2.29 × 10 ⁻⁴	51
H1H320P	3.17 × 10 ⁻⁴	36
H1M300	1.52 × 10 ⁻⁴	76
H1M504	5.04 × 10 ⁻⁴	23
H1M497	6.60 × 10 ⁻⁵	175
H1M503	8.73 × 10 ⁻⁵	132
H1M496	4.45 × 10 ⁻⁵	260

Example 4

Effect of pH on Antigen Binding Affinity

The effects of pH on antigen binding affinity for CHO cell-produced fully human anti-hPCSK9 mAbs was assessed as described above. The mAbs tested are fully human versions of H1H316P ("316P") (HCVR/LCVR SEQ ID NO: 90/92; CDR sequences SEQ ID NO: 76/78/80 and 84/86/88)

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and H1M300N ("300N") (HCVR/LCVR SEQ ID NO: 218/226; CDR sequences SEQ ID NO:220/222/224 and 228/230/232). Human PCSK9-myc-myc-his (hPCSK9-mmh) was captured on an anti-myc mAb surface either at a high density (about 35 to 45 resonance units) (RU) or at a low density (about 5 to 14 RU). Each antibody, at 50 nM in HBST (pH 7.4 or pH 5.5) was injected over the captured hPCSK9 surface at a flow rate of 100 µl/ml for 1.5 min at 25° C. and antigen-antibody dissociation was monitored for 10 min. Control I: anti-hPCSK9 mAb SEQ ID NO:79/101 (WO 2008/063382) (K_D=pM; T_{1/2}=min).

TABLE 5

Antibody	High hPCSK9 Density Surface				Low hPCSK9 Density Surface			
	pH 7.4		pH 5.5		pH 7.4		pH 5.5	
	K _D	T _{1/2}	K _D	T _{1/2}	K _D	T _{1/2}	K _D	T _{1/2}
316P	191	74	144	83	339	45	188	58
300N	65	507	1180	26	310	119	1380	13
Control I	20000	29	ND	ND	ND	ND	ND	ND

The antigen binding properties of 316P and 300N at pH 7.4 or pH 5.5 were determined by a modified BIAcore™ assay as described above. Briefly, mAbs were immobilized onto BIAcore™ CM5 sensor chips via amine coupling. Varying concentrations of myc-myc-his tagged hPCSK9, mouse PCSK9 (mPCSK9, SEQ ID NO:757), hPCSK9 with a gain of function (GOF) point mutation of D374Y (hPCSK9(D374Y), cynomolgus monkey (*Macaca fascicularis*) PCSK9 (mf-PCSK9, SEQ ID NO:761) (mfPCSK9), rat (*Rattus norvegicus*) PCSK9 (rPCSK9, SEQ ID NO:763), and his-tagged Syrian golden hamster (*Mesocricetus auratus*) PCSK9 (maPCSK9, SEQ ID NO:762) (maPCSK9), ranging from 11 to 100 nM, were injected over the antibody surface at the flow rate of 100 µl/ml for 1.5 min and antigen-antibody dissociation was monitored in real time for 5 min at either 25° C. (Table 6) or 37° C. (Table 7). Control II: anti-hPCSK9 mAbs SEQ ID NO:67/12 (WO 2009/026558) (NB: no binding was observed under the experimental condition) (K_D=pM; T_{1/2}=min).

TABLE 6

Antigen	pH Effect at 25° C.			
	pH 7.4		pH 5.5	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh	316P			
	1260	36	22	39
	4460	10	63	11
	2490	15	166	13
	1420	42	8	23
	8350	8	87	8
hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh	300N			
	1100	76	3100	5
	NB	NB	NB	NB
	1310	46	9030	3
	2170	31	38500	0.4
	NB	NB	NB	NB
hPCSK9-mmh mPCSK9-mmh	Control I			
	33100	14	1740	31
	NB	NB	NB	NB

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TABLE 6-continued

pH Effect at 25° C.				
Antigen	pH 7.4		pH 5.5	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9(D347Y)-mmh	71000	11	7320	30
mfPCSK9-mmh	362000	0.2	67200	3
maPCSK9-h	NB	NB	NB	NB
rPCSK9-mmh	NB	NB	NB	NB
Control II				
hPCSK9-mmh	143	266	2	212
mPCSK9-mmh	3500	11	33	12
hPCSK9(D347Y)-mmh	191	155	49	56
mfPCSK9-mmh	102	262	12	63
maPCSK9-h	6500	3	ND	ND
rPCSK9-mmh	22400	2	106	5

TABLE 7

pH Effect at 37° C.				
Antigen	pH 7.4		pH 5.5	
	K _D	T _{1/2}	K _D	T _{1/2}
316P				
hPCSK9-mmh	4000	9	142	11
mPCSK9-mmh	12200	3	13600	3
hPCSK9(D347Y)-mmh	6660	4	1560	5
mfPCSK9-mmh	3770	11	44	5
maPCSK9-h	21700	2	ND	ND
rPCSK9-mmh	55100	2	399	1
300N				
hPCSK9-mmh	2470	20	11900	1
mPCSK9-mmh	NB	NB	NB	NB
hPCSK9(D347Y)-mmh	2610	14	28000	1
mfPCSK9-mmh	4810	8	65200	0.1
maPCSK9-h	NB	NB	NB	NB
rPCSK9-mmh	NB	NB	NB	NB
Control I				
hPCSK9-mmh	45900	0.1	11300	3
mPCSK9-mmh	NB	NB	NB	NB
hPCSK9(D347Y)-mmh	169000	0.4	27000	3
mfPCSK9-mmh	500000	0.6	5360	0.3
maPCSK9-h	NB	NB	NB	NB
rPCSK9	NB	NB	NB	NB
Control II				
hPCSK9-mmh	284	87	20	44
mPCSK9-mmh	8680	3	89	3
hPCSK9(D347Y)-mmh	251	57	483	26
mfPCSK9-mmh	180	127	214	65
maPCSK9-h	8830	0.5	ND	ND
rPCSK9p-mmh	30200	1	233	1

Example 5

Anti-hPCSK9 mAbs Binding to hPCSK9 with Point Mutation D374Y

The binding affinity of selected anti-hPCSK9 mAbs to hPCSK9 with a gain of function (GOF) point mutation of D374Y (hPCSK9(D374Y)-mmh) was determined as described above. Each antibody was captured at a flowrate of 40 µl/min for 8-30 sec on a goat anti-human IgG polyclonal antibody surface created through direct chemical coupling to a BIACORE™ chip to form a captured antibody surface. hPCSK9(D374Y)-mmh at varying concentrations of 1.78 nM to 100 nM was injected over the captured antibody surface at

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a flowrate of 50 µl/min for 5 min, and the dissociation of hPCSK9(D374Y)-mmh and antibody was monitored for 15 min at 25° C. Control III: anti-hPCSK9 mAbs SEQ ID NO:49/23 (WO 2009/026558) (K_D=pM; T_{1/2}=min).

TABLE 8

Antibody	K _D	T _{1/2}
316P	1780	14
300N	1060	49
Control I	23600	25
Control II	66	216
Control III	1020	126

Example 6

Binding Specificity of Anti-hPCSK9 mAbs

316P, 300N, and Control I anti-hPCSK9 mAbs were captured on an amine-coupled anti-hFc CM5 chip on BIA-CORE™2000. Tagged (myc-myc-his) human PCSK9, human PCSK1 (hPCSK1) (SEQ ID NO:759), human PCSK7 (hPCSK7) (SEQ ID NO:760), or mouse PCSK9 were injected (100 nM) over the captured mAb surface and allowed to bind at 25° C. for 5 min. Changes in RU were recorded. Results: 300N and Control I bound only to hPCSK9, and 316P bound both hPCSK9 and mPCSK9.

The binding specificities of anti-hPCSK9 mAbs were determined by ELISA. Briefly, anti-hPCSK9 antibody was coated on a 96-well plate. Human PCSK9-mmh, mPCSK9-mmh, maPCSK9-h, hPCSK1-mmh, or hPCSK7-mmh, at 1.2 nM, were added to antibody-coated plates and incubated at RT for 1 hr. Plate-bound PCSK protein was then detected by HRP-conjugated anti-His antibody. Results show that 316P binds human, mouse, and hamster PCSK9, whereas 300N and Control I only bound hPCSK9. None of the anti-hPCSK9 mAbs exhibited significant binding to hPCSK1 or hPCSK7.

Example 7

Cross-Reactivity of Anti-hPCSK9 mAbs

Cross-reactivity of anti-hPCSK9 mAbs with mmPCSK9, mfPCSK9, mPCSK9, maPCSK9, or rPCSK9 was determined using BIACORE™3000. Briefly, anti-hPCSK9 mAbs were captured on an anti-hFc surface created through direct chemical coupling to a BIACORE™ chip. Purified tagged hPCSK9, hPCSK9(D374Y), mmPCSK9, mfPCSK9, mPCSK9, maPCSK9, or rPCSK9, each at 1.56 nM to 50 nM, was injected over the antibody surface at either 25° C. or 37° C. Binding between 316P, 300N, Control I, Control II, or Control III and the PCSK9 proteins was determined (K_D=pM; T_{1/2}=min) (ND=not determined).

TABLE 9

316P mAb				
Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9-mmh	1800	9	580	36
hPCSK9(D374Y)-mmh	4200	4	1690	15
mmPCSK9-mmh	1800	21	550	92
mfPCSK9-mmh	1800	11	520	60

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TABLE 9-continued

316P mAb				
Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
mPCSK9-mmh	4700	3	2300	11
maPCSK9-h	19000	1	6810	5
rPCSK9-mmh	37500	1	14500	2

TABLE 10

300N mAb				
Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9-mmh	2400	22	740	110
hPCSK9(D374Y)-mmh	2200	14	900	65
mmPCSK9-mmh	1600	26	610	79
mfPCSK9-mmh	3800	11	1500	45
mPCSK9-mmh	NB	NB	NB	NB
maPCSK9-h	NB	NB	NB	NB
rPCSK9-mmh	NB	NB	NB	NB

TABLE 11

Control I mAb				
Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9-mmh	226000	2	27500	16
hPCSK9(D374Y)-mmh	ND	ND	23600	25
mmPCSK9-mmh	420000	3	291000	2
mfPCSK9-mmh	14300	10	24900	14
mPCSK9-mmh	NB	NB	NB	NB
maPCSK9-h	NB	NB	NB	NB
rPCSK9-mmh	NB	NB	NB	NB

TABLE 12

Control II mAb				
Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9-mmh	91	162	61	372
hPCSK9(D374Y)-mmh	93	90	66	216
mfPCSK9-mmh	33	252	26	546
mPCSK9-mmh	4700	3	2300	11
maPCSK9-h	60800	0.4	25000	2
rPCSK9-mmh	14100	1	6900	3

TABLE 13

Control III mAb				
Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
hPCSK9-mmh	380	378	490	450
hPCSK9(D374Y)-mmh	130	660	1000	126
mfPCSK9-mmh	110	750	340	396
mPCSK9-mmh	33500	1	10900	4

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TABLE 13-continued

Antigen	37° C.		25° C.	
	K _D	T _{1/2}	K _D	T _{1/2}
maPCSK9-h	780	107	2100	67
rPCSK9-mmh	NB	NB	33200	2

Example 8

Inhibition of Binding Between hPCSK9 and hLDLR Domains

The ability of selected anti-hPCSK9 mAbs to block hPCSK9 binding to human LDLR full length extracellular domain (hLDLR-ecto SEQ ID NO:758), hLDLR EGF-A domain (amino acids 313-355 of SED ID NO:758), or hLDLR EGF-AB domains (amino acids of 314-393 of SEQ ID NO:758) (LDLR Genbank number NM_000527) was evaluated using BIACORE™. 3000. Briefly, hLDLR-ecto, EGF-A-hFc, or EGF-AB-hFc protein was amine-coupled on a CM5 chip to create a receptor or receptor fragment surface. Selected anti-hPCSK9 mAbs, at 62.5 nM (2.5 fold excess over antigen), were premixed with 25 nM of hPCSK9-mmh, followed by 40 min incubation at 25° C. to allow antibody-antigen binding to reach equilibrium to form equilibrated solutions. The equilibrated solutions were injected over the receptor or receptor fragment surfaces at 2 μl/min for 40 min at 25° C. Changes in RU due to the binding of the anti-hPCSK9 mAbs to hLDLR-ecto, EGF-A-hFc, or EGF-AB-hFc were determined. Results show that H1H316P and H1M300N blocked the binding of hPCSK9-mmh to hLDLR-ecto, hLDLR EGF-A domain, and hLDLR EGF-AB domains; H1H320P blocked the binding of hPCSK9-mmh to hLDLR-ecto and hLDLR EGF-A domain; and H1H321P blocked the binding of hPCSK9-mmh to hLDLR EGF-A domain.

The ability of the mAbs to block hPCSK9 binding to hLDLR-ecto, hLDLR EGF-A domain, or hLDLR EGF-AB domains was also evaluated with an ELISA-based immunoassay. Briefly, hLDLR-ecto, hLDLR EGF-A-hFc or hLDLR EGF-AB-hFc, each at 2 μg/ml, was coated on a 96-well plate in PBS buffer overnight at 4° C., and nonspecific binding sites blocked with BSA. This plate was used to measure free hPCSK9-mmh in a PCSK9-mmh solution pre-equilibrated with varying concentrations of anti-hPCSK9 mAbs. A constant amount of hPCSK9-mmh (500 μM) was pre-mixed with varied amounts of antibody, ranging from 0 to ~50 nM in serial dilutions, followed by 1 hr incubation at room temperature (RT) to allow antibody-antigen binding to reach equilibrium. The equilibrated sample solutions were transferred to receptor or receptor fragment coated plates. After 1 hour of binding, the plates were washed and bound hPCSK9-mmh detected using HRP conjugated anti-myc antibody. IC₅₀ values (in pM) were determined as the amount of antibody required to achieve 50% reduction of hPCSK9-mmh bound to the plate-coated receptor or receptor fragment. The results show that specific mAbs functionally block PCSK9 from binding the three receptors at both neutral pH (7.2) and acidic pH (5.5).

TABLE 14

Ab	Plate Coating Surface					
	pH 7.2			pH 5.5		
	hLDLR-ecto	EGF-A	EGF-AB	hLDLR-ecto	EGF-A	EGF-AB
316P	<125	<125	<125	<125	<125	<125
300N	144	146	<125	1492	538	447
Control I	—	>100,000	>100,000	—	>100,000	>100,000
Control II	288	510	274	411	528	508
Control III	303	635	391	742	787	1073

The ability of the mAbs to block hPCSK9 GOF mutant hPCSK9(D374Y)-mmh binding to hLDLR EGF-A domain or hLDLR EGF-AB domain (IC₅₀ values in pM) was also evaluated with the ELISA-based immunoassay described above using a constant amount of 0.05 nM hPCSK9(D374Y)-mmh.

TABLE 15

	pH 7.2		pH 5.5	
	Plate Coating Surface			
	EGF-A	EGF-AB	EGF-A	EGF-AB
316P	203	139	1123	1139
300N	135	142	3463	3935
Control I	>100,000	>100,000	>100,000	>100,000
Control II	72	57	129	118
Control III	537	427	803	692

The ability of the mAbs to block either mmPCSK9 or mPCSK9 binding to hLDLR-ecto domain, hLDLR EGF-A domain, or hLDLR EGF-AB domain (IC₅₀ values in pM) was evaluated at neutral pH (7.2) with the ELISA-based immunoassay described above using a constant amount of 1 nM of mmh-tagged mmPCSK9 or 1 nM of mPCSK9.

TABLE 16

	1 nM mmPCSK9-mmh			1 nM mPCSK9-mmh	
	hLDLR-ecto	EGF-A	EGF-AB	EGF-A	EGF-AB
316P	<250	<250	<250	<250	<250
300N	255	256	290	>33000	>33000

The ability of the mAbs to block hPCSK9, mmPCSK9, rPCSK9, maPCSK9, mfPCSK9, or mPCSK9 binding to hLDLR EGF-A domain (IC₅₀ values in pM) was evaluated at neutral pH (7.2) (Table 17) acidic pH (5.5, Table 18) with the ELISA-based immunoassay described above using a constant amount of 0.5 nM of hPCSK9-mmh, 1 nM of mmPCSK9-mmh, 1 nM of rPCSK9-mmh, 1 nM of maPCSK9-h, 0.3 nM of mfPCSK9-mmh, or 1 nM of mPCSK9-mmh.

TABLE 17

	hPCSK9	mmPCSK9	rPCSK9	maPCSK9	mfPCSK9	mPCSK9
316P	<125	<250	2662	349	75	305
300N	182	460	>100000	>100000	473	>100000
Control I	—	>100000	>100000	>100000	>100000	>100000
Control II	146	83	2572	2038	361	855
Control III	249	293	>100000	245	572	>100000

TABLE 18

	hPCSK9	mmPCSK9	rPCSK9	maPCSK9	mPCSK9
316P	<125	<250	42880	1299	991
300N	223	3704	>100000	>100000	>100000
Control I	>10000	>100000	>100000	>100000	>100000
Control II	154	<250	11640	8339	2826
Control III	390	376	>100000	414	>100000

The ability of 316P and Control I to block hPCSK9 binding to hLDLR was also determined. Briefly, either recombinant hLDLR or hLDLR-EGFA-mFc was immobilized onto BIA-CORE™ CM5 chips via amine coupling. An antigen-antibody mixture of 100 nM hPCSK9-mmh and 316P, Control I mAb, or a non-hPCSK9 specific mAb (each at 250 nM) was incubated at RT for 1 hr, and then injected over the hLDLR or hLDLR-EGFA surface at the flow rate of 10 µl/ml for 15 min at 25° C. Changes in RU due to the binding between the free hPCSK9-mmh in the mixture to either hLDLR or hLDLR-EGFA were recorded. The binding of hPCSK9 to either hLDLR or hLDLR-EGFA was completely blocked by 316P and 300N but not by Control I mAb.

Example 9

Epitope Mapping

In order to determine epitope-binding specificity, three chimeric PCSK9-mmh proteins were generated in which specific human PCSK9 domains were substituted with mouse PCSK9 domains. Chimeric protein #1 consists of a mouse PCSK9 pro-domain (amino acid residues 1-155 of SEQ ID NO:757) followed by a human PCSK9 catalytic domain (residues 153-425 of SEQ ID NO:755) and a mouse PCSK9 C-terminal domain (residues 429-694 SEQ ID NO:757) (mPro-hCat-mC-term-mmh). Chimeric protein #2 consists of a human PCSK9 pro-domain (residues 1-152 of SEQ ID NO:755) followed by a mouse PCSK9 catalytic domain (residues 156-428 of SEQ ID NO:757) and a mouse PCSK9 C-terminal (hPro-mCat-mC-term-mmh). Chimeric protein #3 consists of mouse PCSK9 pro-domain and a mouse PCSK9 catalytic domain followed by a human PCSK9 C-terminal domain (residues 426-692 of SEQ ID NO:755) (mPro-mCat-hC-term-mmh). In addition, hPCSK9 with a point mutation of D374Y (hPCSK9 (D374Y)-mmh) was generated.

Binding specificity of mAbs to test proteins hPCSK9-mmh, mouse PCSK9-mmh, chimeric proteins #1, #2, and #3, and hPCSK9 (D374Y)-mmh were tested as follows: the mAbs were coated on a 96-well plate overnight at 4° C., then each test protein (1.2 nM) was added to the plate. After 1 hr binding at RT, the plate was washed and bound test protein detected using HRP-conjugated anti-myc polyclonal antibody (++=OD>1.0; +=OD 0.4-1.0; -=OD<0.4).

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TABLE 19

Antibody	hPCSK9	mPCSK9	Chimeric Protein			hPCSK9(D374Y)
			#1	#2	#3	
H1M300	++	-	++	+	-	++
H1M309	++	-	-	-	++	++
H1M312	++	-	-	-	++	++
H1M492	++	-	-	-	-	+
H1M493	++	-	-	-	++	++
H1M494	++	-	-	+	++	++
H1M495	++	-	-	-	++	++
H1M496	++	-	-	-	++	++
H1M497	++	-	-	++	+	++
H1M498	++	-	-	-	+	++
H1M499	++	-	-	-	++	++
H1M500	++	-	++	-	-	++
H1M502	++	-	-	-	++	++
H1M503	++	-	-	++	-	++
H1M504	++	-	-	-	-	+
H1M505	++	-	++	+	-	++
H1M508	++	-	-	-	++	++
H1H318P	++	-	++	-	-	++
H1H334P	++	-	++	-	-	++
H1H316P	++	++	++	++	++	++
H1H320P	++	-	-	++	-	++
Control I	++	-	-	-	++	++

Binding specificity of 316P, 300N and control anti-hPCSK9 mAbs to hPCSK9-mmh, mPCSK9-mmh, mmPCSK9-mmh, mfPCSK9-mmh, rPCSK9-mmh, chimeric proteins #1, #2, and #3, and hPCSK9 (D374Y)-mmh were tested as described above except that the protein concentration is 1.7 nM (—=OD<0.7; +=OD 0.7-1.5; ++=OD>1.5).

TABLE 20

	316P	300N	Control I	Control II	Control III
hPCSK9-mmh	++	++	++	++	++
mPCSK9-mmh	++	-	-	++	++
mmPCSK9-mmh	++	++	++	++	++
mfPCSK9-mmh	++	++	++	++	++
rPCSK9-mmh	++	-	-	++	+
Chimeric Protein #1	++	++	-	++	++
Chimeric Protein #2	++	++	-	++	++
Chimeric Protein #3	++	+	++	++	++
hPCSK9 (D374Y)	++	++	++	++	++

Similar results for selected mAbs were obtained by BIACORE™ binding assay. Briefly, 316P, 300N, or Control I mAb was captured on an amine-coupled anti-hFc CM5 chip and 100 nM of each protein injected over the mAb-captured surface. Changes in RU due to the binding of each protein to the mAb surface was determined.

TABLE 21

Antibody	hPCSK9	mPCSK9	Chimeric Protein		
			#1	#2	#3
316P	500	505	529	451	467
300N	320	13	243	76	10
Control I	65	7	4	3	69

To further assess the binding specificity of 316P, which cross-reacts with mPCSK9-mmh, a cross-competition ELISA assay was developed to determine binding domain specificity. Briefly, mAbs specific for chimeric protein #1, #2, or #3, were first coated on a 96-well plate overnight at 1 µg/ml. Human PCSK9-mmh (2 µg/ml) was then added to each well followed by 1 hr incubation at RT. 316P (1 µg/ml) was added and incubated for another hour at RT. Plate-bound

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316P was detected using HRP-conjugated anti-hFc polyclonal antibody. Although 316P binding to hPCSK9-mmh was not affected by the presence of mAbs specific for either chimeric protein #2 or chimeric protein #3, 316P binding to hPCSK9-mmh was greatly reduced by the presence of antibody specific for chimeric protein #1.

Example 10

BIACORE™-Based Antigen Binding Profile Assessment

Antibody binding profiles were also established for 316P, 300N, Control I, II, and III mAbs using BIACORE™1000. Briefly, hPCSK9-mmh was captured on an anti-myc surface. A first anti-hPCSK9 mAb (50 µg/ml) was injected over the PCSK9-bound surface for 10 min, at a flow rate of 10 µl/min at 25° C. A second anti-hPCSK9 mAb (50 µg/ml) was then injected over the first mAb-bound surface for 10 min, at a flow rate of 10 µl/min at 25° C. Ability of the first mAb to block binding of the second mAb was measured and is expressed as percent inhibition.

TABLE 22

First mAb	Second mAb				
	316P	300N	Control I	Control II	Control III
316P	100	101	27	99	101
300N	77	100	12	82	-2
Control I	6	12	100	6	9
Control II	91	102	-6	100	3
Control III	73	10	-12	1	100

Example 11

Increase of LDL Uptake by Anti-hPCSK9 Antibodies

The ability of anti-hPCSK9 mAbs to increase LDL uptake in vitro was determined using a human hepatocellular liver carcinoma cell line (HepG2). HepG2 cells were seeded onto 96-well plates at 9×10^4 cells/well in DMEM complete media and incubated at 37° C., 5% CO₂, for 6 hr to form HepG2 monolayers. Human PCSK9-mmh, at 50 nM in lipoprotein deficient medium (LPDS), and a test mAb was added in various concentrations from 500 nM to 0.98 nM in LPDS medium. Data are expressed as IC₅₀ values for each experiment (IC₅₀=antibody concentration at which increases LDL uptake by 50%). In addition, the experiment also showed that both 316P and 300N were able to completely reverse the inhibitory effect of hPCSK9 on LDL uptake, while Control I mAb or H1M508 anti-hPCSK9 mAb reversed the inhibitory effect by about 50%.

TABLE 23

Antibody	IC ₅₀ (nM)
316P	21.30
300N	22.12
Control I	>250
H1M508	>250

The ability of anti-hPCSK9 mAbs to reverse the inhibitory effect on LDL uptake by PCSK9 protein from different mammalian species was also tested in a HepG2 cell line as

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described above. Briefly, HepG2 cells were incubated overnight with serial dilutions of antibody in LPDS medium (beginning with 500 nM) and 50 nM of hPCSK9-mmh, mfPCSK9-mmh, mPCSK9-mmh, rPCSK9-mmh, or maPCSK9-h. HepG2 cells were also incubated overnight with serial dilutions of antibody in LPDS (beginning with 50 nM) and 1 nM hPCSK9(D374Y). As shown in Table 24, while 316P was able to completely reverse the inhibitory effect on LDL by all PCSK9 proteins tested, 300N was only able to reverse the inhibitory effect on LDL uptake by hPCSK9, hPCSK9 (D374Y), and mfPCSK9. Values are expressed as nM IC₅₀.

TABLE 24

	316P	300N	Control I	Control II	Control III
hPCSK9-mmh	14.1	12.6	>500	13.4	12.4
hPCSK9(D374Y)-mmh	2.1	1.1	>50	0.7	0.6
mfPCSK9-mmh	14.7	13.4	>500	14.2	13.6
mPCSK9-mmh	21.2	>500	>500	19	>500
rPCSK9-mmh	27.7	>500	>500	21.9	>500
maPCSK9-h	14.4	>500	>500	29.5	12.7

Example 12

Neutralization of Biological Effect of hPCSK9 In Vivo

To assess the biological effect of neutralizing PCSK9, hPCSK9 was over-expressed in C57BL/6 mice by hydrodynamic delivery (HDD) of DNA constructs encoding full-length hPCSK9-mmh. 4 mice (C57BL/6) were injected with empty vector/saline (control), and 16 mice were injected with a 50 µg hPCSK9-mmh-DNA/saline mixture in the tail vein equal to 10% of their body weight. At day 7 after HDD, delivery of hPCSK9 resulted in a 1.6-fold elevation of total cholesterol, 3.4-fold elevation in LDL-cholesterol (LDL-C) and a 1.9-fold elevation in non-HDL cholesterol (relative to control). Serum hPCSK9 levels on day 7 were all greater than 1 µg/ml, as assessed by quantitative ELISA.

Administration of HIM300N on day 6 after HDD to 3 experimental groups (1, 5 or 10 mg/kg) (n=4 per group) via intraperitoneal (i.p.) injection resulted in a significant attenuation of serum cholesterol levels. At 18 hours after administration, total cholesterol was reduced by 9.8%, 26.3% and 26.8%, LDL-C was reduced by 5.1%, 52.3% and 56.7%, and non-HDL cholesterol was reduced by 7.4%, 33.8% and 28.6% in the 1, 5 or 10 mg/kg HIM300N treated groups, respectively.

Example 13

Pharmacokinetic and Serum Chemistry Study in Monkeys

A pharmacokinetic (PK) study was conducted in naïve male cynomolgus monkeys (*Macaca fascicularis*) with a body weight range between 5-7 kg and aged between 3-5 years.

Group assignments. The monkeys were assigned into 5 treatment groups: Treatment Group 1 (n=3) received control buffer (10 mM sodium phosphate, pH 6, 1 ml/kg); Treatment Group 2 (n=3) received 1 ml/kg of 316P (5 mg/ml); Treatment Group 3 (n=3) received 1 ml/kg 300N (5 mg/ml); Treatment Group 4 (n=3) received 1 ml/kg 316P (15 mg/ml); and Treat-

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ment Group 5 (n=3) received 1 ml/kg 300N (15 mg/ml). All treatments were administered by IV bolus followed by a 1 ml saline flush. Total dose volume (ml) was calculated on the most recent body weight (each animal was weighed twice during acclimation and once weekly throughout the study). A single dose of test mAb or buffer control was administered on Day 1.

Animal care. Animals were housed in a temperature- and humidity-monitored environment. The targeted range of temperature and relative humidity was between 18-29° C. and 30-70%, respectively. An automatic lighting system provided a 12-hour diurnal cycle. The dark cycle could be interrupted for study- or facility-related activities. The animals were individually housed in cages that comply with the Animal Welfare Act and recommendations set forth in The Guide for the Care and Use of Laboratory Animals (National Research Council 1996).

Diet and Feeding. Animals were fed twice per day according to SNBL USA SOPs. Animals were fasted when required by specific procedures (, prior to blood draws for serum chemistry, urine collection, or when procedures involving sedation are performed). The diet was routinely analyzed for contaminants and found to be within manufacturer's specifications. No contaminants were expected to be present at levels that would interfere with the outcome of the study.

Experimental Design. An appropriate number of animals were selected from SNBL USA stock. Animals were examined for health by veterinary staff, and had undergone serum chemistry, hematology, and coagulation screening. Sixteen males, confirmed healthy, were assigned to the study. Fifteen males were assigned to specific study groups and the remaining animal was available as a spare. A stratified randomization scheme incorporating serum cholesterol level (based on the average of two draws in acclimation) was used to assign animals to study groups.

Acclimation Period. Previously quarantined animals were acclimated to the study room for a minimum of 14 days prior to initiation of dosing. Acclimation phase data was collected from all animals, including the spare. All animals were assessed for behavioral abnormalities that could affect performance on study. The spare animal was returned to stock after day 1.

Blood collection. Blood was collected by venipuncture from a peripheral vein from restrained, conscious animals. Whenever possible, blood was collected via a single draw and then divided appropriately.

PK Study. Blood samples (1.5 ml) were collected at pre-dose, 2 min, 15, min, 30 min, 1 hr, 2 hr, 4 hr, 8 hr, 12 hr, 24 hr, and subsequently once every 24 hr in serum separator tubes (SST). Specimen storage serum is transferred to 2 vials and stored at -60° C. or below.

Serum samples were analyzed using an optimized ELISA (enzyme-linked immunosorbent assay) procedure. Briefly, a microtiter plate was first coated with hPCSK9-mmh. Test mAb 316P or 300N was then captured on the hPCSK9-mmh plate. The captured 316P or 300N was detected using a biotinylated mouse anti-hIgG4 followed by binding to NeutrAvidin-HRP. Varying concentrations of 316P or 300N, ranging from 100 to 1.56 ng/ml, were used as standards. One percent monkey serum (assay matrix) in the absence of 316P or 300N was used as the zero (0 ng/ml) standard. The results, shown in FIG. 2, indicate a dose-dependent increase in serum 316P and 300N levels. PK parameters were analyzed using WinNonlin software (Noncompartmental analysis, Model 201-IV bolus administration).

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TABLE 25

PK Parameter	316P		300N	
	5 mg/kg	15 mg/kg	5 mg/kg	15 mg/kg
T_{max} (h)	0.428	0.105	4.02	0.428
C_{max} (μ g/ml)	184	527	226	1223
$T_{1/2}$ (h)	83	184	215	366

Serum Chemistry. Blood samples were collected at pre-dose, 12 hr, 48 hr, and subsequently once every 48 hr, for clinical chemistry analysis, in particular lipid profiles (cholesterol, LDL-C, HDL-C, triglycerides). With the exception of the 12 hr post-dose sample, all animals were subject to an overnight fast prior to sample collection. The sample volume was approximately 1 ml. Chemistry parameters were determined using an Olympus automated analyzer. Parameters measured (Xybion code): Albumin (ALB); Alkaline Phosphatase (ALP); Alanine Aminotransferase (ALT); Aspartate Transaminase (AST); Total Bilirubin (TBIL); Calcium (Ca); Total Cholesterol (TChol); Creatine Kinase (CK); Creatinine (CRN); Gamma Glutamyltransaminase (GGT); Glucose (GLU); Inorganic Phosphorus (IP); Total Protein (TP); Triglyceride (TRIG); Blood Urea Nitrogen (BUN); Globulin (GLOB); Albumin/Globulin Ratio (A/G); Chloride (Cl); Potassium (K); Sodium (Na); LDL and HDL cholesterol. Residual serum was stored at -20° C. or below and disposed of no sooner than one week after analysis.

Results from samples through Day 105 post-dose time point are shown in FIGS. 3-7. There was a reduction in total cholesterol and LDL-C in animals receiving 316P and 300N, regardless of dose, within 24 hours of the first dose. Serum total cholesterol reduced rapidly and robustly ($\sim 35\%$, FIG. 3). A robust decrease of $\sim 80\%$ was seen in LDL-C (FIGS. 4-5) by day 6. In animals that received a 15 mg/kg dose of 300N, the reduction in both total cholesterol ($\sim 10\text{-}15\%$ reduction) and LDL-C ($\sim 40\%$ reduction) continued to at least day 80 of the study. In addition, HDL-C was elevated in animals that received 316P at 15 mg/kg (FIG. 6). Animals that received a higher dose (15 mg/kg) of either 316P or 300N also showed a reduction in triglycerides during the course of study (FIG. 7). 316P exhibited maximal suppression of LDL-C levels of up to 80% relative to baseline. The length of this suppression was dose-dependent with at least 60% suppression (relative to baseline LDL-C levels) lasting approximately 18 days (5 mg/kg dose) and approximately 45 days (15 mg/kg dose). 300N exhibits a distinct pharmacodynamic profile from 316P. LDL-C suppression by 300N was sustained for a much longer period of time at comparable doses (50% LDL-C suppression for 28 days following a 5 mg/kg dose and 50% LDL-C suppression for approximately 90 days following a 15 mg/kg dose). There was little or no measurable change in liver function as determined by ALT and AST measurements. All animals receiving an anti-PCSK9 antibody in the study exhibited a rapid suppression of LDL-C and total cholesterol.

A similar LDL-C lowering effect of 316P and 300N was also observed in cynomolgus monkeys that received a single subcutaneous (SC) administration of either 5 mg/kg 316P or 5 mg/kg 300N (FIG. 8). Both 316P and 300N dramatically suppressed LDL-C levels and maintained an LDL-C lowering effect for approximately 15 and 30 days, respectively (FIG. 8). The pharmacodynamic effect (approximately 40% LDL-C suppression) approximately correlates with functional antibody levels in monkey serum (FIG. 9). As antibody levels decrease below 10 μ g/ml, LDL-C suppression appeared to diminish as well. In addition, 300N demonstrated

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a substantially longer circulating half-life than 316P and hence a longer observed LDL-C suppression.

TABLE 26

PK Parameter	316P	300N
T_{max} (h)	60	84
C_{max} (μ g/ml)	46	63
$T_{1/2}$ (h)	64	286

Example 14

Attenuation of LDL Receptor Degradation by Anti-hPCSK9 Antibodies

To assess the biological effect of PCSK9 on hepatic LDL receptor levels and subsequent effects on serum LDL-C levels, hPCSK9 was administered to mice expressing hPCSK9 but not mPCSK9 (PCSK9^{hu/hu} mice) by intravenous injection. Specifically, PCSK9^{hu/hu} mice were injected with PBS (control), or 1.2 mg/kg hPCSK9-mmh via the tail vein. Six hours after delivery of hPCSK9, a 1.4-fold elevation (relative to baseline level) in total cholesterol and a 2.3-fold elevation in LDL-C in serum were observed. Analysis of hepatic LDL receptor levels in a separate cohort (n=3) of animals 0.4 hours after hPCSK9 administration revealed a significant reduction in detectable LDL receptor in liver homogenates.

To assess the biological effect of anti-hPCSK9 on hepatic LDL receptor levels and subsequent effects on serum LDL-C levels, 316P and a non-hPCSK9 specific mAb were administered to PCSK9^{hu/hu} mice at equivalent dose (5 mg/kg) 20 hours prior to the hPCSK9-mmh protein injection described above. Four hours after the hPCSK9 administration, mice were sacrificed and a total of eight tissues (liver, brain, lung, kidney, heart, ileum, adrenal, and pancreas) were collected and levels of LDL receptor were determined by Western blot. Changes in LDL receptor levels were only observed in liver. In comparison to PBS control dosing, administration of 316P significantly blocked the PCSK9-mediated increases in total cholesterol and LDL cholesterol (LDL-C=2.49 mg/dl at baseline and 3.1 mg/dl 6 hours after PCSK9; a 25% increase compared to 135% with vehicle). Prior administration of the non-hPCSK9 specific mAb blocked LDL-C increases by approximately 27% from PBS alone (LDL-C=4.1 mg/dl compared to PBS 5.6 mg/dl). Analysis of LDL receptor levels in a separate cohort of mice (n=3 per treatment group) revealed a significant reduction in LDL receptor levels with PCSK9 administration, which was blocked by 316P but not by the non-hPCSK9 specific mAb (FIG. 10).

Effect of different doses of 316P was also evaluated in PCSK9^{hu/hu} mice with both elevated LDL-C and elevated hPCSK9 levels. PCSK9^{hu/hu} mice were first placed on a high carbohydrate diet for 8 weeks, resulting in a ~ 2 -fold elevation in both LDL-C and hPCSK9 levels. Either 316P or a non-hPCSK9 specific mAb, each at 1 mg/kg, 5 mg/kg, or 10 mg/kg, were administered to the mice. Sera were collected 24 hours later and LDL-C levels were analyzed. 316P was effective in decreasing LDL-C levels in a dose-dependent manner (FIG. 11). In addition, 316P administered at a dose of 10 mg/kg, rapidly reduced LDL-C levels back to original (pre-diet) values within 24 hours.

Example 15

Mouse PK Studies

A PK study was conducted in 6-week-old C57BL/6 mice and 11-15 week old hPCSK9 heterozygous mice. A single

injection of Control I, 316P, or 300N, each at 10 mg/kg, was administered SC. Serum bleeds were measured for hIgG levels at 0 hr (pre-bleed), 6 hr, day 1, 3, 6, 10, 14, 21, 28, 35, 42 and 56, for a total of 12 time points, using an anti-hFc capture and anti-hFc detection sandwich ELISA (FIGS. 12 and 13). All mAbs achieved their T_{max} at approximately 3 days with corresponding C_{max} levels of approximately 47-115 $\mu\text{g/ml}$ for C57BL/6 mice and 55-196 $\mu\text{g/ml}$ for hPCSK9 heterozygous mice. At Day 56, Control I mAb levels were about 12 $\mu\text{g/ml}$ and 300N levels were about 11 $\mu\text{g/ml}$ whereas 316P levels were about less than 0.02 $\mu\text{g/ml}$ in C57BL/6 mice. At Day 56 in hPCSK9 heterozygous mice, Control I mAb levels were about 29 $\mu\text{g/ml}$, while both 300N and 316P levels were below the quantifiable limit (BQL) of 0.02 $\mu\text{g/ml}$.

Example 16

Anti-hPCSK9 Antibody Binding to Mutant/Variant hPCSK9

To further assess binding between hPCSK9 and anti-hPCSK9 mAbs, 21 variant hPCSK9 proteins in which each variant contained a single point mutation and two variant hPCSK9 proteins each contained a double mutation were generated. Each selected antibody was captured on a F(ab')₂ anti-hIgG surface created through direct chemical coupling to a BIACORETM chip to form a captured antibody surface. Each mmh-tagged variant hPCSK9 at varying concentrations from 100 nM to 25 nM was then injected over the captured antibody surface at a flowrate of 60 $\mu\text{l/min}$ for 240 sec, and the dissociation of variant hPCSK9 and antibody was monitored in real time for 20 min at 25° C. nb: no binding was observed under these experimental conditions (K_D =M $\times 10^{-9}$; $T_{1/2}$ =min; WT=wildtype).

TABLE 27

	316P		300N		Control I		Control II		Control III	
	K_D	$T_{1/2}$	K_D	$T_{1/2}$	K_D	$T_{1/2}$	K_D	$T_{1/2}$	K_D	$T_{1/2}$
WT	1.00	37	0.69	120	30.6	16	0.10	333	0.60	481
P70A	1.42	32	1.68	80	19.0	16	0.24	168	0.90	325
S127R	2.40	36	1.87	110	25.0	18	0.26	288	0.55	550
D129G	1.27	36	1.40	88	22.9	18	0.19	257	0.75	445
S147F	1.29	32	9.07	24	21.1	15	0.22	178	0.23	1468
S153R	5.64	4	0.56	141	36.6	17	0.09	322	3.33	60
E159R	6.96	5	0.82	94	31.7	16	0.08	350	2.97	68
T162R	0.98	43	0.58	140	29.0	17	0.09	322	0.48	362
D192R	1.35	28	0.75	119	30.2	15	0.09	326	nb	nb
R194E	0.38	71	0.65	129	31.4	16	0.07	389	nb	nb
E197R	1.42	27	0.67	115	30.2	17	0.09	339	nb	nb
R215H	0.86	41	1.03	98	37.8	17	0.65	49	0.74	272
R215E	0.90	43	1.81	77	44.0	16	4.48	12	0.78	276
F216L	1.83	32	0.99	121	21.2	15	1.35	39	0.33	880
R237E	2.48	15	1.03	109	29.6	15	0.07	481	5.89	43
D238R	410	1	0.78	123	25.9	19	0.24	144	0.14	1273
A341R	1.54	21	0.34	190	28.7	18	0.08	340	0.88	200
D343R	7.88	6	1.18	89	27.0	16	0.08	402	4.13	66
R357H	6.26	30	6.53	66	26.4	13	0.63	165	1.91	896
E366K	2.92	13	36.0	2	28.8	18	0.46	69	0.38	808
D374Y	2.04	15	0.66	83	25.0	17	0.08	285	1.02	161
V380M	0.48	63	2.82	28	25.9	17	0.15	177	0.35	711
P70A, S147F	1.18	34	7.87	24	23.5	18	0.23	164	0.79	348
E366K, V380M	3.33	12	78.3	1	25.5	18	0.59	60	0.52	551

The results show that when residue D238 was mutated, the binding affinity of 316P for hPCSK9 was reduced >400-fold, from a K_D of 1×10^{-9} M to 410×10^{-9} M; and $T_{1/2}$ shortened about 30-fold, from 37 to 1 min, indicating that 316P binds an epitope on hPCSK9 comprising D238 of hPCSK9 (SEQ ID NO:755). Additionally, BIACORETM assays show that 316P

binding affinity and $T_{1/2}$ were reduced about 5- to 10-fold when a residue at 153, 159 or 343 was mutated. Specifically, K_D was reduced from about 1×10^{-9} M to between about $5-8 \times 10^{-9}$ M when any one of S153, E159 or D343 were mutated; while $T_{1/2}$ was decreased from about 37 min to between about 4-6 min.

300N binding to hPCSK9 was reduced about 50-fold when the residue at position 366 was mutated, resulting in a decreased K_D of from about 0.7×10^{-9} M to about 36×10^{-9} M and a shorter $T_{1/2}$ from about 120 to 2 min. These results indicate that 300N binds an epitope on hPCSK9 comprising E366 of hPCSK9 (SEQ ID NO:755). Additionally, the BIACORETM assays show that 300N binding affinity and $T_{1/2}$ were reduced between 2- to >10-fold when a residue at 147 or 380 was mutated. Specifically, K_D was reduced from about 0.69×10^{-9} M to between about $2-9 \times 10^{-9}$ M when any of S147 or V380 were mutated; while $T_{1/2}$ was shortened from about 120 min to between about 24-66 min. Compared to 316P, 300N binding to hPCSK9 was not reduced by a mutation at residue 238.

In contrast, Control I antibody did not exhibit an altered binding affinity or $T_{1/2}$ in response to any of the positional mutations tested; Control II antibody exhibited a 40-fold decreased affinity when residue 215 was mutated (R215E) (from $\sim 0.1 \times 10^{-9}$ to $\sim 4.5 \times 10^{-9}$), and $T_{1/2}$ was about 27-fold shorter (from ~ 333 to 12 min); while Control III antibody exhibited a decreased affinity when residue 237 was mutated (K_D decreased from $\sim 0.6 \times 10^{-9}$ to $\sim 5.9 \times 10^{-9}$, and $T_{1/2}$ decreased from ~ 481 to ~ 43 min).

Binding specificity of 316P, 300N, and control anti-hPCSK9 mAbs to hPCSK9 variants was tested using an ELISA-based immunoassay. Anti-PCSK9 mAbs were coated on a 96-well plate overnight at 4° C. Each mmh-tagged vari-

ant hPCSK9 in CHO-k1 transient transfection lysate supernatants was added to the antibody-coated plate at various concentrations ranging from 0 to 5 nM. After 1 hr binding at RT, the plate was washed and bound variant hPCSK9 was detected using HRP-conjugated anti-myc polyclonal antibody ($-OD < 0.7$; $+OD 0.7-1.5$; $++OD > 1.5$).

TABLE 28

hPCSK9 or Variant	316P	300N	Control I	Control II	Control III
hPCSK9(WT)	++	++	++	++	++
hPCSK9(S127R)	++	++	++	++	++
hPCSK9(D129G)	++	++	++	++	++
hPCSK9(S153R)	++	++	++	++	++
hPCSK9(R215H)	++	++	++	++	++
hPCSK9(F216L)	++	++	++	++	++
hPCSK9(R237E)	++	++	++	++	++
hPCSK9(D238R)	-	++	++	++	++
hPCSK9(A341R)	++	++	++	++	++
hPCSK9(D343R)	++	++	++	++	++
hPCSK9(R357H)	++	++	++	++	++
hPCSK9(E159R)	++	++	++	++	++
hPCSK9(T162R)	++	++	++	++	++
hPCSK9(D192R)	++	++	++	++	-
hPCSK9(R194E)	++	++	++	++	-
hPCSK9(E197R)	++	++	++	++	-
hPCSK9(R215E)	++	++	++	++	++
hPCSK9(P70A)	++	++	++	++	++
hPCSK9(S147F)	++	++	++	++	++
hPCSK9(E366K)	++	+	++	++	++
hPCSK9(V380M)	++	++	++	++	++
hPCSK9(P70A, S147F)	++	++	++	++	++
hPCSK9(E366K, V380M)	++	+	++	++	++

Example 17

Effect of 316P on Normolipemic and Hyperlipemic Hamster

The ability of anti-PCSK9 mAb 316P to reduce serum LDL-C was tested in normolipemic or hyperlipemic Gold Syrian hamsters (*Mesocricetus auratus*). Male Syrian Hamsters, age 6-8 weeks, weighing between 80-100 grams, were allowed to acclimate for a period of 7 days before entry into the study. All animals were placed on either a standard chow diet or a hyperlipemic diet of chow supplemented with 0.1% cholesterol and 10% coconut oil. The 316P mAb was delivered to hamsters by a single subcutaneous injection at doses of 1, 3, or 10 mg/kg for normolipemic hamsters and at doses of 3, 10, or 30 mg/kg for hyperlipemic hamsters. Serum samples were taken from all groups at 24 hr and 7, 14, and 22 days post injection, at which time serum lipid levels were assessed and compared to baseline levels taken 7 days prior to the administration of the mAbs. Circulating total cholesterol and LDL-C in normolipemic hamsters was significantly reduced in a dose-dependent manner compared to vehicle injection. As shown in FIG. 14, administration of 316P effectively reduced LDL-C levels by up to 60% seven days post injection at the highest dose (10 mg/kg) tested. Similar cholesterol reducing effect of 316P was not observed in hyperlipemic hamsters.

Example 18

A Randomized, Double-Blind, Placebo-Controlled, Ascending Single-to-Multi-Dose Study of the Safety, Tolerability, and Bioeffect of Subcutaneously Administered Human Anti-PCSK9 Antibody in Patients with and without Concomitant Atorvastatin

The objective of this study was to determine whether a fully human monoclonal antibody to PCSK9 (mAb316P) is effective and safe as either a primary or adjunctive agent to lower LDLc in patients with Heterozygous Familial Hypercholesterolemia (HeFH) or other forms of primary hypercholesterolemia (nonFH).

This study was a randomized, double-blind, placebo-controlled, multiple ascending dose Clinical trial enrolling 61 adults with either documented HeFH (n=21) or nonFH (n=30), on diet plus stable atorvastatin therapy (atorvaRx) or nonFH (n=10) on diet alone. Subjects on stable atorvastatin therapy had LDLc ≥ 2.6 mmol/L and those on diet alone had LDLc ≥ 3.4 mmol/L. mAb316P at doses of 50, 100 and 150 mg was administered subcutaneously (sc) at 1, 29 and 43 days. The primary endpoint was the incidence and severity of treatment emergent adverse events (TEAE). The primary efficacy endpoint was percent and absolute change in serum LDLc from baseline to each visit. Additional endpoints included apolipoprotein (apo) B, total cholesterol, HDLc, VLDLc, and the ratio of apoB to apoA1.

109 patients were screened, and 61 patients were randomized (14 placebo, 47 mAb316P) with 100% completing 148+/-7 days of treatment and follow up. Compared to the nonFH cohort, the FH group was younger (mean 40 vs 52 yrs), had more males (81% vs 57%) and was on higher doses of atorvastatin (52% on 40 mg vs 3%). Baseline LDLc was 3.45, 2.88 and 4.46 mmol/L respectively in the FH, nonFH atorvaRx and nonFH diet only groups respectively. Response to mAb316P (expressed as percent change in calculated serum LDL-C from baseline to each visit) is shown Tables 29 and 30. Treatment with mAb316P resulted in mean % reductions in LDLc on top of statins on day 57 of 35.6%, 50.2% and 57.5% at the 50, 100 and 150 mg doses, respectively, in the combined FH and nonFH populations. There did not appear to be differences in response between FH and nonFH or those on or not on statin therapy.

Favourable changes were also observed in HDLc and apoA1. No serious adverse events were seen and treatment was generally well tolerated. No drug-related adverse effects were seen on liver function testing or other laboratory parameters.

TABLE 29

Percent Change in Calculated Serum LDL-C From Baseline to Each Visit*								
Ab Dose: patients:	FH Patients on Atorvastatin				Non-FH Patients on Atorvastatin			
	PBO [#] (N = 6)	50 mg (N = 5)	100 mg (N = 5)	150 mg (N = 5)	PBO [#] (N = 6)	50 mg (N = 8)	100 mg (N = 8)	150 mg (N = 8)
Baseline	—	—	—	—	—	—	—	—
Day 1	—	—	—	—	—	—	—	—
Visit 5	2.03 (6.119)	-0.42 (4.603)	-7.50 (6.084)	-5.88 (10.366)	3.16 (9.748)	-8.98 (5.819)	-10.09 (11.047)	-14.29 (8.751)
Day 2	—	—	—	—	—	—	—	—
Visit 6	0.39 (7.522)	-4.81 (7.306)	-20.91 (10.160)	-15.21 (11.538)	5.67 (8.135)	-21.28 (5.678)	-27.27 (16.699)	-21.00 (14.256)
Day 3	—	—	—	—	—	—	—	—

TABLE 29-continued

Ab Dose: patients:	Percent Change in Calculated Serum LDL-C From Baseline to Each Visit*							
	FH Patients on Atorvastatin				Non-FH Patients on Atorvastatin			
	PBO# (N = 6)	50 mg (N = 5)	100 mg (N = 5)	150 mg (N = 5)	PBO# (N = 6)	50 mg (N = 8)	100 mg (N = 8)	150 mg (N = 8)
Visit 7	-2.79	-30.44	-50.96	-40.81	-6.62	-43.13	-56.95	-46.81
Day 8 ±3	(5.318)	(10.776)	(16.227)	(20.082)	(8.384)	(6.406)	(19.049)	(19.233)
Visit 8	6.36	-31.42	-53.67	-52.95	4.48	-38.71	-54.36	-62.00
Day 15 ±3	(19.607)	(18.218)	(12.128)	(17.130)	(7.389)	(11.028)	(7.819)	(16.531)
Visit 9	10.20	-4.99	-21.07	-27.03	-0.63	-2.24	-11.48	-17.64
Day 29 ±3	(14.274)	(9.479)	(16.407)	(21.567)	(13.983)	(16.704)	(20.396)	(14.132)
Visit 10	1.86	-32.31	-47.59	-44.47	7.54	-30.88	-50.53	-55.72
Day 43 ±3	(14.283)	(15.685)	(13.104)	(27.321)	(10.473)	(13.053)	(10.389)	(11.393)
Visit 11	3.45	-39.26	-53.64	-55.80	5.84	-33.36	-48.04	-58.52
Day 57 ±3	(9.693)	(8.294)	(12.404)	(15.596)	(14.883)	(8.700)	(9.366)	(17.918)
Visit 12	2.30	-9.02	-19.17	-23.24	3.54	-2.77	-13.80	-15.84
Day 71 ±3	(18.929)	(7.955)	(16.643)	(29.233)	(17.026)	(11.065)	(25.640)	(13.593)
Visit 13	-1.70	-2.72	-7.04	-9.82	10.90	-2.01	9.18	6.66
Day 85 ±3	(14.163)	(16.512)	(15.835)	(21.450)	(23.826)	(10.720)	(28.556)	(14.575)
Visit 14	4.93	5.76	-1.76	4.32	4.62	1.23	-2.53	14.77
Day 99 ±3	(18.181)	(10.957)	(9.717)	(20.651)	(16.912)	(16.703)	(13.430)	(16.167)
Visit 15	0.21	2.29	0.36	8.26	-0.92	1.76	0.89	13.06
Day 120 ±3	(17.738)	(7.043)	(14.954)	(50.237)	(23.154)	(12.863)	(13.837)	(16.902)
Visit 16	4.67	-3.02	5.32	4.23	1.79	5.40	8.63	12.43
Day 148 ±3	(18.920)	(6.420)	(21.592)	(35.706)	(28.237)	(17.012)	(21.463)	(19.139)

#PBO = placebo

*Values represent Mean percent change from baseline (Standard Deviation)

TABLE 30

Ab Dose: patients:	Percent Change in Calculated Serum LDL-C From Baseline to Each Visit*					
	FH and Non-FH Patients on Atorvastatin, Combined				Non-FH Patients Not on Atorvastatin	
	PBO# (N = 12)	50 mg (N = 13)	100 mg (N = 13)	150 mg (N = 13)	PBO# (N = 2)	150 mg (N = 8)
Baseline	—	—	—	—	—	—
Day 1	—	—	—	—	—	—
Visit 5	2.60	-5.69	-9.10	-11.05	7.13	-7.28
Day 2	(7.782)	(6.753)	(9.233)	(9.930)	(2.911)	(4.156)
Visit 6	3.03	-14.94	-24.82	-18.78	11.64	-11.37
Day 3	(7.963)	(10.302)	(14.403)	(13.097)	(2.323)	(7.661)
Visit 7	-4.70	-38.25	-54.65	-44.50	12.52	-41.59
Day 8 ±3	(6.985)	(10.193)	(17.567)	(18.959)	(13.260)	(13.106)
Visit 8	5.42	-35.90	-54.09	-58.52	2.75	-44.68
Day 15 ±3	(14.161)	(13.971)	(9.209)	(16.681)	(17.896)	(15.461)
Visit 9	4.79	-3.30	-15.17	-21.25	15.09	-38.57
Day 29 ±3	(14.610)	(13.952)	(18.867)	(17.152)	(20.319)	(14.306)
Visit 10	4.70	-31.43	-49.40	-51.39	4.71	-50.88
Day 43 ±3	(12.304)	(13.488)	(11.064)	(18.893)	(6.661)	(11.674)
Visit 11	4.64	-35.63	-50.19	-57.47	6.09	-54.41
Day 57 ±3	(12.040)	(8.717)	(10.513)	(16.439)	(28.082)	(12.175)
Visit 12	2.92	-5.17	-15.86	-18.68	16.05	-42.16
Day 71 ±3	(17.177)	(10.126)	(21.982)	(20.167)	(25.084)	(29.771)
Visit 13	4.60	-2.28	2.94	0.32	14.58	-30.13
Day 85 ±3	(19.813)	(12.572)	(25.034)	(18.627)	(7.290)	(21.347)
Visit 14	4.78	2.98	-2.23	10.75	7.50	-11.83
Day 99 ±3	(16.742)	(14.423)	(11.698)	(17.963)	(12.321)	(18.493)
Visit 15	-0.35	1.97	0.68	11.21	25.69	-8.36
Day 120 ±3	(19.674)	(10.636)	(13.649)	(31.840)	(14.125)	(7.430)
Visit 16	3.23	2.16	7.35	9.28	-6.29	-0.74
Day 148 ±3	(22.965)	(14.168)	(20.662)	(25.611)	(15.014)	(13.169)

#PBO = placebo

*Values represent Mean percent change from baseline (Standard Deviation)

60

It can be concluded from this study that mAb316P is an effective therapeutic option for patients with heFH or non-FH, with elevated cholesterol, on statin therapy or on diet alone.

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various

modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and the accompanying figures.

65

Such modifications are intended to fall within the scope of the appended claims.

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          20           25           30
Asp Met His Trp Val Arg Gln Ser Thr Gly Lys Gly Leu Glu Trp Val
          35           40           45
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
          50           55           60
Gly Arg Phe Thr Ile Thr Arg Glu Lys Ala Lys Asn Ser Val Tyr Leu
          65           70           75           80
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val
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ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagcc 180

aggttcagtg gcattgggctc tgggacagag ttcactctca ttatcagcag cctgcagtct 240

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

Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Thr Arg Glu Lys Ala Lys Asn Ser Val Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val
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Glu Arg Ala Ala Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
          20             25             30
Leu Ala Trp Tyr His Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
          35             40             45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
          50             55             60
Ile Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Ser
65             70             75             80
Glu Asp Phe Ala Phe Tyr Phe Cys Gln Gln Tyr Asn Asn Trp Pro Pro
          85             90             95
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          100            105
  
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acaggaaaaa gtctggagtg ggtctcagct attggttcta ccggtgacac atactatcca      180
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 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
 20 25 30
 Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
 50 55 60
 Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
 65 70 75 80
 Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val
 85 90 95
 Arg Glu Gly Trp Glu Val Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
 100 105 110
 Val Thr Val Ser Ser
 115

<210> SEQ ID NO 23

<211> LENGTH: 324

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 23

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgtagc agcaacttag cctggtacca gcagaaacct 120
 ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatccagcc 180
 aggttcagtg gcagtggggc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag tataataact ggctccatt cactttcggc 300
 cctgggacca aagtgatat caaa 324

<210> SEQ ID NO 24

<211> LENGTH: 108

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 24

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

-continued

<210> SEQ ID NO 25
 <211> LENGTH: 342
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 25

```
cagggtgcagc tgggtgcagtc tgggggagggc gtggtccagc ctgggagggtc cctgagactc      60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct      120
ccaggcaagg ggctggagtg ggtggcggtt ataggatttg atggaagtaa tatacattat      180
ggagactccg tgagggggcg aatcatcata tccagagaca attccgagaa cacgttgtat      240
ctggaaatga acagcctgag agccgaggac acggcaatgt actattgtgc gagagagaag      300
ggttttagact ggggccaggg aaccacggtc accgtctcct ca                          342
```

<210> SEQ ID NO 26
 <211> LENGTH: 114
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 26

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

<210> SEQ ID NO 27
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 27

```
ggattcacct tcagtagcta tggc      24
```

<210> SEQ ID NO 28
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 28

```
Gly Phe Thr Phe Ser Ser Tyr Gly
  1           5
```

-continued

<210> SEQ ID NO 29
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 29

ataggatttg atggaagtaa tata

24

<210> SEQ ID NO 30
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 30

Ile Gly Phe Asp Gly Ser Asn Ile
 1 5

<210> SEQ ID NO 31
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 31

gcgagagaga agggtttaga c

21

<210> SEQ ID NO 32
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 32

Ala Arg Glu Lys Gly Leu Asp
 1 5

<210> SEQ ID NO 33
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 33

gccatccaga tgacccagtc tccttcaccc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggccagtca gagtattagt agctggttgg cctgggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240

gatgatTTTT caacttatta ctgccaacag tataatagtt attacacttt tggccagggg 300

accaaggtgg aaatcaaacy a 321

<210> SEQ ID NO 34
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 34

Ala Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser 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 Tyr Thr
 85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105

<210> SEQ ID NO 35

<211> LENGTH: 18

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 35

cagagtatta gtagctgg

18

<210> SEQ ID NO 36

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 36

Gln Ser Ile Ser Ser Trp
 1 5

<210> SEQ ID NO 37

<211> LENGTH: 9

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 37

aaggcgtct

9

<210> SEQ ID NO 38

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 38

Lys Ala Ser
 1

<210> SEQ ID NO 39

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 39

caacagtata atagttatta cact

24

<210> SEQ ID NO 40

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 40

Gln Gln Tyr Asn Ser Tyr Tyr Thr
1 5

<210> SEQ ID NO 41

<211> LENGTH: 342

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 41

cagggtgcagc tgggtggagtc tgggggagggc gtgggtccagc ctgggagggtc cctgagactc 60

tcctgtgtcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccagggt 120

ccagggaagg ggctggagtg ggtggcggtt ataggatttg atggaagtaa tatacattat 180

ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat 240

ctggaaatga acagcctgag agccgaggac acggcaatgt actattgtgc gagagagaag 300

ggtttagact ggggccaggg aaccctggtc accgtctcct ca 342

<210> SEQ ID NO 42

<211> LENGTH: 114

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 42

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

Ser Ser

<210> SEQ ID NO 43

<211> LENGTH: 318

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 43

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggccagtca gagtattagt agctgggttg cctggatatca gcagaaacca    120
gggaaagccc ctaagctect gatctataag gcgtctagtt tagaaagtgg ggtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatacagcag cctgcagcct    240
gatgattttg caacttatta ctgccaacag tataatagtt attacacttt tggccagggg    300
accaagctgg agatcaaa                                     318

```

<210> SEQ ID NO 44

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 44

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10            15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
          20            25            30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
      35            40            45
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Tyr Thr
          85            90            95
Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
      100            105

```

<210> SEQ ID NO 45

<211> LENGTH: 342

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 45

```

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc      60
tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct    120
ccaggcaagg ggctggagtg ggtggcagtt ataggatttg atggaagtaa tatatactat    180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cagcgtgtat    240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagagaag    300
ggtttagact ggggccaggg aaccctggtc accgtctcct ca                          342

```

<210> SEQ ID NO 46

<211> LENGTH: 114

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 46

```

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg

```

-continued

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	Gly Phe Asp Gly Ser Asn Ile 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	80
Leu Gln Met	Asn Ser Leu Arg Ala Glu Asp Thr	Ala Val Tyr Tyr Cys	
	85	90	95
Ala Arg Glu	Lys Gly Leu Asp Trp Gly Gln Gly Thr	Leu Val Thr Val	
	100	105	110

Ser Ser

<210> SEQ ID NO 47

<211> LENGTH: 319

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 47

```

gacatccaga tgaccagtc tccttcacac ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggccagtc gagtattagt agctgggttg cctgggtatca gcagaaacca      120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca      180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct      240
gatgattttg caacttatta ctgccaacag tataatagtt attacacttt tggccagggg      300
accaagctgg agatcaaac                                     319

```

<210> SEQ ID NO 48

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 48

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly	
1 5 10 15	
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp	
20 25 30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile	
35 40 45	
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Tyr Thr	
85 90 95	
Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> SEQ ID NO 49

<211> LENGTH: 342

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 49

```

caggtgcagc tgcaggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc      60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct      120
ccaggcaagg ggctggagtg ggtggcggtt ataggatttg atggaagtaa tatatattat      180
ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttggtat      240
ctggaaatga acagcctgag agccgaggac acggcagtgt attattgtgc gagagagaag      300
ggttttagact ggggccaggg aaccctggtc actgtctcct ca                          342

```

<210> SEQ ID NO 50

<211> LENGTH: 114

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 50

```

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

```

<210> SEQ ID NO 51

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 51

```

ggattcacct tcagtagcta tggc

```

24

<210> SEQ ID NO 52

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 52

```

Gly Phe Thr Phe Ser Ser Tyr Gly
 1             5

```

<210> SEQ ID NO 53

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 53

ataggatttg atggaagtaa tata

24

<210> SEQ ID NO 54
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 54

Ile Gly Phe Asp Gly Ser Asn Ile
 1 5

<210> SEQ ID NO 55
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 55

gcgagagaga agggtttaga c

21

<210> SEQ ID NO 56
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 56

Ala Arg Glu Lys Gly Leu Asp
 1 5

<210> SEQ ID NO 57
 <211> LENGTH: 342
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 57

gccatccaga tgaccagtc tccagactcc ctggetgtgt ctctgggcga gagggccacc 60
 atcaactgca agtcagcca gagtgttttt cacacctcca acaataagaa ctacttagtt 120
 tggatatcagc agaaaccagg acagcctcct aagttgctcc tttactgggc ctctaccgg 180
 gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240
 atcagcagcc tgcaggctga agatgtggca aattattact gtcaccaata ttacagtatt 300
 ccgtggacgt tcggccaagg gaccaaggty gagatcaaac ga 342

<210> SEQ ID NO 58
 <211> LENGTH: 114
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 58

Ala Ile Gln Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

-continued

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Phe His Thr
 20 25 30

Ser Asn Asn Lys Asn Tyr Leu Val Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Leu 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 Asn Tyr Tyr Cys His Gln
 85 90 95

Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
 100 105 110

Lys Arg

<210> SEQ ID NO 59
 <211> LENGTH: 36
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 59

cagagtgttt ttcacacctc caacaataag aactac

36

<210> SEQ ID NO 60
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 60

Gln Ser Val Phe His Thr Ser Asn Asn Lys Asn Tyr
 1 5 10

<210> SEQ ID NO 61
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 61

tgggcctct

9

<210> SEQ ID NO 62
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 62

Trp Ala Ser
 1

<210> SEQ ID NO 63
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 63

-continued

 caccaatatt acagtattcc gtggacg

27

<210> SEQ ID NO 64
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 64

His Gln Tyr Tyr Ser Ile Pro Trp Thr
 1 5

<210> SEQ ID NO 65
 <211> LENGTH: 342
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 65

cagggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctgggaggtc cctgagactc	60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct	120
ccaggcaagg ggctggagtg ggtggcgctt ataggatttg atggaagtaa tatatattat	180
ggagactccg tgaggggccc aatcatcata tccagagaca attccgagaa cacgttgat	240
ctggaaatga acagcctgag agccgaggac acggcagtgt attattgtgc gagagagaag	300
ggtttagact ggggccaggg aaccctggtc accgtctcct ca	342

<210> SEQ ID NO 66
 <211> LENGTH: 114
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 66

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

<210> SEQ ID NO 67
 <211> LENGTH: 339
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 67

-continued

```

gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc      60
atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagtt      120
tggtatcagc agaaaccagg acagcctcct aagttgctcc tttactgggc ctctaccgg      180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc      240
atcagcagcc tgcaggtga agatgtggca aattattact gtcaccaata ttacagtatt      300
ccgtggacgt tcggccaagg gaccaagggtg gaaatcaaa                               339

```

```

<210> SEQ ID NO 68
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 68

```

```

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 Phe His Thr
          20             25             30
Ser Asn Asn Lys Asn Tyr Leu Val Trp Tyr Gln Gln Lys Pro Gly Gln
          35             40             45
Pro Pro Lys Leu Leu Leu 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 Asn Tyr Tyr Cys His Gln
          85             90             95
Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
          100            105            110

```

```

Lys

```

```

<210> SEQ ID NO 69
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 69

```

```

caggtgcagc tgggtggagtc tgggggaggc gtgtccagc ctgggaggtc cctgagactc      60
tctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct      120
ccaggcaagg ggctggagtg ggtggcagtt ataggatttg atggaagtaa tatatactat      180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cagctgtat      240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagagaag      300
ggtttagact ggggccaggg aacctgggtc accgtctcct ca                               342

```

```

<210> SEQ ID NO 70
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 70

```

```

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1             5             10             15

```

-continued

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 Gly Phe Asp Gly Ser Asn Ile 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 Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Leu Val Thr Val
 100 105 110

Ser Ser

<210> SEQ ID NO 71
 <211> LENGTH: 339
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 71

gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc 60
 atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagct 120
 tggtagccagc agaaaccagg acagctctct aagctgctca tttactgggc ctctaccggg 180
 gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240
 atcagcagcc tgcagcgtga agatgtggca gtttattact gtcaccaata ttacagtatt 300
 ccgtggacgt tcggccaagg gaccaaggtg gaaatcaaa 339

<210> SEQ ID NO 72
 <211> LENGTH: 113
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 72

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 Phe His Thr
 20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala 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 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 His Gln
 85 90 95

Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
 100 105 110

Lys

<210> SEQ ID NO 73
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 73

```

gaagtgcagc tgggtgcagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc      60
tcctgtgcag cctctggatt cacctttaac aactatgcc aactatgcc tgaactgggt ccgccaggct  120
ccaggaaagg gactggactg ggtctcaact attagtggta gcggtgggtac taaaaactac      180
gcagactccg tgaagggccg ttctcattatt tcccagagaca gttccaaaca cacgctgtat      240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct      300
aactggggaa atttcgatct ctgggggccgt ggcaccacgg tcactgtctc ctca          354

```

<210> SEQ ID NO 74

<211> LENGTH: 118

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 74

```

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

```

<210> SEQ ID NO 75

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 75

```

ggattcacct ttaacaacta tgcc

```

24

<210> SEQ ID NO 76

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 76

```

Gly Phe Thr Phe Asn Asn Tyr Ala
 1             5

```

<210> SEQ ID NO 77

<211> LENGTH: 24

<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 77

attagtggta gcggtggtac taca

24

<210> SEQ ID NO 78
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 78

Ile Ser Gly Ser Gly Gly Thr Thr
 1 5

<210> SEQ ID NO 79
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 79

gcgaaagatt ctaactgggg aaatttcgat ctc

33

<210> SEQ ID NO 80
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 80

Ala Lys Asp Ser Asn Trp Gly Asn Phe Asp Leu
 1 5 10

<210> SEQ ID NO 81
 <211> LENGTH: 342
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 81

gacatccaga tgaccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc 60

atcaactgca agtccagcca gagtgtttta tacagggtcca acaataggaa cttcttaggt 120

tggtaccagc agaaaccagg gcagcctcct aatctactca tttactgggc atctaccgg 180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240

atcagcagcc tgcaggctga agatgtggca gtttattact gtcaacaata ttatactact 300

ccgtacactt ttggccaggg gaccaagggtg gaaatcaaac ga 342

<210> SEQ ID NO 82
 <211> LENGTH: 114
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 82

Asp Ile Gln Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

-continued

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Arg
 20 25 30
 Ser Asn Asn Arg Asn Phe Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45
 Pro Pro Asn 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 Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
 100 105 110

Lys Arg

<210> SEQ ID NO 83
 <211> LENGTH: 36
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 83

cagagtgttt tatacaggtc caacaatagg aacttc

36

<210> SEQ ID NO 84
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 84

Gln Ser Val Leu Tyr Arg Ser Asn Asn Arg Asn Phe
 1 5 10

<210> SEQ ID NO 85
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 85

tgggcatct

9

<210> SEQ ID NO 86
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 86

Trp Ala Ser
 1

<210> SEQ ID NO 87
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 87

-continued

caacaatatt atactactcc gtacact

27

<210> SEQ ID NO 88
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic
 <400> SEQUENCE: 88

Gln Gln Tyr Tyr Thr Thr Pro Tyr Thr
 1 5

<210> SEQ ID NO 89
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic
 <400> SEQUENCE: 89

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
 tcctgtgcag cctctggatt cacctttaac aactatgccca tgaactgggt ccgccaggct 120
 ccaggaaagg gactggactg ggtctcaact attagtggta gcggtgggtac tacaaactac 180
 gcagactccg tgaagggccg ttctcattatt tcccagagaca gttccaaaaca cacgctgtat 240
 ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct 300
 aactggggaa atttcgatct ctggggccgt ggcaccctgg tcactgtctc ctca 354

<210> SEQ ID NO 90
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic
 <400> SEQUENCE: 90

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 Asn Asn Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp Val
 35 40 45

Ser Thr Ile Ser Gly Ser Gly Gly Thr Thr Asn Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Ile Ile Ser Arg Asp Ser Ser Lys His Thr Leu Tyr
 65 70 75 80

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

Ala Lys Asp Ser Asn Trp Gly Asn Phe Asp Leu Trp Gly Arg Gly Thr
 100 105 110

Leu Val Thr Val Ser Ser
 115

<210> SEQ ID NO 91
 <211> LENGTH: 339
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 91

```

gacatcgtga tgaccagtc tccagactcc ctggtgtgt ctctgggga gagggccacc      60
atcaactgca agtccagcca gagtgtttta tacaggtcca acaataggaa cttcttaggt    120
tggtaccagc agaaaccagg gcagcctcct aatctactca tttactgggc atctaccgg      180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc    240
atcagcagcc tgcaggtga agatgtggca gtttattact gtcaacaata ttatactact    300
ccgtacactt ttggccaggg gaccaagctg gagatcaaa                          339

```

<210> SEQ ID NO 92

<211> LENGTH: 113

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 92

```

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 Arg
          20             25             30
Ser Asn Asn Arg Asn Phe Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln
          35             40             45
Pro Pro Asn 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 Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
          100            105            110

```

Lys

<210> SEQ ID NO 93

<211> LENGTH: 354

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 93

```

gaggtgcagc tgggtggagtc tggggggagcc ttggtacagc ctgggggggtc cctgagactc      60
tctgtgtcag cctctggatt cacctttaac aactatgccg tgagctgggt ccgccaggct    120
ccaggggaagg ggctggagtg ggtctcagct attagtggta gcggtggtag tacatactac    180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct    300
aactggggaa atttcgatct ctggggccgt ggcaccctgg tcaactgtctc ctca          354

```

<210> SEQ ID NO 94

<211> LENGTH: 118

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 94

```

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

```

-continued

1	5	10	15
Ser Leu Arg	Leu Ser Cys Ala Ala Ser	Gly Phe Thr Phe Asn Asn Tyr	
	20	25	30
Ala Met 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 Thr 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
Leu Gln Met	Asn Ser Leu Arg Ala Glu Asp Thr	Ala Val Tyr Tyr Cys	
	85	90	95
Ala Lys Asp	Ser Asn Trp Gly Asn Phe Asp Leu Trp Gly	Arg Gly Thr	
	100	105	110
Leu Val Thr	Val Ser Ser		
	115		

<210> SEQ ID NO 95
 <211> LENGTH: 339
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 95

gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc	60
atcaactgca agtccagcca gagtgtttta tacaggtcca acaataggaa cttcttagct	120
tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctaccgg	180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc	240
atcagcagcc tgcaggtgca agatgtggca gtttattact gtcaacaata ttatactact	300
ccgtacactt ttggccaggg gaccaagctg gagatcaaa	339

<210> SEQ ID NO 96
 <211> LENGTH: 113
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 96

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly	
1	15
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Arg	
20	30
Ser Asn Asn Arg Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln	
35	45
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val	
50	60
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr	
65	80
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln	
85	95
Tyr Tyr Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile	
100	110

Lys

<210> SEQ ID NO 97

-continued

<211> LENGTH: 351
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 97

```
cagggtgcagc tgggtgcagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc      60
tcctgtgcag tctctggatt caccctcagt agctacgata tgcactgggt ccgccaacct      120
acaggaaaag gtctggagtg ggtctcagct attggttcta ctggtgacac atactatcca      180
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt      240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agaggggatgg      300
gacgtaccct ttgacttctg gggccaggga accctggtca ccgtctctc a                  351
```

<210> SEQ ID NO 98
 <211> LENGTH: 117
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 98

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

<210> SEQ ID NO 99
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 99

```
ggattcacc ctagtagcta cgat      24
```

<210> SEQ ID NO 100
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 100

```
Gly Phe Thr Leu Ser Ser Tyr Asp
  1             5
```

-continued

```

<210> SEQ ID NO 101
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 101

```

```

attggttcta ctggtgacac a

```

21

```

<210> SEQ ID NO 102
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 102

```

```

Ile Gly Ser Thr Gly Asp Thr
 1             5

```

```

<210> SEQ ID NO 103
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 103

```

```

gcaagagagg gatgggacgt accctttgac ttc

```

33

```

<210> SEQ ID NO 104
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 104

```

```

Ala Arg Glu Gly Trp Asp Val Pro Phe Asp Phe
 1             5             10

```

```

<210> SEQ ID NO 105
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 105

```

```

gccatccagt tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

```

```

atcacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca 120

```

```

gggaaagccc ctaagctcct gatctatgct gcatccagtt taaaaagtgg ggtcccatca 180

```

```

cggttcagcg gcagtggatc tggcacagat ttcactctca ccatcagcag cctgcagcct 240

```

```

gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa 300

```

```

gggaccaagg tggagatcaa acga 324

```

```

<210> SEQ ID NO 106
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 106

```


-continued

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 Asp Ile Arg Asn Asp
 20 25 30
 Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 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 Leu Gln Asp Tyr Asn Tyr Pro Trp
 85 90 95
 Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105

<210> SEQ ID NO 107
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 107

caggacatta gaaatgat

18

<210> SEQ ID NO 108
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 108

Gln Asp Ile Arg Asn Asp
 1 5

<210> SEQ ID NO 109
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 109

gctgcatcc

9

<210> SEQ ID NO 110
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 110

Ala Ala Ser
 1

<210> SEQ ID NO 111
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 111

ctacaagatt acaattaccc gtggacg

27

<210> SEQ ID NO 112

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 112

Leu Gln Asp Tyr Asn Tyr Pro Trp Thr
 1 5

<210> SEQ ID NO 113

<211> LENGTH: 351

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 113

gagggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60
 tctgtgtcag tctctggatt caccctcagt agctacgata tgcactgggt ccgccaacct 120
 acaggaaaaa gtctggagtg ggtctcagct attggttcta ctggtgacac atactatcca 180
 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
 caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggatgg 300
 gacgtaccct ttgacttctg gggccaggga accctgggtca ccgtctcctc a 351

<210> SEQ ID NO 114

<211> LENGTH: 117

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 114

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

<210> SEQ ID NO 115

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 115

```

gccatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggcaagtca ggacattaga aatgatttag gctgggtatca gcagaaacca      120
gggaaagccc ctaagctcct gatctatgct gcattccagtt tacaaagtgg ggtcccatca      180
cggttcagcg gcagtggatc tggcacagat ttcactctca ccatcagcag cctgcagcct      240
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa      300
gggaccaagg tggaaatcaa a                                           321

```

<210> SEQ ID NO 116

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 116

```

Ala 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 Ile Arg Asn Asp
          20             25             30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 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 Leu Gln Asp Tyr Asn Tyr Pro Trp
          85             90             95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
          100             105

```

<210> SEQ ID NO 117

<211> LENGTH: 351

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 117

```

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc      60
tcctgtgcag cctctggatt caccctcagt agctacgata tgcactgggt ccgccaagct      120
acaggaaaag gtctggagtg ggtctcagct attggttcta ctggtgacac atactatcca      180
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt      240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggatgg      300
gacgtaccct ttgacttctg gggccaggga accctggtca ccgtctcttc a           351

```

<210> SEQ ID NO 118

<211> LENGTH: 117

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 118

```

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1             5             10             15

```

-continued

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
 20 25 30

Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

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

Val Thr Val Ser Ser
 115

<210> SEQ ID NO 119
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 119

```
gccatccaga tgaccagtc tccatctccc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca      120
gggaaagccc ctaagctcct gatctatgct gcattccagtt tacaaagtgg ggtcccatca      180
aggttcagcg gcagtggatc tggcacagat ttcactctca ccatcagcag cctgcagcct      240
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtaggac gttcggccaa      300
gggaccaagg tggaaatcaa a                                     321
```

<210> SEQ ID NO 120
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 120

Ala 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 Ile Arg Asn Asp
 20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 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 Leu Gln Asp Tyr Asn Tyr Pro Trp
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 121
 <211> LENGTH: 384
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 121

cagggtgcagc tgcaggagtc gggggccagga ctggtgaagc ctteggagac cctgtccctc 60
acctgcactg tctctgggga ctccatcaat acttactact ggagctgggt ccggcagccc 120
ccaggggaagg gactggagtg gattgggtat atctattata gtggaaccac caactacaac 180
ccctccctca agagtcgagt caccatatca atagacacgc ccaggaacca gttctccctg 240
aagctgatct ctgtgaccgc agcggacacg gccgtgtatt actgtgcgag agagaggatt 300
actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa 360
gggaccacgg tcaccgtctc ctca 384

<210> SEQ ID NO 122

<211> LENGTH: 128

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 122

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

<210> SEQ ID NO 123

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 123

ggggactcca tcaatactta ctac 24

<210> SEQ ID NO 124

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 124

Gly Asp Ser Ile Asn Thr Tyr Tyr
1 5

<210> SEQ ID NO 125

-continued

<211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 125

atctattata gtggaaccac c

21

<210> SEQ ID NO 126
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 126

Ile Tyr Tyr Ser Gly Thr Thr
 1 5

<210> SEQ ID NO 127
 <211> LENGTH: 66
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 127

gcgagagaga ggattactat gattcgggga gttaccctct actattactc ctacggtatg

60

gacgtc

66

<210> SEQ ID NO 128
 <211> LENGTH: 22
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 128

Ala Arg Glu Arg Ile Thr Met Ile Arg Gly Val Thr Leu Tyr Tyr Tyr
 1 5 10 15

Ser Tyr Gly Met Asp Val
 20

<210> SEQ ID NO 129
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 129

gacatccaga tgaccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc

60

atcacttgct gggccagtca ggacattagc agttatttag cctgggtatca gcaaaaacca

120

gggtagagccc ctaagctcct gatctatgct gcattccactt tgcaaagtgg ggtcccatca

180

agggtcggcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct

240

gaagattttg caacttatta ctgtcaacag cttaatagtt accctcggac gttcggccaa

300

gggaccaagg tggaaatcaa acga

324

<210> SEQ ID NO 130
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence

-continued

```

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 130

Asp Ile Gln Met Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
 1             5             10            15

Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Asp Ile Ser Ser Tyr
          20             25            30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Ile Ala Pro Lys Leu Leu Ile
          35             40            45

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Gly Gly
          50             55            60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
          65             70            75            80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Arg
          85             90            95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
          100            105

```

```

<210> SEQ ID NO 131
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 131

```

```

caggacatta gcagttat

```

18

```

<210> SEQ ID NO 132
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 132

```

```

Gln Asp Ile Ser Ser Tyr
 1             5

```

```

<210> SEQ ID NO 133
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 133

```

```

gctgcatcc

```

9

```

<210> SEQ ID NO 134
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 134

```

```

Ala Ala Ser
 1

```

```

<210> SEQ ID NO 135
<211> LENGTH: 27
<212> TYPE: DNA

```

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 135

caacagctta atagttaccc tcggacg

27

<210> SEQ ID NO 136
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 136

Gln Gln Leu Asn Ser Tyr Pro Arg Thr
 1 5

<210> SEQ ID NO 137
 <211> LENGTH: 384
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 137

cagggtgcagc tgcaggagtc ggggccagga ctggtgaagc cttcggagac cctgtccctc 60
 acctgcactg tctctgggga ctccatcaat acttactact ggagctgggt ccggcagccc 120
 ccaggaaggg gactggagtg gattgggtat atctattata gtggaaccac caactacaac 180
 ccctccctca agagtcgagt caccatata atagacacgc ccaggaacca gttctccctg 240
 aagctgatct ctgtgaccgc agcggacacg gccgtgtatt actgtgcgag agagaggatt 300
 actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa 360
 gggaccacgg tcaccgtctc ctca 384

<210> SEQ ID NO 138
 <211> LENGTH: 128
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 138

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

-continued

<210> SEQ ID NO 139
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 139

```

gacatccaga tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgct gggccagtcg ggacattagc agttatttag cctggatca gcaaaaacca      120
gggatagccc ctaagctcct gatctatgct gcattccactt tgcaaagtgg ggtcccatca      180
aggttcggcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct      240
gaagattttg caacttatta ctgtcaacag cttaatatgt accctcggac gttcggccaa      300
gggaccaagg tggaaatcaa a                                           321

```

<210> SEQ ID NO 140
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 140

```

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

```

<210> SEQ ID NO 141
 <211> LENGTH: 384
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 141

```

cagggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc      60
acctgcactg tctctgggga ctccatcaat acttactact ggagctggat ccggcagccc      120
ccaggaaggg gactggagtg gattgggtat atctattata gtggaaccac caactacaac      180
ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg      240
aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcgag agagaggatt      300
actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa      360
gggaccacgg tcaccgtctc ctca                                           384

```

<210> SEQ ID NO 142
 <211> LENGTH: 128
 <212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 142

```

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

```

<210> SEQ ID NO 143
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 143

```

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggcaagtca ggacattagc agttatttag gctgggtatca gcagaaacca    120
gggaaagccc ctaagcgctt gatctatgct gcattccagtt tgcaaagtgg ggtcccatca    180
aggttcagcg gcagtggtac tgggacagaa ttcactctca caatcagcag cctgcagcct    240
gaagattttg caacttatta ctgtcaacag cttaatatgtt accctcggac gttcggccaa    300
gggaccaagg tggaaatcaa a                                     321

```

<210> SEQ ID NO 144
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 144

```

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 Ile Ser Ser Tyr
          20             25             30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg 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 Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65             70             75             80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Arg
          85             90             95

```

-continued

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 145
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 145

cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctgggta cacctttacc aactatggta tcagctgggt gcgacaggcc 120
cctggacaag gacttgagtt aatgggatgg attagtggtt acaatggtaa cacaaactat 180
gcacaagaac tccaggccag agtcaccatg accacagaca catccacgag cacagcctac 240
atggagctga ggaacctgag atctgacgac acggccgtat attactgtgc gagagataga 300
gtcgtttagt cagctgctaa ttactacttt tattctatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

<210> SEQ ID NO 146
<211> LENGTH: 126
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 146

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

<210> SEQ ID NO 147
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 147

ggttacacct ttaccaacta tgggt

24

<210> SEQ ID NO 148
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 148

Gly Tyr Thr Phe Thr Asn Tyr Gly
 1 5

<210> SEQ ID NO 149

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 149

attagtgggtt acaatggtaa caca

24

<210> SEQ ID NO 150

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 150

Ile Ser Gly Tyr Asn Gly Asn Thr
 1 5

<210> SEQ ID NO 151

<211> LENGTH: 57

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 151

gcgagagata gagtcgttgt agcagctgct aattactact tttattctat ggacgtc

57

<210> SEQ ID NO 152

<211> LENGTH: 19

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 152

Ala Arg Asp Arg Val Val Val Ala Ala Ala Asn Tyr Tyr Phe Tyr Ser
 1 5 10 15

Met Asp Val

<210> SEQ ID NO 153

<211> LENGTH: 339

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 153

gccatccaga tgaccagtc tccactctcc ctgtccgtca cccttgga ggcggcctcc 60

atctcctgca ggtctagtca aagcctcgta tacagtgatg gagacaccta cttgaattgg 120

tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180

tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgctttcac actgaaaatc 240

agcgggggtgg aggccgagga tggtggggtt tactactgca tgcaagctac aactggcct 300

cggacgttcg gccaaaggac caaggtggaa atcaaacga 339

-continued

<210> SEQ ID NO 154
 <211> LENGTH: 113
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 154
 Ala Ile Gln Met Thr Gln Ser Pro Leu Ser Leu Ser Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
 20 25 30
 Asp Gly Asp Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
 35 40 45
 Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Gly Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

Arg

<210> SEQ ID NO 155
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 155

caaagcctcg tatacagtga tggagacacc tac

33

<210> SEQ ID NO 156
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 156

Gln Ser Leu Val Tyr Ser Asp Gly Asp Thr Tyr
 1 5 10

<210> SEQ ID NO 157
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 157

aaggtttct

9

<210> SEQ ID NO 158
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 158

-continued

Lys Val Ser

1

<210> SEQ ID NO 159
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 159

atgcaagcta cacactggcc tcggacg

27

<210> SEQ ID NO 160
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 160

Met Gln Ala Thr His Trp Pro Arg Thr

1

5

<210> SEQ ID NO 161
 <211> LENGTH: 378
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 161

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctgggta cacctttacc aactatggta tcagctgggt gcgacaggcc 120

cctggacaag gacttgagtt aatgggatgg attagtgggt acaatggtaa cacaaactat 180

gcacaagaac tccagccag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggaacctgag atctgacgac acggccgtat attactgtgc gagagataga 300

gtcgtttagt cagctgctaa ttactacttt tattctatgg acgtctgggg ccaagggacc 360

acggtcaccg tctcctca 378

<210> SEQ ID NO 162
 <211> LENGTH: 126
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 162

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

-continued

Ala Arg Asp Arg Val Val Val Ala Ala Ala Asn Tyr Tyr Phe Tyr Ser
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 163
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 163

gatgttgatga tgactcagtc tccactctcc ctgtccgtea cccttgagaca gccggcctcc 60
atctcctgca ggtctagtca aagcctcgta tacagtgatg gagacaccta cttgaattgg 120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgctttcac actgaaaatc 240
agcgggggtgg aggccgagga tgttgggggtt tactactgca tgcaagctac acactggcct 300
cggacgttcg gccaaaggac caagtgga atcaaa 336

<210> SEQ ID NO 164
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 164

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

<210> SEQ ID NO 165
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 165

cagggttcagc tgggtcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctgggta cacctttacc aactatggta tcagctgggt gcgacaggcc 120
cctggacaag ggcttgatgt gatgggatgg attagtgggt acaatggtaa cacaaactat 180
gcacagaagc tccaggcgag agtcaccatg accacagaca catccacgag cacagcctac 240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagataga 300
gtcgttgtag cagctgctaa ttactacttt tattctatgg acgtctgggg ccaagggacc 360

-continued

acggtcaccg tctcctca

378

<210> SEQ ID NO 166
 <211> LENGTH: 126
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 166

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

<210> SEQ ID NO 167
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 167

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60
 atctcctgca ggtctagtc aagcctcgta tacagtgatg gagacaccta cttgaattgg 120
 ttccagcaga gccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180
 tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240
 agcaggggtgg aggctgagga tggtggggtt tattactgca tgcaagctac aactggcct 300
 cggacgttcg gccaaaggac caaggtggaa atcaaa 336

<210> SEQ ID NO 168
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 168

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
 20 25 30
 Asp Gly Asp Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
 35 40 45
 Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
 50 55 60

-continued

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

Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> SEQ ID NO 169
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 169

cagggtccact tgaaggagtc tgggtcctacg ctggtgaaac ccacacagac cctcacgctg 60
acctgcacct tctctggatt ctcaactcatc actagtggag tgggtgtggg ctggattcgt 120
cagccccccg gaaaggccct ggagtggctt gcaactcattt attggaatgg tgataagcgc 180
tacagcccat ctctgaagag caggctcacc atcaccaagg acacctccaa aaaccagggtg 240
gtccttaca tgaccaacat ggacctgtg gacacagcca catattactg tgcacacagg 300
ataactgaaa ctagtacta cttctactac ggtatggacg tctggggcca agggaccacg 360
gtcacccgtct cctca 375

<210> SEQ ID NO 170
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 170

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

<210> SEQ ID NO 171
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 171

ggattctcac tcatcactag tggagtgggt

30

-continued

<210> SEQ ID NO 172
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 172

Gly Phe Ser Leu Ile Thr Ser Gly Val Gly
 1 5 10

<210> SEQ ID NO 173
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 173

atattattgga atgggtgataa g 21

<210> SEQ ID NO 174
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 174

Ile Tyr Trp Asn Gly Asp Lys
 1 5

<210> SEQ ID NO 175
 <211> LENGTH: 51
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 175

gcacacagga taactgaaac tagttactac ttctactacg gtatggacgt c 51

<210> SEQ ID NO 176
 <211> LENGTH: 17
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 176

Ala His Arg Ile Thr Glu Thr Ser Tyr Tyr Phe Tyr Tyr Gly Met Asp
 1 5 10 15

Val

<210> SEQ ID NO 177
 <211> LENGTH: 339
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 177

gacatccaga tgacccagtc tccactctcc ctgcccgtea cccctggaga gccggcctcc 60

atctcctgca ggtctagtca gagcctcctg catagtcatg gatacgacta tttggattgg 120

tacctgcaga agccagggca gtctccacag ctctgatctc atttgggttc taatcggggc 180

-continued

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tccgggggtcc ctgacaggtt cagtggcagt ggatcaggea cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttgggggtt tattactgca tgcaagctct acaaactccg 300
ctcactttcg gcggagggaac caaggtggaa atcaaacga 339

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<210> SEQ ID NO 178
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 178

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Asp Ile Gln 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
His Gly Tyr Asp 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

```

```

<210> SEQ ID NO 179
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

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<400> SEQUENCE: 179

```

```

cagagcctcc tgcatagtca tggatacgac tat 33

```

```

<210> SEQ ID NO 180
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

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<400> SEQUENCE: 180

```

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Gln Ser Leu Leu His Ser His Gly Tyr Asp Tyr
 1             5             10

```

```

<210> SEQ ID NO 181
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

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<400> SEQUENCE: 181

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ttgggttct 9

```

```

<210> SEQ ID NO 182
<211> LENGTH: 3

```

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 182

Leu Gly Ser
1

<210> SEQ ID NO 183
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 183

atgcaagctc tacaaactcc gctcact

27

<210> SEQ ID NO 184
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 184

Met Gln Ala Leu Gln Thr Pro Leu Thr
1 5

<210> SEQ ID NO 185
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 185

cagatcacct tgaaggagtc tggctcctacg ctggtgaaac ccacacagac cctcacgctg 60
acctgcacct tctctggatt ctcactcatc actagtggag tgggtgtggg ctggattcgt 120
cagccccccg gaaaggccct ggagtggctt gcaactcattt attggaatgg tgataagcgc 180
tacagcccat ctctgaagag caggctcacc atcaccaagg acacctccaa aaaccagggtg 240
gtccttacaa tgaccaacat ggacctgtg gacacagcca catattactg tgcacacagg 300
ataactgaaa ctagtacta cttctactac ggtatggacg tctggggcca agggaccacg 360
gtcacctgtc cctca 375

<210> SEQ ID NO 186
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 186

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1 5 10 15
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ile Thr Ser
20 25 30
Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45
Trp Leu Ala Leu Ile Tyr Trp Asn Gly Asp Lys Arg Tyr Ser Pro Ser
50 55 60

-continued

Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
 65 70 75 80
 Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
 85 90 95
 Cys Ala His Arg Ile Thr Glu Thr Ser Tyr Tyr Phe Tyr Tyr Gly Met
 100 105 110
 Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120 125

<210> SEQ ID NO 187
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 187

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
 atctcctgca ggtctagtc gagcctctcg catagtcatg gatacgacta tttggattgg 120
 tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcggggc 180
 tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
 agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaaactccg 300
 ctcactttcg gcggaggggac caaggtggag atcaaa 336

<210> SEQ ID NO 188
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 188

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
 His Gly Tyr Asp 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> SEQ ID NO 189
 <211> LENGTH: 375
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 189

cagatcacct tgaaggagtc tggctcctacg ctggtgaaac ccacacagac cctcaccgtg 60
 acctgcacct tctctggatt ctcactcatc actagtggag tgggtgtggg ctggatccgt 120

-continued

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cagccccag gaaaggccct ggagtggcct gcactcattt attggaatgg tgataagcgc 180
tacagcccat ctctgaagag caggctcacc atcaccaagg acacctccaa aaaccagggtg 240
gtccttataa tgaccaacat ggacctgtg gacacagcca catattactg tgcacacagg 300
ataactgaaa ctagttacta cttctactac ggtatggacg tctggggcca agggaccacg 360
gtcacgtct cctca 375

```

```

<210> SEQ ID NO 190
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 190

```

```

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

```

```

<210> SEQ ID NO 191
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 191

```

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctcttgca ggtctagtca gagcctctcg catagtcatg gatacgacta tttggattgg 120
tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcggggc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct acaaaactcc 300
ctcactttcg gcggagggac caagtgagg atcaaa 336

```

```

<210> SEQ ID NO 192
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 192

```

```

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

```

-continued

20	25	30	
His Gly Tyr Asp 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> SEQ ID NO 193			
<211> LENGTH: 375			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic			
 <400> SEQUENCE: 193			
cagatcacct tgaaggagtc tggctcctact ctggtgaaac cctcacagac cctcacgctg			60
acctgcacct tctctgggtt ctcaactcagc actagtggag tgggtgtggg ctggatccgt			120
cagccccag gaaagccct ggagtggctt gcactcattt attggaattc tgataagcgc			180
tacagcccat ctctgaagag caggctcacc atcaccaagg acacctcaa aaaccaggta			240
gtccttataa tgaccaacat ggacctgtg gacacagcca catattactg tgcacacaga			300
catgacagct cgtcctacta cttctactac ggtatggacg tctggggcca agggatcacg			360
gtcacctgtc cctca			375

<210> SEQ ID NO 194			
<211> LENGTH: 125			
<212> TYPE: PRT			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic			
 <400> SEQUENCE: 194			
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Ser Gln			
1	5	10	15
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser			
20	25	30	
Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu			
35	40	45	
Trp Leu Ala Leu Ile Tyr Trp Asn Ser Asp Lys Arg Tyr Ser Pro Ser			
50	55	60	
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val			
65	70	75	80
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr			
85	90	95	
Cys Ala His Arg His Asp Ser Ser Ser Tyr Tyr Phe Tyr Tyr Gly Met			
100	105	110	
Asp Val Trp Gly Gln Gly Ile Thr Val Thr Val Ser Ser			
115	120	125	

<210> SEQ ID NO 195
 <211> LENGTH: 30
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 195

gggttctcac tcagcactag tggagtgggt

30

<210> SEQ ID NO 196
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 196

Gly Phe Ser Leu Ser Thr Ser Gly Val Gly
1 5 10

<210> SEQ ID NO 197
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 197

atttattgga attctgataa g

21

<210> SEQ ID NO 198
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 198

Ile Tyr Trp Asn Ser Asp Lys
1 5

<210> SEQ ID NO 199
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 199

gcacacagac atgacagctc gtcctactac ttctactacg gtatggacgt c

51

<210> SEQ ID NO 200
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 200

Ala His Arg His Asp Ser Ser Ser Tyr Tyr Phe Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> SEQ ID NO 201
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 201

```

gacatccaga tgaccagtc tccgctctcc ctgcccgtca ccctggaga gccggcctcc    60
atctcctgca ggtctagtc gagcctctc catagtcatg gatacaacta tttggattgg    120
tacctgcaga agccagggca gtctccacaa ctctgatct atttgggttc taatcgggcc    180
tccgggggtcc ctgacagggt cagtggcggg ggatcaggca cagattttac actgaaaatc    240
agcagagtgg aggctgagga tgttgggatt tattactgca tgcaagctct acagactcct    300
ctcactttcg gcggaggggac caaggtggag atcaaacga                        339

```

<210> SEQ ID NO 202

<211> LENGTH: 113

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 202

```

Asp Ile Gln 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
His 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 Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65             70             75             80
Ser Arg Val Glu Ala Glu Asp Val Gly Ile 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

<210> SEQ ID NO 203

<211> LENGTH: 33

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 203

```

cagagcctcc tccatagtca tggatacaac tat                                33

```

<210> SEQ ID NO 204

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 204

```

Gln Ser Leu Leu His Ser His Gly Tyr Asn Tyr
 1             5             10

```

<210> SEQ ID NO 205

<211> LENGTH: 9

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 205

ttgggttct

9

<210> SEQ ID NO 206

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 206

Leu Gly Ser

1

<210> SEQ ID NO 207

<211> LENGTH: 27

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 207

atgcaagctc tacagactcc tctcact

27

<210> SEQ ID NO 208

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 208

Met Gln Ala Leu Gln Thr Pro Leu Thr

1

5

<210> SEQ ID NO 209

<211> LENGTH: 375

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 209

cagatcacct tgaaggagtc tggctcctact ctggtgaaac cctcacagac cctcagcgtg 60

acctgcacct tctctggggt ctcactcagc actagtggag tgggtgtggg ctggatccgt 120

cagccccag gaaagccct ggagtggctt gcactcattt attggaattc tgataagcgc 180

tacagcccat ctctgaagag caggctcacc atcaccaagg acacctcaa aaaccaggta 240

gtccttaca tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga 300

catgacagct cgtcctacta cttctactac ggtatggacg tctggggcca agggaccacg 360

gtcacctct cctca 375

<210> SEQ ID NO 210

<211> LENGTH: 125

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 210

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Ser Gln

1

5

10

15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser

-continued

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

<210> SEQ ID NO 211
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 211

gatattgtga tgactcagtc tccgctctcc ctgcccgtca cccctggaga gccggcctcc	60
atctctctgca ggtctagtc gagcctctc catagtcacg gatacaacta tttggattgg	120
tacctgcaga agccagggca gtctccacaa ctctgatct atttgggttc taatcgggcc	180
tccgggggtcc ctgacaggtt cagtggcggg ggatcaggca cagattttac actgaaaatc	240
agcagagtgg aggctgagga tgttgggatt tattactgca tgcaagctct acagactcct	300
ctcactttcg gcggaggggac caagtgaggag atcaaa	336

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

<400> SEQUENCE: 212

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			
His	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	Gly	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Lys	Ile
65				70				75					80		
Ser	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Ile	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> SEQ ID NO 213
 <211> LENGTH: 375
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 213

```

cagatcacct tgaaggagtc tggctcctacg ctggtgaaac ccacacagac cctcacgctg      60
acctgcacct tctctggggt ctcactcagc actagtggag tgggtgtggg ctggatccgt      120
cagccccag gaaagccct ggagtggctt gcaactcattt attggaattc tgataagcgc      180
tacagcccat ctctgaagag caggctcacc atcaccaagg acacctccaa aaaccagggtg      240
gtccttaciaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga      300
catgacagct cgtcctacta cttctactac ggtatggacg tctggggcca agggaccacg      360
gtcacccgtct cctca                                         375

```

<210> SEQ ID NO 214

<211> LENGTH: 125

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 214

```

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

```

<210> SEQ ID NO 215

<211> LENGTH: 336

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 215

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc      60
atctcctgca ggtctagtca gagcctctcc catagtcatg gatacaacta tttggattgg      120
tacctgcaga agccagggca gtctccacag ctctgatctt atttgggttc taatcggggc      180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc      240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct acagactcct      300
ctcactttcg gcggaggggac caaggtggag atcaaa                                         336

```

<210> SEQ ID NO 216

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 216

```

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
His 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> SEQ ID NO 217

<211> LENGTH: 381

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 217

```

gagatgcaac tgggtggagtc tggggggaggc ttggtccagc ctgggggggtc cctgagactc      60
tcctgtgcag cctctggatt cacctttagt agtcactgga tgaagtgggt ccgccaggct      120
ccaggaaggg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat      180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgttt      240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt      300
gtactaatgg tctatgatat ggactactac tactacggta tggacgtctg gggccaaggg      360
accacggtca ccgtctcctc a                                381

```

<210> SEQ ID NO 218

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 218

```

Glu Met 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 Ser His
          20             25             30
Trp Met Lys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
          35             40             45
Ala Asn Ile Asn 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 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 Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr
          100            105            110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

```

-continued

115	120	125
<210> SEQ ID NO 219 <211> LENGTH: 24 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 219 ggattcacct ttagtagtca ctgg		
		24
<210> SEQ ID NO 220 <211> LENGTH: 8 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 220 Gly Phe Thr Phe Ser Ser His Trp 1 5		
<210> SEQ ID NO 221 <211> LENGTH: 24 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 221 ataaaccaag atggaagtga gaaa		
		24
<210> SEQ ID NO 222 <211> LENGTH: 8 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 222 Ile Asn Gln Asp Gly Ser Glu Lys 1 5		
<210> SEQ ID NO 223 <211> LENGTH: 60 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 223 gcgagagata ttgtactaat ggtctatgat atggactact actactacgg tatggacgtc		
		60
<210> SEQ ID NO 224 <211> LENGTH: 20 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 224 Ala Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr 1 5 10 15 Gly Met Asp Val 20		

-continued

<210> SEQ ID NO 225
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 225

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc      60
atctcctgca ggtctagtca gagcctcctg catagtaatg gaaacaacta tttggattgg      120
tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcgggcc      180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc      240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaaaactct acaaaactccg      300
ctcactttcg gcggaggggac caagtgagg atcaaa                                336
  
```

<210> SEQ ID NO 226
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 226

```

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1             5             10            15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
      20             25            30
Asn Gly Asn 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 Thr
      85             90            95
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
      100            105           110
  
```

<210> SEQ ID NO 227
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 227

```

cagagcctcc tgcataagtaa tggaaacaac tat                                33
  
```

<210> SEQ ID NO 228
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 228

```

Gln Ser Leu Leu His Ser Asn Gly Asn Asn Tyr
 1             5             10
  
```

<210> SEQ ID NO 229

-continued

<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 229

ttgggttct

9

<210> SEQ ID NO 230
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 230

Leu Gly Ser
1

<210> SEQ ID NO 231
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 231

atgcaaactc tacaaactcc gctcact

27

<210> SEQ ID NO 232
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 232

Met Gln Thr Leu Gln Thr Pro Leu Thr
1 5

<210> SEQ ID NO 233
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 233

gagggtgcagc tgggtggagtc tggggggaggc ttggtccagc ctgggggggtc cctgagactc 60
tctgtgtcag cctctggatt cacctttagt agtcactgga tgaagtgggt ccgccaggct 120
ccaggaaggg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat 180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgttt 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt 300
gtactaatgg tctatgatat ggactactac tactacggta tggacgtctg gggccaaggg 360
accacggtca cegtctcctc a 381

<210> SEQ ID NO 234
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 234

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 Ser His
 20 25 30
 Trp Met Lys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Asn Ile Asn 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 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 Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr
 100 105 110
 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120 125

<210> SEQ ID NO 235

<211> LENGTH: 336

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 235

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
 atctcctgca ggtctagtc gagcctcctg catagtaatg gaaacaacta tttggattgg 120
 tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcggggc 180
 tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
 agcagagtgg aggctgagga tgttgggggt tattactgca tgcaaaactct acaaaactccg 300
 ctcactttcg gcggaggggac caaggtggag atcaaa 336

<210> SEQ ID NO 236

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 236

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu His Ser
 20 25 30
 Asn Gly Asn 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 Thr
 85 90 95
 Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

-continued

<210> SEQ ID NO 237
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 237

```

gaggtgcagc tgggtggagtc tgggggaggc ttggtccagc ctgggggggtc cctgagactc      60
tctctgtcag cctctggatt cacctttagt agtcactgga tgagctgggt ccgccagget      120
ccaggaaggg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat      180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctactgtat      240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt      300
gtactaatgg tctatgatat ggactactac tactacggta tggacgtctg ggggcaaggg      360
accacgggtca ccgtctcctc a                                          381
  
```

<210> SEQ ID NO 238
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 238

```

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 Ser His
             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 Asn 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 Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr
             100            105            110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
             115            120            125
  
```

<210> SEQ ID NO 239
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 239

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gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc      60
atctcctgca ggtctagtca gagcctcctg catagtaatg gaaacaacta tttggattgg      120
tacctgcaga agccagggca gtctccacag ctctgatctt atttgggttc taatcggggc      180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc      240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaaactct acaaactccg      300
ctcactttcg gcggaggggc caaggtggag atcaaa                               336
  
```

-continued

<210> SEQ ID NO 240
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 240

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Pro	Gly
1				5					10					15	
Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser
			20					25					30		
Asn	Gly	Asn	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	Thr
				85				90						95	
Leu	Gln	Thr	Pro	Leu	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
			100					105					110		

<210> SEQ ID NO 241
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 241

cagggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctgggaggtc cctgagactc tctgtgacag tctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt gtactagtga tgtatgatag agactatcac tactatggga tggacgtctg gggccaaggg accacggtca ccgtctcctc a	60 120 180 240 300 360 381
--	--

<210> SEQ ID NO 242
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 242

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	Val	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	Ala	Ile	Ser	Tyr	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Val	Asp	Ser	Val
		50				55					60				
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Lys	Thr	Leu	Tyr
65					70					75				80	
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Asn	Cys

-continued

	85		90		95										
Ala	Lys	Asn	Ile	Val	Leu	Val	Met	Tyr	Asp	Ile	Asp	Tyr	His	Tyr	Tyr
	100							105					110		

Gly	Met	Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
	115						120					125		

<210> SEQ ID NO 243
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 243

ggattcacct tcagtagcta tggc

24

<210> SEQ ID NO 244
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 244

Gly	Phe	Thr	Phe	Ser	Ser	Tyr	Gly
1				5			

<210> SEQ ID NO 245
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 245

atatcatatg atggaagtaa taaa

24

<210> SEQ ID NO 246
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 246

Ile	Ser	Tyr	Asp	Gly	Ser	Asn	Lys
1				5			

<210> SEQ ID NO 247
 <211> LENGTH: 60
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 247

gcgaaaaata ttgtactagt gatgtatgat atagactatc actactatgg gatggacgtc

60

<210> SEQ ID NO 248
 <211> LENGTH: 20
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 248

-continued

Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr
1 5 10 15

Gly Met Asp Val
20

<210> SEQ ID NO 249
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 249

gatattgtga tgactcagtc tccactctcc ctgcccgtea cccctggaga gccggcctcc 60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg 120
tacctgcaga agccagggca gtctccacaa ctctgatct atttgggttt taatcgggcc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct acaaaactct 300
ctcactttcg gcggagggac caagtgagg atcaga 336

<210> SEQ ID NO 250
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 250

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu 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 Phe 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 Arg
100 105 110

<210> SEQ ID NO 251
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 251

cagagcctcc tgcataagtaa tggatacaac tat 33

<210> SEQ ID NO 252
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 252

-continued

Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
1 5 10

<210> SEQ ID NO 253
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 253

ttgggtttt

9

<210> SEQ ID NO 254
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 254

Leu Gly Phe
1

<210> SEQ ID NO 255
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 255

atgcaagctc tacaaactcc tctcact

27

<210> SEQ ID NO 256
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 256

Met Gln Ala Leu Gln Thr Pro Leu Thr
1 5

<210> SEQ ID NO 257
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 257

cagggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tctgtgtcag tctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat 180
gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt 300
gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg gggccaaggg 360
accacgggtca cegtctcctc a 381

<210> SEQ ID NO 258

<400> SEQUENCE: 258

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<400> SEQUENCE: 259

gatatattgtga	tgactcagtc	tccactctcc	ctgcccgctca	cccttgagaga	gccggcctcc	60
atctcctgca	ggtctagtc	gagcctcctg	catagtaatg	gatacaacta	tttggaattg	120
tacctgcaga	agccagggca	gtctccacaa	ctcctgatct	atttgggttt	taatcggggc	180
tccgggggtcc	ctgacaggtt	cagtggcagc	ggatcaggca	cagattttac	actgaaaaac	240
agcagagtgg	aggtctagga	tgttgggggt	tattactgca	tgcaagctct	acaaactcct	300
ctcactttcg	gcggaggggc	caaggtggag	atcaaaa			336

<400> SEQUENCE: 260

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala

-continued

	85	90	95	
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys				
	100	105	110	

<210> SEQ ID NO 261
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 261

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc	60
tctgtgacag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct	120
ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat	180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaaatatt	300
gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg ggggcaaggg	360
accacggtca ccgtctcctc a	381

<210> SEQ ID NO 262
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 262

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 Ser Tyr Asp 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	
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr	
100 105 110	
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser	
115 120 125	

<210> SEQ ID NO 263
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 263

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc	60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg	120
tacctgcaga agccagggca gtctccacag ctctgatct atttgggttt taatcgggcc	180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc	240

-continued

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agcagagtgg aggctgagga tgttgggggtt tattactgca tgcaagctct acaaactcct    300
ctcactttcg gcggaggggac caaggtggag atcaaaa                                336

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<210> SEQ ID NO 264
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 264

```

```

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1             5             10             15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu 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 Phe 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> SEQ ID NO 265
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 265

```

```

cagggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctgggaggtc cctgagactc    60
tctctgtgcag tctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct    120
ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat    180
gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat    240
ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt    300
gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg gggccaaggg    360
accacggtca ccgtctcctc a                                381

```

```

<210> SEQ ID NO 266
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 266

```

```

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 Val 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 Ala Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Val Asp Ser Val

```

-continued

50	55	60
Lys Gly Arg Phe Thr	Ile Ser Arg Asp Asn Ser	Lys Lys Thr Leu Tyr
65	70	75 80
Leu Gln Met Asn Ser	Leu Arg Ala Glu Asp Thr	Ala Val Tyr Asn Cys
	85	90 95
Ala Lys Asn Ile Val	Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr	
	100	105 110
Gly Met Asp Val Trp	Gly Gln Gly Thr Thr Val Thr Val Ser Ser	
	115	120 125

<210> SEQ ID NO 267
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 267

 ggattcacct tcagtagcta tggc 24

<210> SEQ ID NO 268
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 268

 Gly Phe Thr Phe Ser Ser Tyr Gly
 1 5

<210> SEQ ID NO 269
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 269

 atatcatatg atggaagtaa taaa 24

<210> SEQ ID NO 270
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 270

 Ile Ser Tyr Asp Gly Ser Asn Lys
 1 5

<210> SEQ ID NO 271
 <211> LENGTH: 60
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 271

 gcgaaaaata ttgtactagt gatgtatgat atagactatc actactatgg gatggacgtc 60

<210> SEQ ID NO 272
 <211> LENGTH: 20
 <212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 272

Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr
 1 5 10 15

Gly Met Asp Val
 20

<210> SEQ ID NO 273
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 273

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
 atctctctgca ggtctagtca gagcctctcg catagtaatg gatacaacta tttggattgg 120
 tacctgcaga agccagggca gtctccacaa ctctgatct atttgggttt taatcgggcc 180
 tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
 agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct acaaaactcct 300
 ctcactttcg gcggaggggac caaggtggag atcaga 336

<210> SEQ ID NO 274
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 274

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu 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 Phe 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 Arg
 100 105 110

<210> SEQ ID NO 275
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 275

cagagcctcc tgcataagtaa tggatacaac tat 33

<210> SEQ ID NO 276
 <211> LENGTH: 11

-continued

<212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 276

Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
 1 5 10

<210> SEQ ID NO 277
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 277

ttgggtttt

9

<210> SEQ ID NO 278
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 278

Leu Gly Phe
 1

<210> SEQ ID NO 279
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 279

atgcaagctc tacaaactcc tctcact

27

<210> SEQ ID NO 280
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 280

Met Gln Ala Leu Gln Thr Pro Leu Thr
 1 5

<210> SEQ ID NO 281
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 281

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
 tctgtgtcag tctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
 ccaggcaagg ggctggagtc ggtggcagct atatcatatg atggaagtaa taaatactat 180
 gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat 240
 ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt 300

-continued

gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg gggccaaggg 360
accacggtca ccgtctcctc a 381

<210> SEQ ID NO 282
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 282

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 Val 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 Ala Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Val Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Lys Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Asn Cys
85 90 95
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr
100 105 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 283
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 283

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg 120
tacctgcaga agccagggca gtctccacaa ctctgatct atttgggttt taatcggggc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct aaaaactcct 300
ctcactttcg gcggagggac caaggtggag atcaaa 336

<210> SEQ ID NO 284
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 284

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu 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 Phe Asn Arg Ala Ser Gly Val Pro

-continued

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> SEQ ID NO 285
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 285

cagggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc	60
tctgtgtcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct	120
ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat	180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaaatatt	300
gtactagtga tgtatgatag agactatcac tactatggga tggacgtctg ggggcaaggg	360
accacggtca ccgtctcctc a	381

<210> SEQ ID NO 286
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 286

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg	
1	15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr	
20	30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
35	45
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val	
50	60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr	
65	80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
85	95
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr	
100	110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser	
115	125

<210> SEQ ID NO 287
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 287

gatattgtga tgactcagtc tccactctcc ctgcccgta cccctggaga gccggcctcc	60
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-continued

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atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg 120
tacctgcaga agccagggca gtctccacag ctctgatct atttgggttt taatcggggc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct acaaaactct 300
ctcactttcg gcggaggggac caagggtggag atcaaa 336

```

```

<210> SEQ ID NO 288
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 288

```

```

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1             5             10             15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu 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 Phe 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> SEQ ID NO 289
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 289

```

```

cagatcacct tgaaggagtc tggctcctacg ctggtaaaac ccacacagac cctcacgctg 60
acctgcacct tctctggggt ctcactcagc gctagtggag tgggtgtggg ctgggtccgt 120
cagcccccag gaaagggcct ggagtggctt gcactcattt attggaatga tgataagcgt 180
tacagcccat ctctaagaa cagcctcacc atcaccaagg acacctccaa aaaccagggtg 240
gtccttataa tgaccaacat ggacctgtg gacacagcca catattactg tgcacacaga 300
atacatctat ggtcctactt ctactacggt atggacgtct ggggccaaagg gaccacggtc 360
accgtctcct ca 372

```

```

<210> SEQ ID NO 290
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 290

```

```

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

```

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

<400> SEQUENCE: 291

qqgttctcac tcagcctag tqgaqtgggt

30

```
<210> SEQ ID NO 292
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

<400> SEQUENCE: 292

Gly Phe Ser Leu Ser Ala Ser Gly Val Gly
1 5 10

```
<210> SEQ ID NO 293
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

<400> SEQUENCE: 293

atttattgga atqatgataa g

21

```
<210> SEQ ID NO 294
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

<400> SEQUENCE: 294

Ile Tyr Trp Asn Asp Asp Lys
1 5

```
<210> SEQ ID NO 295
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

<400> SEQUENCE: 295

-continued

gcacacagaa tacatctatg gtctacttc tactacggta tggacgtc

48

<210> SEQ ID NO 296
 <211> LENGTH: 16
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 296

Ala His Arg Ile His Leu Trp Ser Tyr Phe Tyr Tyr Gly Met Asp Val
 1 5 10 15

<210> SEQ ID NO 297
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 297

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
 atctctctgca ggtctagtca gactctctcg catagtaatg gatacaacta tttcgattgg 120
 tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcggggc 180
 tccgggggtcc ctgacagatt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
 agcagagtgg aggctgagga tgttggaatt tattactgca tgcaagctct aaaaactcct 300
 ctcactttcg gcggaggggac caagtgagg atcaga 336

<210> SEQ ID NO 298
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 298

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr Leu Leu His Ser
 20 25 30
 Asn Gly Tyr Asn Tyr Phe 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 Ile Tyr Tyr Cys Met Gln Ala
 85 90 95
 Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Arg
 100 105 110

<210> SEQ ID NO 299
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 299

cagactctcc tgcataagtaa tggatacaac tat

33

-continued

<210> SEQ ID NO 300
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 300

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

<210> SEQ ID NO 301
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 301

ttgggttct

9

<210> SEQ ID NO 302
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 302

Leu Gly Ser
 1

<210> SEQ ID NO 303
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 303

atgcaagctc tacaaactcc tctcact

27

<210> SEQ ID NO 304
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 304

Met Gln Ala Leu Gln Thr Pro Leu Thr
 1 5

<210> SEQ ID NO 305
 <211> LENGTH: 372
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 305

cagatcacct tgaaggagtc tggctcctacg ctggtaaaac ccacacagac cctcacgctg 60

acctgcacct tctctggggt ctcactcagc gctagtggag tgggtgtggg ctgggtccgt 120

cagccccag gaaaggccct ggagtggctt gcactcattt attggaatga tgataagcgt 180

tacagcccat ctctaagaa cagcctcacc atcaccaagg acacctccaa aaaccagggtg 240

-continued

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gtccttaca tgaccaacat ggacctgtg gacacagcca catattactg tgcacacaga 300
atacatctat ggtcctactt ctactacggt atggacgtct ggggccaagg gaccacggtc 360
accgtctcct ca 372

```

```

<210> SEQ ID NO 306
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 306

```

```

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

```

```

<210> SEQ ID NO 307
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 307

```

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctcctgca ggtctagtc gactctcctg catagtaatg gatacaacta ttctgattgg 120
tacctgcaga agccagggca gtctccacag ctctgatctt atttgggttc taatcggggc 180
tccgggggtcc ctgacagatt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttggaatt tattactgca tgcaagctct acaaaactct 300
ctcactttcg gcggaggggac caaggtggag atcaaaa 336

```

```

<210> SEQ ID NO 308
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 308

```

```

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1             5             10             15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr Leu Leu His Ser
          20             25             30
Asn Gly Tyr Asn Tyr Phe Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser

```

-continued

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
Ser Arg Val Glu Ala Glu Asp Val Gly Ile 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> SEQ ID NO 309
 <211> LENGTH: 372
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 309

cagatcacct tgaaggagtc tggctcctacg ctggtgaaac ccacacagac cctcacgctg	60
acctgcacct tctctgggtt ctcactcagc gctagtggag tgggtgtggg ctggatccgt	120
cagccccag gaaagccct ggagtggctt gcactcattt attggaatga tgataagcgc	180
tacagcccat ctctgaagag caggctcacc atcaccaagg acacctcaa aaaccagggtg	240
gtccttataa tgaccaacat ggacctgtg gacacagcca catattactg tgcacacaga	300
atacatctat ggtcctactt ctactacggt atggacgtct gggggcaagg gaccacggtc	360
accgtctcct ca	372

<210> SEQ ID NO 310
 <211> LENGTH: 124
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 310

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln	
1	15
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Ala Ser	
20	30
Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu	
35	45
Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser	
50	60
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val	
65	80
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr	
85	95
Cys Ala His Arg Ile His Leu Trp Ser Tyr Phe Tyr Tyr Gly Met Asp	
100	110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser	
115	120

<210> SEQ ID NO 311
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 311

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccttgagaga gccggcctcc      60
atctcctgca ggtctagtc gactctcctg catagtaatg gatacaacta tttggattgg      120
tacctgcaga agccagggca gtctccacag ctectgatct atttgggttc taatcggggc      180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc      240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct acaaaactct      300
ctcactttcg gcggaggggac caaggtggag atcaaaa                                336

```

<210> SEQ ID NO 312

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 312

```

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1             5             10             15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr 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> SEQ ID NO 313

<211> LENGTH: 381

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 313

```

cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc      60
tcttgaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc      120
cctggacaag ggcttgagtg gatgggatgg atcagcgggtt acaatggtaa acaaaacgat      180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt      300
ttagtagtac cacctgccct taattattcc tactacgtta tggacgtctg gggccaaggg      360
accacggtca ccgtctcctc a                                              381

```

<210> SEQ ID NO 314

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 314

```

Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Asn Pro Gly Ala

```

-continued

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

<210> SEQ ID NO 315
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 315

ggttacacct ttaccaccta tggt

24

<210> SEQ ID NO 316
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 316

Gly Tyr Thr Phe Thr Thr Tyr Gly
1 5

<210> SEQ ID NO 317
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 317

atcagcgggtt acaatggtaa aaca

24

<210> SEQ ID NO 318
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 318

Ile Ser Gly Tyr Asn Gly Lys Thr
1 5

<210> SEQ ID NO 319
 <211> LENGTH: 60
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 319

tcgagagatc gtttagtagt accacctgcc cttaattatt cctactacgt tatggacgtc 60

<210> SEQ ID NO 320

<211> LENGTH: 20

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 320

Ser	Arg	Asp	Arg	Leu	Val	Val	Pro	Pro	Ala	Leu	Asn	Tyr	Ser	Tyr	Tyr
1				5					10					15	

Val	Met	Asp	Val
			20

<210> SEQ ID NO 321

<211> LENGTH: 336

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 321

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttgagaca gccggcctcc 60

atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120

tctcagcaga ggccagggtca atctccaagg cgcctaattt ataaggtttc taaccggggac 180

tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240

agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaagggtac acactggccg 300

tacacttttg gccagggggac caagctggag atcaaa 336

<210> SEQ ID NO 322

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 322

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	Arg	Ser	Ser	Gln	Ser	Leu	Val	Tyr	Ser
		20					25					30			

Asp	Gly	Asn	Thr	Tyr	Leu	Asn	Trp	Ser	Gln	Gln	Arg	Pro	Gly	Gln	Ser
	35						40					45			

Pro	Arg	Arg	Leu	Ile	Tyr	Lys	Val	Ser	Asn	Arg	Asp	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	Gly
			85					90						95	

Thr	His	Trp	Pro	Tyr	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100				105							110	

<210> SEQ ID NO 323

<211> LENGTH: 33

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 323

caaagcctcg tatacagtga tggaaacacc tac

33

<210> SEQ ID NO 324

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 324

Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr
1 5 10

<210> SEQ ID NO 325

<211> LENGTH: 9

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 325

aaggtttct

9

<210> SEQ ID NO 326

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 326

Lys Val Ser
1

<210> SEQ ID NO 327

<211> LENGTH: 27

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 327

atgcaaggta cacactggcc gtacact

27

<210> SEQ ID NO 328

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 328

Met Gln Gly Thr His Trp Pro Tyr Thr
1 5

<210> SEQ ID NO 329

<211> LENGTH: 381

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 329

cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc

60

-continued

```

tcttgaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc 120
cctggacaag ggcttgatg gatgggatgg atcagcgggt acaatggtaa aacaaacgat 180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac 240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt 300
ttagtagtac cacctgccct taattattcc tactacgtta tggacgtctg gggccaaggg 360
accacggtea ccgtctcttc a 381

```

```

<210> SEQ ID NO 330
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 330

```

```

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

```

```

<210> SEQ ID NO 331
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 331

```

```

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaaca gccggcctcc 60
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120
tctcagcaga ggccagggtca atctccaagg cgcctaattt ataaggtttc taaccgggac 180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240
agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaaggtag acactggccg 300
tacacttttg gccaggggac caagctggag atcaaa 336

```

```

<210> SEQ ID NO 332
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 332

```

```

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly

```

-continued

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

<210> SEQ ID NO 333
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 333

```

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc      60
tcttgcaagg cttctgggta cacctttacc acctatggta tcagctgggt ggcacaggcc      120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat      180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt      300
ttagtagtac cacctgccct taattattcc tactacgtta tggacgtctg ggggcaaggg      360
accacgggtca ccgctccttc a                                     381

```

<210> SEQ ID NO 334
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 334

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

<210> SEQ ID NO 335

-continued

<211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 335

```

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttgagaca gccggcctcc      60
atctcctgca ggtctagtc aagcctcgta tacagtgatg gaaacaccta cttgaattgg      120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac      180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc      240
agcagggttg aggtcgagga tgttggggtt tattactgca tgcaaggtag acactggccg      300
tacacttttg gccaggggac caagctggag atcaaa      336
  
```

<210> SEQ ID NO 336
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 336

```

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
          20             25             30
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
          35             40             45
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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 Gly
          85             90             95
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100            105            110
  
```

<210> SEQ ID NO 337
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 337

```

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc      60
tctgtgcagc cctctggatt caccttcagt agctatagca tggactgggt ccgccaggct      120
ccaggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac      180
gcagactctg tgaagggccg attcaccatc tccagagaca ccgccaagaa ctcactgtat      240
ctgcaaatga acagcctgag agacgaggac acggctgttt attactgtgc gagagagggc      300
agtagcagac tttttgacta ctggggccag ggaaccctgg tcaccgtctc ctca      354
  
```

<210> SEQ ID NO 338
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 338

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

<210> SEQ ID NO 339

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 339

ggattcacct tcagtagcta tagc

24

<210> SEQ ID NO 340

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 340

Gly Phe Thr Phe Ser Ser Tyr Ser
 1 5

<210> SEQ ID NO 341

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 341

attagtagta gtagtagtta cata

24

<210> SEQ ID NO 342

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 342

Ile Ser Ser Ser Ser Ser Tyr Ile
 1 5

<210> SEQ ID NO 343

<211> LENGTH: 33

-continued

<212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 343

gcgagagagg gcagtagcag actttttgac tac

33

<210> SEQ ID NO 344
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 344

Ala Arg Glu Gly Ser Ser Arg Leu Phe Asp Tyr
 1 5 10

<210> SEQ ID NO 345
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 345

gacatccaga tgacccagtc tccttcacac ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggccagtc gagtattagt agctggttg cctgggtatca gcagagacca 120

gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaagggtg agtcccatca 180

aggttcagcg gcagtggtgc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240

gaggattttg caacttatta ctgccaacag tataatagtt attggtacac ttttgccag 300

gggaccaagc tggagatcaa a 321

<210> SEQ ID NO 346
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 346

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Gly 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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Trp Tyr
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> SEQ ID NO 347
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 347

cagagtatta gtagctgg

18

<210> SEQ ID NO 348
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 348

Gln Ser Ile Ser Ser Trp
1 5

<210> SEQ ID NO 349
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 349

aaggcgtct

9

<210> SEQ ID NO 350
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 350

Lys Ala Ser
1

<210> SEQ ID NO 351
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 351

caacagtata atagttattg gtacact

27

<210> SEQ ID NO 352
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 352

Gln Gln Tyr Asn Ser Tyr Trp Tyr Thr
1 5

<210> SEQ ID NO 353
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 353

-continued

```

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc    60
tctctgtcag cctctggatt caccttcagt agctatagca tggactgggt cgcaggagct    120
ccaggaaggg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac    180
gcagactctg tgaagggccg attcaccatc tccagagaca cgcgaagaa ctactgtat    240
ctgcaaatga acagcctgag agacgaggac acggtgttt attactgtgc gagagagggc    300
agtagcagac tttttgacta ctggggccag ggaaccctgg tcaccgtctc ctca    354

```

```

<210> SEQ ID NO 354
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 354

```

```

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

```

```

<210> SEQ ID NO 355
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 355

```

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc    60
atcacttgcc gggccagtc gagtattagt agctggttg cctgggtatca gcagagacca    120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaagggtg agtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct    240
gaggattttg caacttatta ctgccaacag tataatagtt attggtacac ttttggccag    300
gggaccaagc tggagatcaa a    321

```

```

<210> SEQ ID NO 356
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 356

```

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10             15

```

-continued

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

<210> SEQ ID NO 357
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 357

gaggtgcagc tgggtggagtc tggggggaggc ctggtcaagc ctgggggggtc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct 120
 ccaggggaagg ggctgggagtg ggtctcatcc attagtagta gtagtagtta catatactac 180
 gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcaactgtat 240
 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagagggc 300
 agtagcagac tttttgacta ctgggggcaa ggaaccctgg tcaccgtctc ctca 354

<210> SEQ ID NO 358
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 358

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

<210> SEQ ID NO 359
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 359

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc    60
atcacttgcc gggccagtc gagtattagt agctgggttg cctgggtatca gcagaaacca    120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct    240
gatgattttg caacttatta ctgccaacag tataatagtt attggtacac ttttgccag    300
gggaccaagc tggagatcaa a                                           321

```

<210> SEQ ID NO 360

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 360

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10             15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
                20             25             30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35             40             45
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Trp Tyr
                85             90             95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        100             105

```

<210> SEQ ID NO 361

<211> LENGTH: 384

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 361

```

caggtgcacc tgggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc    60
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct    120
ccaggaaggg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat    180
gtggactctg tggaggggccg attcatcatt tccagggaca acgccaagaa ctattgtat    240
ctacatatga acagcctcag agccgacgac acggccgtgt attactgtgc gagagatcag    300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa    360
gggaccacgg tcaccgtcgc ctca                                           384

```

<210> SEQ ID NO 362

<211> LENGTH: 128

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 362

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

<210> SEQ ID NO 363

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 363

ggattcacct tcagtgacca ctac

24

<210> SEQ ID NO 364

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 364

Gly Phe Thr Phe Ser Asp His Tyr
 1 5

<210> SEQ ID NO 365

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 365

attagtaatg atggtggtac caaa

24

<210> SEQ ID NO 366

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 366

Ile Ser Asn Asp Gly Gly Thr Lys
 1 5

<210> SEQ ID NO 367

<211> LENGTH: 63

<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 367

gcgagagatc agggatatat tggctacgac tcgtattatt actattccta cggtatggac 60
 gtc 63

<210> SEQ ID NO 368
 <211> LENGTH: 21
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 368

Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser
 1 5 10 15
 Tyr Gly Met Asp Val
 20

<210> SEQ ID NO 369
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 369

aaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc 60
 ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa 120
 tctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcagtggt gtctgggacc gacttcactc tcaccatcag cggactggag 240
 cctgaagatt ttgaagtgtg ttattgtcaa gtatatggta actcactcac tctcggcgga 300
 gggaccaagg tggagatcaa g 321

<210> SEQ ID NO 370
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 370

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

-continued

<210> SEQ ID NO 371
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 371

cagagtgtta acaacaaatt c

21

<210> SEQ ID NO 372
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 372

Gln Ser Val Asn Asn Lys Phe
1 5

<210> SEQ ID NO 373
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 373

ggtgcatcc

9

<210> SEQ ID NO 374
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 374

Gly Ala Ser
1

<210> SEQ ID NO 375
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 375

caagtatatg gtaactcact cact

24

<210> SEQ ID NO 376
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 376

Gln Val Tyr Gly Asn Ser Leu Thr
1 5

<210> SEQ ID NO 377
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 377

```

caggtgcagc tgggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc      60
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct      120
ccaggaaggg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat      180
gtggactctg tggaggggccg attcatcatt tccagggaca acgccaagaa ctcattgtat      240
ctacatatga acagcctcag agccgacgac acggccgtgt attactgtgc gagagatcag      300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa      360
gggaccacgg tcaccgtctc ctca                                          384

```

<210> SEQ ID NO 378

<211> LENGTH: 128

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 378

```

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

```

<210> SEQ ID NO 379

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 379

```

gaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc      60
ctctcctgta gggccagtca gagtgtaaac aacaaattct tagcctggta ccagcagaaa      120
tctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca      180
gacaggttca gtggcagtggt gtctgggacc gacttcactc tcaccatcag cggactggag      240
cctgaagatt ttgaagtgta ttattgtcaa gtatatggta actcactcac tctcggcgga      300
gggaccaagg tggagatcaa a                                          321

```

<210> SEQ ID NO 380

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 380

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

<210> SEQ ID NO 381

<211> LENGTH: 384

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 381

cagggtgcagc tgggtggagtc tgggggagggc ttggtcaagc ctggaggggc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct 120
 ccagggaagg ggctggagtg ggtttcatat attagtaatg atggtgggtac caaatactac 180
 gcagactctg tgaagggccg attcaccatc tccagggaca acgccaagaa ctcaactgtat 240
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatcag 300
 ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctgggggcaa 360
 gggaccacgg tcaccgtctc ctca 384

<210> SEQ ID NO 382

<211> LENGTH: 128

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 382

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

-continued

Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 383
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 383

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcateca gcagggccac tggcatccca 180
 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtg ttactgtcaa gtatatggta actcactcac ttctcgcgga 300
 gggaccaagg tggagatcaa a 321

<210> SEQ ID NO 384
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 384

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 Ser Val Asn Asn Lys
20 25 30
 Phe 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 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 Val Tyr Gly Asn Ser Leu
85 90 95
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 385
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 385

gaggtgcaga aggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc 60
 tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct 120
 ccaggaaggg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
 gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat 240
 ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc 300
 agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca 360

<210> SEQ ID NO 386

-continued

```

<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 386

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

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
      20             25             30

Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35             40             45

Ser Ser Ile Arg Ser Ser Ser Asn Tyr 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 Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
      85             90             95

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
 100             105             110

Gly Thr Leu Val Thr Val Ser Ser
 115             120

```

```

<210> SEQ ID NO 387
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 387

```

```

ggattcacct tcagtactta taac

```

24

```

<210> SEQ ID NO 388
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 388

```

```

Gly Phe Thr Phe Ser Thr Tyr Asn
 1             5

```

```

<210> SEQ ID NO 389
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 389

```

```

attaggagta gtagtaatta cata

```

24

```

<210> SEQ ID NO 390
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 390

```

```

Ile Arg Ser Ser Ser Asn Tyr Ile

```


-continued

1 5

<210> SEQ ID NO 391
 <211> LENGTH: 39
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 391

gcgagagatg gcagcagttg gtacgactac tctgactac 39

<210> SEQ ID NO 392
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 392

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
 1 5 10

<210> SEQ ID NO 393
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 393

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca acagatacca 120
 gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180
 aggttcagcg gcagtcggtc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300
 gggaccaagg tggaaatcaa a 321

<210> SEQ ID NO 394
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 394

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

-continued

<210> SEQ ID NO 395
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 395

cagagtatta gtagctgg

18

<210> SEQ ID NO 396
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 396

Gln Ser Ile Ser Ser Trp
1 5

<210> SEQ ID NO 397
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 397

aaggcgtct

9

<210> SEQ ID NO 398
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 398

Lys Ala Ser
1

<210> SEQ ID NO 399
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 399

caacagtata ttagttattc tcggacg

27

<210> SEQ ID NO 400
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 400

Gln Gln Tyr Ile Ser Tyr Ser Arg Thr
1 5

<210> SEQ ID NO 401
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 401

```

gaggtgcagc tgggtggagtc tggggggaggc ctggtcaagc cggggggggtc cctgagactc    60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct    120
ccaggggaagg gactgggagt ggtctcatcc attaggagta gtagtaatta catatactac    180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat    240
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc    300
agcagttggt acgactactc tgactactgg ggccagggaa ccctgggtcac cgtctcctca    360

```

<210> SEQ ID NO 402

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 402

```

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

```

<210> SEQ ID NO 403

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 403

```

gacatccaga tgacccagtc tccttcaccc ctgtctgcat ctgtaggaga cagagtcacc    60
atcacttgcc gggccagtcg gagtattagt agctgggttg cctgggtatca acagatacca    120
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca    180
aggttcagcg gcagtggtac tgggacagaa ttcactctca tcatcagcag cctgcagcct    240
gatgatTTTT caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa    300
gggaccaagg tggaaatcaa a                                     321

```

<210> SEQ ID NO 404

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 404

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

<210> SEQ ID NO 405

<211> LENGTH: 360

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 405

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt acttataaca tgaactgggt ccgccaggct 120
 ccaggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
 gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240
 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc 300
 agcagttggt acgactactc tgactactgg ggccaaggaa ccctgggtcac cgtctcctca 360

<210> SEQ ID NO 406

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 406

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

-continued

<210> SEQ ID NO 407
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 407

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca gcagaaacca    120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca    180
agggttcagc gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct    240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa    300
gggaccaagg tggaaatcaa a                                              321
  
```

<210> SEQ ID NO 408
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 408

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10            15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
          20            25            30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
      35            40            45
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Ile Ser Tyr Ser Arg
          85            90            95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
      100           105
  
```

<210> SEQ ID NO 409
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 409

```

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc cggggggggtc cctgagactc      60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct    120
ccaggaaggg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac    180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat    240
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc    300
agcagttggt acgactactc tgactactgg ggccagggaa ccctgggtcac cgtctcctca    360
  
```

<210> SEQ ID NO 410
 <211> LENGTH: 120
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence

-continued

```

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 410

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

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
      20             25             30

Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35             40             45

Ser Ser Ile Arg Ser Ser Ser Asn Tyr 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 Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
      85             90             95

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
 100             105             110

Gly Thr Leu Val Thr Val Ser Ser
 115             120

```

```

<210> SEQ ID NO 411
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 411

```

```

ggattcacct tcagtactta taac

```

24

```

<210> SEQ ID NO 412
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 412

```

```

Gly Phe Thr Phe Ser Thr Tyr Asn
 1             5

```

```

<210> SEQ ID NO 413
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 413

```

```

attaggagta gtagtaatta cata

```

24

```

<210> SEQ ID NO 414
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 414

```

```

Ile Arg Ser Ser Ser Asn Tyr Ile
 1             5

```

-continued

<210> SEQ ID NO 415
 <211> LENGTH: 39
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 415

gcgagagatg gcagcagttg gtacgactac tctgactac 39

<210> SEQ ID NO 416
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 416

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
 1 5 10

<210> SEQ ID NO 417
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 417

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca acagatacca 120
 gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180
 aggttcagcg gcagtggtgc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300
 gggaccaagg tggaaatcaa a 321

<210> SEQ ID NO 418
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 418

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

<210> SEQ ID NO 419
 <211> LENGTH: 18

-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 419

cagagtatta gtagctgg

18

<210> SEQ ID NO 420
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 420

Gln Ser Ile Ser Ser Trp
1 5

<210> SEQ ID NO 421
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 421

aaggcgtct

9

<210> SEQ ID NO 422
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 422

Lys Ala Ser
1

<210> SEQ ID NO 423
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 423

caacagtata ttagttattc tcggacg

27

<210> SEQ ID NO 424
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 424

Gln Gln Tyr Ile Ser Tyr Ser Arg Thr
1 5

<210> SEQ ID NO 425
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 425

```

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc cggggggggtc cctgagactc    60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct    120
ccaggggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac    180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttactgtat    240
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc    300
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca    360

```

<210> SEQ ID NO 426

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 426

```

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

```

<210> SEQ ID NO 427

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 427

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc    60
atcacttgcc gggccagtc gagtattagt agctgggttg cctgggtatca acagatacca    120
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct    240
gatgatTTTT caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa    300
gggaccaagg tggaaatcaa a                                           321

```

<210> SEQ ID NO 428

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 428

-continued

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

<210> SEQ ID NO 429
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 429

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt acttataaca tgaactgggt ccgccaggct 120
 ccaggaaggg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
 gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240
 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc 300
 agcagttggt acgactactc tgactactgg ggccaaggaa ccctgggtcac cgtctcctca 360

<210> SEQ ID NO 430
 <211> LENGTH: 120
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 430

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

<210> SEQ ID NO 431
 <211> LENGTH: 321

-continued

<212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 431

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggccagtca gagtattagt agctgggttg cctggatatca gcagaaacca    120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatacagcag cctgcagcct    240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa    300
gggaccaagg tggaaatcaa a                                              321
  
```

<210> SEQ ID NO 432
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 432

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10            15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
          20            25            30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
          35            40            45
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Ile Ser Tyr Ser Arg
          85            90            95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
          100           105
  
```

<210> SEQ ID NO 433
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 433

```

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc cggggggggc cctgagactc      60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct    120
ccaggaaggg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac    180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagag ttcactgtat    240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc    300
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca    360
  
```

<210> SEQ ID NO 434
 <211> LENGTH: 120
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 434

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

<210> SEQ ID NO 435

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 435

ggattcacct tcagtactta taac

24

<210> SEQ ID NO 436

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 436

Gly Phe Thr Phe Ser Thr Tyr Asn
 1 5

<210> SEQ ID NO 437

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 437

attaggagta gtagtaatta cata

24

<210> SEQ ID NO 438

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 438

Ile Arg Ser Ser Ser Asn Tyr Ile
 1 5

<210> SEQ ID NO 439

<211> LENGTH: 39

<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 439

gcgagagatg gcagcagttg gtacgactac tctgactac 39

<210> SEQ ID NO 440
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 440

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
 1 5 10

<210> SEQ ID NO 441
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 441

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca acaggtacca 120
 gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180
 aggttcagcg gcagtcgagc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300
 gggaccaagg tggaaatcaa a 321

<210> SEQ ID NO 442
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 442

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

<210> SEQ ID NO 443
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 443

cagagtatta gtagctgg

18

<210> SEQ ID NO 444

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 444

Gln Ser Ile Ser Ser Trp

1

5

<210> SEQ ID NO 445

<211> LENGTH: 9

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 445

aaggcgtct

9

<210> SEQ ID NO 446

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 446

Lys Ala Ser

1

<210> SEQ ID NO 447

<211> LENGTH: 27

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 447

caacagtata ttagttattc tcggacg

27

<210> SEQ ID NO 448

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 448

Gln Gln Tyr Ile Ser Tyr Ser Arg Thr

1

5

<210> SEQ ID NO 449

<211> LENGTH: 360

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 449

gagggtgcagc tgggtggagtc tggggggaggc ctggtcaagc cggggggggtc cctgagactc

60

-continued

```

tctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct 120
ccaggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagag ttactgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc 300
agcagttggt acgactactc tgactactgg ggccaggga ccttggtcac cgtctcctca 360

```

```

<210> SEQ ID NO 450
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 450

```

```

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

```

```

<210> SEQ ID NO 451
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 451

```

```

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca acaggtacca 120
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240
gatgatTTTT caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300
gggaccaagg tggaaatcaa a 321

```

```

<210> SEQ ID NO 452
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 452

```

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10             15

```

-continued

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

<210> SEQ ID NO 453
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 453

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt acttataaca tgaactgggt ccgccaggct 120
 ccaggaaggg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
 gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240
 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc 300
 agcagtttgt acgactactc tgactactgg ggccagggaa ccctgggtcac cgtctcctca 360

<210> SEQ ID NO 454
 <211> LENGTH: 120
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 454

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

<210> SEQ ID NO 455
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 455

gacatccaga tgacccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc	60
atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca gcagaaacca	120
gggaaagccc ctaagctect gatctataag gcgtctagtt tagaaagtgg ggtcccatca	180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatacagcag cctgcagcct	240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa	300
gggaccaagg tggaaatcaa a	321

<210> SEQ ID NO 456

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 456

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly	
1 5 10 15	
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp	
20 25 30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile	
35 40 45	
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Ile Ser Tyr Ser Arg	
85 90 95	
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	
100 105	

<210> SEQ ID NO 457

<211> LENGTH: 360

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 457

gaggtgcagc tgggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc	60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct	120
ccaggaaggg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac	180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat	240
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc	300
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca	360

<210> SEQ ID NO 458

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 458

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly

-continued

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

<210> SEQ ID NO 459
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 459

ggattcacct tcagtactta taac

24

<210> SEQ ID NO 460
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 460

Gly Phe Thr Phe Ser Thr Tyr Asn
 1 5

<210> SEQ ID NO 461
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 461

attaggagta gtagtaatta cata

24

<210> SEQ ID NO 462
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 462

Ile Arg Ser Ser Ser Asn Tyr Ile
 1 5

<210> SEQ ID NO 463
 <211> LENGTH: 39
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 463

gcgagagatg gcagcagttg gtacgactac tctgactac

39

<210> SEQ ID NO 464

<211> LENGTH: 13

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 464

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
1 5 10

<210> SEQ ID NO 465

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 465

gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggccagtca gagtattagt agctggttgg cctgggtatca acagatacca 120

gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180

aggttcagcg gcagtggtgc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240

gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300

gggaccaagg tggaaatcaa a 321

<210> SEQ ID NO 466

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 466

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

<210> SEQ ID NO 467

<211> LENGTH: 18

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 467

-continued

cagagtatta gtagctgg

18

<210> SEQ ID NO 468
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 468

Gln Ser Ile Ser Ser Trp
 1 5

<210> SEQ ID NO 469
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 469

aaggcgtct

9

<210> SEQ ID NO 470
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 470

Lys Ala Ser
 1

<210> SEQ ID NO 471
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 471

caacagtata ttagttattc tcggacg

27

<210> SEQ ID NO 472
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 472

Gln Gln Tyr Ile Ser Tyr Ser Arg Thr
 1 5

<210> SEQ ID NO 473
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 473

gagggtgcagc tgggtggagtc tggggggaggc ctggtcaagc cggggggggtc cctgagactc 60

tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct 120

-continued

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ccaggggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat 240
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc 300
agcagttggt acgactactc tgactactgg ggccaggga ccttggtcac cgtctcctca 360

```

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<210> SEQ ID NO 474
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 474

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

```

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<210> SEQ ID NO 475
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 475

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gacatccaga tgacccagtc tccttcaccc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca acagatacca 120
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180
aggttcagcg gcagtggtac tgggacagaa ttcactctca tcatcagcag cctgcagcct 240
gatgatTTTT caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300
gggaccaagg tggaaatcaa a 321

```

```

<210> SEQ ID NO 476
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 476

```

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10             15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
          20             25             30

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-continued

Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
 65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 477
 <211> LENGTH: 360
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 477

gagggtgcagc tgggtggagtc tggggggaggc ctggtcaagc ctgggggggtc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt acttataaca tgaactgggt ccgccaggct 120
 ccaggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac 180
 gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctactgtat 240
 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc 300
 agcagttggt acgactactc tgactactgg ggccaaggaa ccctgggtcac cgtctcctca 360

<210> SEQ ID NO 478
 <211> LENGTH: 120
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 478

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
 20 25 30

Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Ser Ile Arg Ser Ser Ser Asn Tyr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 479
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 479

-continued

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gacatccaga tgaccagtc tccttcacc ctgtctgcat ctgtaggaga cagagtcacc    60
atcacttgcc gggccagtca gagtattagt agctgggttg cctgggtatca gcagaaacca    120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca    180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatacagcag cctgcagcct    240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa    300
gggaccaagg tggaaatcaa a                                              321

```

```

<210> SEQ ID NO 480
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 480

```

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1             5             10            15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
          20            25            30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
      35            40            45
Tyr Lys Ala Ser Ser Leu Glu Ser 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 Ile Ser Tyr Ser Arg
          85            90            95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
      100            105

```

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<210> SEQ ID NO 481
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 481

```

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gagggtgaac tagtgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc    60
tcctgtgtag tctctggatt caccttcggt gactacgaca tgcaactgggt cgtcaagct    120
acaggaagag gtctggagtg ggtctcaggt attgctctcg ctggtgacac atcctataca    180
ggctccgtga agggccgatt caccatctcc agagagaatg ccaagaactc cttgcatctt    240
caaatgaaca gcctgacaac cggggacacg gctatatatt attgtgctag agaggatata    300
gcagtgcctg gttttgatta ctggggccag ggaaccctgg tcaccgtctc ctca        354

```

```

<210> SEQ ID NO 482
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 482

```

```

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 Val Val Ser Gly Phe Thr Phe Gly Asp Tyr

```

-continued

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

<210> SEQ ID NO 483
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 483

ggattcacct tcggtgacta cgac

24

<210> SEQ ID NO 484
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 484

Gly Phe Thr Phe Gly Asp Tyr Asp
 1 5

<210> SEQ ID NO 485
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 485

attgctcctg ctggtgacac a

21

<210> SEQ ID NO 486
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 486

Ile Ala Pro Ala Gly Asp Thr
 1 5

<210> SEQ ID NO 487
 <211> LENGTH: 36
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 487

-continued

gctagagagg ataatagcagt gcctgggttt gattac

36

<210> SEQ ID NO 488
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 488

Ala Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr
 1 5 10

<210> SEQ ID NO 489
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 489

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga acgaggcacc 60
 ctctcctgca gggccagtca gagggttagc agcaacttag cctggtagca gcagaaacct 120
 ggccaggctc ccagactcct catctatggt gcacccacga gggccactgg cttcccagcc 180
 aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag tataataagt ggctccggt cactttcggc 300
 cctgggacca aagtgattt caaa 324

<210> SEQ ID NO 490
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 490

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

<210> SEQ ID NO 491
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 491

cagagtgtta gcagcaac

18

-continued

<210> SEQ ID NO 492
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 492

Gln Ser Val Ser Ser Asn
 1 5

<210> SEQ ID NO 493
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 493

ggtgcatcc

9

<210> SEQ ID NO 494
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 494

Gly Ala Ser
 1

<210> SEQ ID NO 495
 <211> LENGTH: 30
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 495

cagcagtata ataagtggcc tccgttcact

30

<210> SEQ ID NO 496
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 496

Gln Gln Tyr Asn Lys Trp Pro Pro Phe Thr
 1 5 10

<210> SEQ ID NO 497
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 497

gaggtgcaac tagtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60

tctgtgtag tctctggatt caccttcggt gactacgaca tgcactgggt ccgtcaagct 120

acaggaagag gtctggagtg ggtctcaggt attgctcctg ctggtgacac atcctataca 180

ggctccgtga agggccgatt caccatctcc agagagaatg ccaagaactc cttgcatctt 240

-continued

caaatgaaca gcctgacaac cggggacacg gctatatatt attgtgctag agaggatata 300
gcagtgccctg gttttgatta ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> SEQ ID NO 498
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 498

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

<210> SEQ ID NO 499
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 499

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga acgaggcacc 60
ctctcctgca gggccagtca gagggttagc agcaacttag cctggtacca gcagaaacct 120
ggccaggctc ccagactcct catctatggt gcacccacga gggccactgg cttcccagcc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttt cagtttatta ctgtcagcag tataataagt ggctccggt cactttcggc 300
cctgggacca aagtgatat caaa 324

<210> SEQ ID NO 500
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 500

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

-continued

Tyr Gly Ala Ser Thr Arg Ala Thr Gly Phe Pro Ala Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
 65 70 75 80

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

Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
 100 105

<210> SEQ ID NO 501
 <211> LENGTH: 354
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 501

gagggtgcagc tgggtggagtc tggggggaggc ttggtacagc ctgggggggtc cctgagactc 60
 tcctgtgcag cctctggatt caccttcggt gactacgaca tgcactgggt ccgccaagct 120
 acaggaaaag gtctggagtg ggtctcagct attgtctctg ctggtgacac atactatcca 180
 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
 caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgctag agaggatata 300
 gcagtgcctg gttttgatta ctgggggcca ggaaccctgg tcaccgtctc ctca 354

<210> SEQ ID NO 502
 <211> LENGTH: 118
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 502

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 Gly Asp Tyr
 20 25 30

Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Ala Ile Ala Pro Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Leu Val Thr Val Ser Ser
 115

<210> SEQ ID NO 503
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 503

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60

-continued

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ctctcctgca gggccagtca gagggttagc agcaacttag cctgggtacca gcagaaacct 120
ggccaggctc ccaggctect catctatggt gcattccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtggggc tgggacagag ttactcttca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataagt ggctccggt cactttcggc 300
cctgggacca aagtggatat caaa 324

```

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<210> SEQ ID NO 504
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

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<400> SEQUENCE: 504

```

```

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

```

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<210> SEQ ID NO 505
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 505

```

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caaatctctc tgggtgcaatc tggacctgag gtgaaggagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctgggta cacctttacc aactacgcta tcagctgggt gcgacaggtc 120
cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat 180
gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac 240
atggagctga ggagcctgag atctgacgac acggccatgt attactgtgc gagagggggc 300
gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

```

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<210> SEQ ID NO 506
<211> LENGTH: 126
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 506

```

```

Gln Ile Leu Leu Val Gln Ser Gly Pro Glu Val Lys Glu 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

```

-continued

Ala Ile Ser Trp Val Arg Gln Val Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala His Glu Val
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys
 85 90 95

Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
 100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120 125

<210> SEQ ID NO 507
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 507

ggttacacct ttaccaacta cgct

24

<210> SEQ ID NO 508
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 508

Gly Tyr Thr Phe Thr Asn Tyr Ala
 1 5

<210> SEQ ID NO 509
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 509

gtcagcgctt acaatgggtca caca

24

<210> SEQ ID NO 510
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 510

Val Ser Ala Tyr Asn Gly His Thr
 1 5

<210> SEQ ID NO 511
 <211> LENGTH: 57
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 511

gcgagagggg gtgtagtcgt gccagttgct cccacttct acaacggtat ggacgtc

57

-continued

<210> SEQ ID NO 512
 <211> LENGTH: 19
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 512

Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
 1 5 10 15

Met Asp Val

<210> SEQ ID NO 513
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 513

gatattgtga tgactcagtt tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
 atctcctgca ggtctagtc gagcctctg catattaatg aatacaacta tttggattgg 120
 tacctaaaga agccagggca gtctccacag ctctgatct atttgggttt taatcggggc 180
 tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
 agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaactccg 300
 tggacgttag gccaaaggac caaggtggaa atcaaa 336

<210> SEQ ID NO 514
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 514

Asp Ile Val Met Thr Gln Phe 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 Ile
 20 25 30

Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Phe 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 Trp Thr Leu Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 515
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 515

cagagcctcc tgcatattaa tgaatacaac tat

-continued

<210> SEQ ID NO 516
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 516

Gln Ser Leu Leu His Ile Asn Glu Tyr Asn Tyr
 1 5 10

<210> SEQ ID NO 517
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 517

ttgggtttt

9

<210> SEQ ID NO 518
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 518

Leu Gly Phe
 1

<210> SEQ ID NO 519
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 519

atgcaagctc ttcaaactcc gtggacg

27

<210> SEQ ID NO 520
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 520

Met Gln Ala Leu Gln Thr Pro Trp Thr
 1 5

<210> SEQ ID NO 521
 <211> LENGTH: 378
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 521

cagggttcagc tgggtgcagtc tggacctgag gtgaaggagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc aactacgcta tcagctgggt gcgacaggtc 120

cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatgggtca cacaaactat 180

-continued

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gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac 240
atggagctga ggagcctgag atctgacgac acggccatgt attactgtgc gagagggggt 300
gtagtctgtc cagttgtctc ccacttctac aacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctca 378

```

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<210> SEQ ID NO 522
<211> LENGTH: 126
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 522

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```

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

```

```

<210> SEQ ID NO 523
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

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<400> SEQUENCE: 523

```

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctctctgca ggtctagtca gagcctctcg catattaatg aatacaacta tttggattgg 120
tacctaaaga agccagggca gtctccacag ctctgatctc atttgggttt taatcggggc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaactccg 300
tggacgttag gccaaaggac caaggtggaa atcaaa 336

```

```

<210> SEQ ID NO 524
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 524

```

```

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 Ile
          20             25            30

```

-continued

Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Phe 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 Trp Thr Leu Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 525
 <211> LENGTH: 378
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 525

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60
 tcctgcaagg cttctgggta cacctttacc aactacgcta tcagctgggt gcgacaggcc 120
 cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatgggtc cacaaactat 180
 gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240
 atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagggggg 300
 gtagtcgtgc cagttgctcc ccactttctac aacggtatgg acgtctgggg gcaaggggacc 360
 acggtcaccg tctcctca 378

<210> SEQ ID NO 526
 <211> LENGTH: 126
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 526

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 Asn Tyr
 20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
 100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120 125

<210> SEQ ID NO 527
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 527

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc      60
atctcctgca ggtctagtca gagectcctg catattaatg aatacaacta tttggattgg      120
tacctgcaga agccagggca gtctccacag ctctgatctc atttgggttc taatcggggc      180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc      240
agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct tcaaaactcc      300
tggacgttcg gccaaaggac caaggtggaa atcaaa                                336

```

<210> SEQ ID NO 528

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 528

```

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 Ile
          20             25             30
Asn Glu 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 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100            105            110

```

<210> SEQ ID NO 529

<211> LENGTH: 351

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 529

```

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc      60
tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca      120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca      180
ggctccgtga tgggcccatt caccatctcc agagacgctg ccaaaaaactc cttctatctt      240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agaggggaata      300
agaacaccct atgattattg gggccaggga gcccggtca cgtctctctc a                                351

```

<210> SEQ ID NO 530

<211> LENGTH: 117

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 530

```

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1             5             10             15

```

-continued

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
 20 25 30

Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Thr Gly Ser Val Met
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Ala Ala Lys Asn Ser Phe Tyr Leu
 65 70 75 80

Glu Met Asn Ser Leu Arg Val Gly Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Ala Arg
 100 105 110

Val Thr Val Ser Ser
 115

<210> SEQ ID NO 531
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 531

ggattcaccc taagtagcta cgac

24

<210> SEQ ID NO 532
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 532

Gly Phe Thr Leu Ser Ser Tyr Asp
 1 5

<210> SEQ ID NO 533
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 533

attggcagta ctggtagacac a

21

<210> SEQ ID NO 534
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 534

Ile Gly Ser Thr Gly Asp Thr
 1 5

<210> SEQ ID NO 535
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 535

gcaagagagg gaataagaac accctatgat tat

33

<210> SEQ ID NO 536

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 536

Ala Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr
1 5 10

<210> SEQ ID NO 537

<211> LENGTH: 324

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 537

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgtagc agcaatgtag cctggtagca gcagaaacct 120

ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagcc 180

aggttcagtg gcagtgggctc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240

gaagattttg cagtttatta ctgtcagcag tataataatt ggctccatt cactttcggc 300

cctgggacca aagtgatat caaa 324

<210> SEQ ID NO 538

<211> LENGTH: 108

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 538

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

<210> SEQ ID NO 539

<211> LENGTH: 18

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 539

-continued

cagagtgtta gcagcaat

18

<210> SEQ ID NO 540
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 540

Gln Ser Val Ser Ser Asn
 1 5

<210> SEQ ID NO 541
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 541

ggtgcatcc

9

<210> SEQ ID NO 542
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 542

Gly Ala Ser
 1

<210> SEQ ID NO 543
 <211> LENGTH: 30
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 543

cagcagtata ataattggcc tccattcact

30

<210> SEQ ID NO 544
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 544

Gln Gln Tyr Asn Asn Trp Pro Pro Phe Thr
 1 5 10

<210> SEQ ID NO 545
 <211> LENGTH: 351
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 545

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60

tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca 120

acaggaaaaa gtctggagtg ggtctcagct attggcagta ctggtgacac atactatata 180

-continued

```

ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaactc cttctatctt    240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agaggggaata    300
agaacaccct atgattattg gggccaggga accctgggtca cgtctcctc a              351

```

```

<210> SEQ ID NO 546
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 546

```

```

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

```

```

<210> SEQ ID NO 547
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 547

```

```

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc    60
ctctcctgca gggccagtca gagtgtagc agcaatgtag cctgggtacca gcagaaacct    120
ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagcc    180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct    240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc    300
cctgggacca aagtgatat caaa              324

```

```

<210> SEQ ID NO 548
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 548

```

```

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 Gln Ser Val Ser Ser Asn
      20             25            30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile

```

-continued

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

<210> SEQ ID NO 549
 <211> LENGTH: 351
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 549

```

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc      60
tctgtgtcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagct      120
acaggaaaaa gtctggagtg ggtctcagct attggcagta ctggtgacac atactatcca      180
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt      240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agaggggaata      300
agaacaccct atgattattg gggccaagga accctggtca ccgtctcctc a                351
  
```

<210> SEQ ID NO 550
 <211> LENGTH: 117
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 550

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

<210> SEQ ID NO 551
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 551

-continued

```

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc      60
ctctcctgca gggccagtca gagtgttagc agcaatttag cctggtaacca gcagaaacct      120
ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagcc      180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct      240
gaagattttg cagtttatta ctgtcagcag tataataatt ggctccatt cactttcggc      300
cctgggacca aagtggatat caaa                                         324

```

```

<210> SEQ ID NO 552
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 552

```

```

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

```

```

<210> SEQ ID NO 553
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 553

```

```

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc      60
tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca      120
acaggaaaaa gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca      180
ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaaactc cttctatctt      240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata      300
agaacaccct atgattattg gggccaggga gcccggtca cgtctcctc a                351

```

```

<210> SEQ ID NO 554
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 554

```

```

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

```

-continued

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

<210> SEQ ID NO 555
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 555

ggattcaccc taagtagcta cgac

24

<210> SEQ ID NO 556
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 556

Gly Phe Thr Leu Ser Ser Tyr Asp
 1 5

<210> SEQ ID NO 557
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 557

attggcagta ctggtgacac a

21

<210> SEQ ID NO 558
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 558

Ile Gly Ser Thr Gly Asp Thr
 1 5

<210> SEQ ID NO 559
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 559

gcaagagagg gaataagaac accctatgat tat

33

-continued

<210> SEQ ID NO 560
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 560

Ala Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr
 1 5 10

<210> SEQ ID NO 561
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 561

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgttagc agcaatgtag cctggtagca gcagaaacct 120
 ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagcc 180
 aggttcagtg gcagtgggctc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240
 gaagattttg cagtttatta ctgtcagcag tataataatt ggctccatt cactttcggc 300
 cctgggacca aagtgatat caaa 324

<210> SEQ ID NO 562
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 562

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

<210> SEQ ID NO 563
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 563

cagagtgtta gcagcaat

-continued

<210> SEQ ID NO 564
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 564

Gln Ser Val Ser Ser Asn
 1 5

<210> SEQ ID NO 565
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 565

ggtgcatcc

9

<210> SEQ ID NO 566
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 566

Gly Ala Ser
 1

<210> SEQ ID NO 567
 <211> LENGTH: 30
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 567

cagcagtata ataattggcc tccattcact

30

<210> SEQ ID NO 568
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 568

Gln Gln Tyr Asn Asn Trp Pro Pro Phe Thr
 1 5 10

<210> SEQ ID NO 569
 <211> LENGTH: 351
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 569

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60

tctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca 120

acaggaaaaa gtctggagtg ggtctcagct attggcagta ctggtgacac atactatata 180

ggctccgtga tgggcccatt caccatctcc agagacgctg ccaaaaactc cttctatctt 240

-continued

```

gaaatgaaca gcttgagagt cggggacacg gctgtatatt actgtgcaag agaggggaata 300
agaacaccct atgattattg gggccaggga accctggtca cgtctcctc a 351

```

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<210> SEQ ID NO 570
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 570

```

```

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

```

```

<210> SEQ ID NO 571
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 571

```

```

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60
ctctcctgca gggccagtc gagtgtagc agcaatgtag cctgggtacca gcagaaacct 120
ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagcc 180
agggtcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc 300
cctgggacca aagtgatat caaa 324

```

```

<210> SEQ ID NO 572
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 572

```

```

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 Gln Ser Val Ser Ser Asn
      20             25            30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
      35             40            45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly

```

-continued

50	55	60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser		
65	70	75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro		
	85	90 95
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys		
	100	105

<210> SEQ ID NO 573
 <211> LENGTH: 351
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 573

gaggtgcagc tgggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc	60
tctgtgtcag cctctggatt caccctaagt agctacgaca tgcactgggt cgcceaagct	120
acaggaaaaa gtctggagtg ggtctcagct attggcagta ctggtgacac atactatcca	180
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt	240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agaggaata	300
agaacaccct atgattattg gggccaagga accctgggtca cgtctcctc a	351

<210> SEQ ID NO 574
 <211> LENGTH: 117
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 574

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

<210> SEQ ID NO 575
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 575

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc	60
ctctcctgca gggccagtca gactgttagc agcaatttag cctggtacca gcagaaacct	120

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```

ggccaggctc ccaggctcct catctatggt gcattccacca gggccactgg tatccagacc 180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatacagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataatt ggctccatt cactttcggc 300
cctgggacca aagtggatat caaa 324

```

```

<210> SEQ ID NO 576
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 576

```

```

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

```

```

<210> SEQ ID NO 577
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 577

```

```

gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccagggaag g cctggagtg ggtctcaggt attaattgga acagtggtag cataggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagca ctccctgtat 240
ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgt aaaagagggtg 300
actacgggat actactacgg tatggacgtc tggggccaag ggaccacggt caccgtctcc 360
tca 363

```

```

<210> SEQ ID NO 578
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 578

```

```

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

```

-continued

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Asn 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 His Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95

Val Lys Glu Val Thr Thr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly
 100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 579
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 579

ggattcacct ttgatgatta tgcc

24

<210> SEQ ID NO 580
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 580

Gly Phe Thr Phe Asp Asp Tyr Ala
 1 5

<210> SEQ ID NO 581
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 581

attaattgga acagtggtag cata

24

<210> SEQ ID NO 582
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 582

Ile Asn Trp Asn Ser Gly Ser Ile
 1 5

<210> SEQ ID NO 583
 <211> LENGTH: 42
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 583

gtaaaagagg tgactacggg atactactac ggtatggacg tc

42

-continued

<210> SEQ ID NO 584
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 584

Val Lys Glu Val Thr Thr Gly Tyr Tyr Tyr Gly Met Asp Val
 1 5 10

<210> SEQ ID NO 585
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 585

gacatccagt tgaccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcatttgcgt gggccagtc gggcattagc agttatttag cctgggtatca gaaaaaacca 120
 gggaaagccc ctaacctcct gatctatgat gcattccactt tgcaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagaa ttcactctca cactcagcag cctgcagcct 240
 gaagattttg caacttatta ctgtcaacag cttaatatatt acccattcac ttctggccct 300
 gggaccaaag tggatatcaa a 321

<210> SEQ ID NO 586
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 586

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

<210> SEQ ID NO 587
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 587

cagggcatta gcagttat

18

<210> SEQ ID NO 588

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<211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 588

Gln Gly Ile Ser Ser Tyr
 1 5

<210> SEQ ID NO 589
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 589

gatgcatcc

9

<210> SEQ ID NO 590
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 590

Asp Ala Ser
 1

<210> SEQ ID NO 591
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 591

caacagctta atatttacctt attcact

27

<210> SEQ ID NO 592
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 592

Gln Gln Leu Asn Ile Tyr Pro Phe Thr
 1 5

<210> SEQ ID NO 593
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 593

gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
 tcctgtgcag cctctggatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
 ccagggaagg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat 180
 gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagca ctccctgtat 240
 ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgt aaaagaggtg 300

-continued

actacgggat actactacgg tatggacgtc tggggccaag ggaccacggt caccgtctcc 360

tca 363

<210> SEQ ID NO 594
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 594

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 Asn 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 His Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95
 Val Lys Glu Val Thr Thr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly
 100 105 110
 Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 595
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 595

gacatccagt tgaccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgct gggccagtca gggcattagc agttatttag cctggatatca gaaaaaacca 120
 gggaaagccc ctaacctcct gatctatgat gcattccactt tgcaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tgggacagaa ttcactctca cactcagcag cctgcagcct 240
 gaagattttg caacttatta ctgtcaacag cttaatatatt acccattcac ttctggccct 300
 gggaccaaaag tggatatcaa a 321

<210> SEQ ID NO 596
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 596

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

-continued

Tyr Asp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Leu Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ile Tyr Pro Phe
 85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
 100 105

<210> SEQ ID NO 597
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 597

```

gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc      60
tcctgtgcag cctctggatt cacctttgat gattatgccca tgcactgggt ccggcaagct      120
ccaggaaggg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat      180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat      240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgt aaaagagggtg      300
actacgggat actactacgg tatggacgtc tgggggcaag ggaccacggt caccgtctcc      360
tca                                                                    363
  
```

<210> SEQ ID NO 598
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 598

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 Asn 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 Lys Glu Val Thr Thr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly
 100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 599
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 599

-continued

```

gacatccagt tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggccagtc gggcattagc agttatttag cctgggtatca gcaaaaacca 120
gggaaagccc ctaagctcct gatctatgat gcattccactt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtcaacag cttaatatatt acccattcac tttcggecct 300
gggaccaaag tggatatcaa a 321

```

```

<210> SEQ ID NO 600
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 600

```

```

Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe 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 Tyr
          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 Thr Leu Gln Ser 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
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ile Tyr Pro Phe
          85             90             95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
          100             105

```

```

<210> SEQ ID NO 601
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 601

```

```

gaggtgcagt tggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctggatt cacgttttagt agctatgcc a tgaactgggt ccgccaggct 120
ccaggaaggg ggctggattg ggtctcaggt atcagtggta atggtggtag cacctactac 180
gcagactccg tgaagggccg gttcaccatc tccagagaca tttccaagaa cacgctgtat 240
gtgcaaatgc acagcctgag agtcgaggac acggccggtt actactgtgc gaaagcccgt 300
tattacgatt ttgggggggg gaatttcgat ctctggggcc gtggcaccca ggtcactgtc 360
tcctca 366

```

```

<210> SEQ ID NO 602
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 602

```

```

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1             5             10             15

```

-continued

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp Val
 35 40 45

Ser Gly Ile Ser Gly Asn Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Ile Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Val Gln Met His Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Lys Ala Arg Tyr Tyr Asp Phe Trp Gly Gly Asn Phe Asp Leu Trp
 100 105 110

Gly Arg Gly Thr Gln Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 603
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 603

ggattcacgt ttagtagcta tgcc

24

<210> SEQ ID NO 604
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 604

Gly Phe Thr Phe Ser Ser Tyr Ala
 1 5

<210> SEQ ID NO 605
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 605

atcagtggtg atggtggtag cacc

24

<210> SEQ ID NO 606
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 606

Ile Ser Gly Asn Gly Gly Ser Thr
 1 5

<210> SEQ ID NO 607
 <211> LENGTH: 45
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 607

-continued

gcgaaagccc gttattacga tttttggggg gggaatttcg atctc

45

<210> SEQ ID NO 608
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 608

Ala Lys Ala Arg Tyr Tyr Asp Phe Trp Gly Gly Asn Phe Asp Leu
 1 5 10 15

<210> SEQ ID NO 609
 <211> LENGTH: 324
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 609

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgtagc atcaggtact tagcctggta tcagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtgtcagtggt gtctgggaca gacttcactc tcaccatcac tagactggag 240
 cctgaagatt ttgcagtcta ttactgtcag caatatggta gttcaccgct cactttcggc 300
 ggagggacca aggtggagat caaa 324

<210> SEQ ID NO 610
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 610

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 Ser Val Ser Ile Arg
 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 Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Val Ser Val Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 611
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 611

cagagtgtta gcatcaggta c

21

-continued

<210> SEQ ID NO 612
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 612

Gln Ser Val Ser Ile Arg Tyr
1 5

<210> SEQ ID NO 613
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 613

ggtgcatcc

9

<210> SEQ ID NO 614
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 614

Gly Ala Ser
1

<210> SEQ ID NO 615
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 615

cagcaatatg gtagttcacc gctcact

27

<210> SEQ ID NO 616
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 616

Gln Gln Tyr Gly Ser Ser Pro Leu Thr
1 5

<210> SEQ ID NO 617
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 617

gaggtgcagt tgttgagtc tgggggagggc ttggtacagc ctgggggggc cctgagactc 60

tcctgtgcag cctctggatt cacgtttagt agctatgcc a tgaactgggt ccgccaggct 120

ccaggaagg ggctggattg ggtctcaggt atcagtggt a atggtggtag cacctactac 180

-continued

```
gcagactccg tgaagggccg gttcaccatc tccagagaca tttccaagaa cacgctgtat 240
gtgcaaatgc acagcctgag agtcgaggac acggccgttt actactgtgc gaaagcccgt 300
tattacgatt tttggggggg gaatttcgat ctctggggcc gtggcaccct ggctactgtc 360
tcctca 366
```

```
<210> SEQ ID NO 618
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

```
<400> SEQUENCE: 618
```

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

```
<210> SEQ ID NO 619
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

```
<400> SEQUENCE: 619
```

```
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgtagc atcagggtact tagcctggta tcagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
gacaggttca gtgtcagtgt gtctgggaca gacttcactc tcaccatcac tagactggag 240
cctgaagatt ttgcagtcta ttactgtcag caatatggta gttcacgct cactttcggc 300
ggagggacca aggtggagat caaa 324
```

```
<210> SEQ ID NO 620
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

```
<400> SEQUENCE: 620
```

```
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 Ser Val Ser Ile Arg
          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	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
	50					55					60				
Val	Ser	Val	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Thr	Arg	Leu	Glu
65					70					75					80
Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Gly	Ser	Ser	Pro
			85						90					95	
Leu	Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys					
		100					105								

```
<210> SEQ ID NO 621
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

<400> SEQUENCE: 621

gaggtgcagc	tgttggagtc	tgggggaggc	ttggtacagc	ctggggggtc	cctgagactc	60
tctctgtcag	cctctggatt	cacgtttagt	agctatgcc	tgagctgggt	ccgccaggct	120
ccagggaagg	ggctggagtg	ggctctcagct	atcagtggt	atggtggtag	cacctactac	180
gcagactccg	tgaagggccg	gttcaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggccgat	attactgtgc	gaaagcccg	300
tattacgatt	tttggggggg	gaatttcgat	ctctgggggc	gtggcaccct	ggtcactgtc	360
tcctca						360

```
<210> SEQ ID NO 622
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

<400> SEQUENCE: 622

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	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35					40					45			
Ser	Ala	Ile	Ser	Gly	Asn	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	Lys	Ala	Arg	Tyr	Tyr	Asp	Phe	Trp	Gly	Gly	Asn	Phe	Asp	Leu	Trp
			100					105					110		
Gly	Arg	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser						
		115					120								

```
<210> SEQ ID NO 623
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
```

-continued

<400> SEQUENCE: 623

```

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcctgca gggccagtca gagtgttagc atcaggtact tagcctggta ccagcagaaa      120
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca      180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag      240
cctgaagatt ttgcagtgtg ttactgtcag caatatggta gttcacgct cactttcggc      300
ggagggacca aggtggagat caaa                                           324

```

<210> SEQ ID NO 624

<211> LENGTH: 108

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 624

```

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 Ser Val Ser Ile Arg
 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 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 Ser Pro
 85            90            95
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100            105

```

<210> SEQ ID NO 625

<211> LENGTH: 381

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 625

```

cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc      60
tcctgcaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc      120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaaacgat      180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt      300
ttagtagtac cacctgccct ttattattcc tactacgtta tggacgtctg gggccaaggg      360
accacggtea ccgtctctc a                                           381

```

<210> SEQ ID NO 626

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 626

-continued

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

<210> SEQ ID NO 627
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 627

ggttacacct ttaccaccta tggt

24

<210> SEQ ID NO 628
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 628

Gly Tyr Thr Phe Thr Thr Tyr Gly
 1 5

<210> SEQ ID NO 629
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 629

atcagcgggtt acaatggtaa aaca

24

<210> SEQ ID NO 630
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 630

Ile Ser Gly Tyr Asn Gly Lys Thr
 1 5

<210> SEQ ID NO 631
 <211> LENGTH: 60
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

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<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 631

tcgagagatc gtttagtagt accacctgcc ctttattatt cctactacgt tatggacgtc 60

<210> SEQ ID NO 632

<211> LENGTH: 20

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 632

Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Ser Tyr Tyr
1 5 10 15Val Met Asp Val
20

<210> SEQ ID NO 633

<211> LENGTH: 336

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 633

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60

atctcctgca ggtctagtc aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120

tttcagcaga ggccaggatc atctccaagg cgcctaattt ataaggtttc taaccgggac 180

tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240

agcaggggtg aggctgagga tgttggggtt tattactgca tgcaaggtag acactggccg 300

tacacttttg gccaggggac caagctggag atcaaa 336

<210> SEQ ID NO 634

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 634

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

<210> SEQ ID NO 635

<211> LENGTH: 33

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 635

caaagcctcg tatacagtga tggaaacacc tac

33

<210> SEQ ID NO 636
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 636

Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr
1 5 10

<210> SEQ ID NO 637
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 637

aaggtttct

9

<210> SEQ ID NO 638
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 638

Lys Val Ser
1

<210> SEQ ID NO 639
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 639

atgcaaggta cacactggcc gtacact

27

<210> SEQ ID NO 640
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 640

Met Gln Gly Thr His Trp Pro Tyr Thr
1 5

<210> SEQ ID NO 641
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 641

-continued

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cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc      60
tcttgcaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc      120
cctggacaag ggcttgagtg gatgggatgg atcagcgggtt acaatggtaa aacaaacgat      180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt      300
ttagtagtac cacctgccct ttattattcc tactacgtta tggacgtctg gggccaaggg      360
accacgggtca ccgtctcctc a                                          381

```

```

<210> SEQ ID NO 642
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 642

```

```

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

```

```

<210> SEQ ID NO 643
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 643

```

```

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc      60
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg      120
tttcagcaga ggccagggtca atctccaagg cgcctaattt ataaggtttc taaccgggac      180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc      240
agcaggggtg aggctgagga tgttggggtt tattactgca tgcaaggtag acactggccg      300
tacacttttg gccaggggac caagctggag atcaaa                                336

```

```

<210> SEQ ID NO 644
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 644

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-continued

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	Arg	Ser	Ser	Gln	Ser	Leu	Val	Tyr	Ser
			20					25					30		
Asp	Gly	Asn	Thr	Tyr	Leu	Asn	Trp	Phe	Gln	Gln	Arg	Pro	Gly	Gln	Ser
		35					40					45			
Pro	Arg	Arg	Leu	Ile	Tyr	Lys	Val	Ser	Asn	Arg	Asp	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	Gly
				85				90						95	
Thr	His	Trp	Pro	Tyr	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105					110		

<210> SEQ ID NO 645

<211> LENGTH: 381

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 645

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc	60
tcctgcaagg cttctgggta cacctttacc acctatggta tcagctgggt gcgacaggcc	120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat	180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac	240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt	300
ttagtagtac cacctgccect ttattattcc tactacgtta tggacgtctg ggggcaaggg	360
accacggtca ccgtctcctc a	381

<210> SEQ ID NO 646

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 646

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

-continued

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<210> SEQ ID NO 647
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 647

gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc      60
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg      120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac      180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc      240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtag acactggccg      300
tacacttttg gccaggggac caagctggag atcaaa                                336

```

```

<210> SEQ ID NO 648
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 648

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
          20            25            30

Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
          35            40            45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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 Gly
          85            90            95

Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100          105           110

```

```

<210> SEQ ID NO 649
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 649

cagggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc      60
tcctgcaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc      120
cctggacaag ggcttgatg gatgggatgg atcagcggtt acaatggtaa aacaaacgat      180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt      300
ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg gggccaaggg      360
accacgggtca ccgtctctc a                                381

```

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<210> SEQ ID NO 650
<211> LENGTH: 127
<212> TYPE: PRT

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-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 650

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

<210> SEQ ID NO 651
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 651

ggttacacct ttaccaccta tggt

24

<210> SEQ ID NO 652
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 652

Gly Tyr Thr Phe Thr Thr Tyr Gly
 1 5

<210> SEQ ID NO 653
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 653

atcagcgggtt acaatggtaa aaca

24

<210> SEQ ID NO 654
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 654

Ile Ser Gly Tyr Asn Gly Lys Thr
 1 5

-continued

<210> SEQ ID NO 655
 <211> LENGTH: 60
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 655

tcgagagatc gtttagtagt accacctgcc cttaattatt actactacgt tatggacgtc 60

<210> SEQ ID NO 656
 <211> LENGTH: 20
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 656

Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Tyr Tyr Tyr
 1 5 10 15

Val Met Asp Val
 20

<210> SEQ ID NO 657
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 657

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60
 atctcctgca ggtctagtc aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120
 ttccagcaga ggccaggatca atctccaagg cgcctaattt ataaggtttc taaccgggac 180
 tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240
 agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaagggtac aactggccg 300
 tacacttttg gccagggggac caagctggag atcaaa 336

<210> SEQ ID NO 658
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 658

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
 20 25 30

Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
 35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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 Gly
 85 90 95

Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

-continued

<210> SEQ ID NO 659
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 659

caaagcctcg tatacagtga tggaaacacc tac

33

<210> SEQ ID NO 660
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 660

Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr
1 5 10

<210> SEQ ID NO 661
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 661

aaggtttct

9

<210> SEQ ID NO 662
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 662

Lys Val Ser
1

<210> SEQ ID NO 663
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 663

atgcaaggta cacactggcc gtacact

27

<210> SEQ ID NO 664
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 664

Met Gln Gly Thr His Trp Pro Tyr Thr
1 5

<210> SEQ ID NO 665
<211> LENGTH: 381
<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 665

```
cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc      60
tctcgcaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc      120
cctggacaag ggcttgatgt gatgggatgg atcagcgggtt acaatggtaa aacaaacgat      180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt      300
ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg gggccaaggg      360
accacgggtca ccgctccttc a                                     381
```

<210> SEQ ID NO 666
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 666

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

<210> SEQ ID NO 667
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 667

```
gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc      60
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg      120
tttcagcaga ggccagggtca atctccaagg cgcctaattt ataaggtttc taaccggggac      180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc      240
agcaggggtg aggctgagga tgttgggggt tattactgca tgcaagggtac acactggccg      300
tacacttttg gccagggggac caagctggag atcaaa                                     336
```

<210> SEQ ID NO 668
 <211> LENGTH: 112
 <212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 668

```

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
          20             25             30
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
          35             40             45
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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 Gly
          85             90             95
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
          100            105            110

```

<210> SEQ ID NO 669
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 669

```

cagggttcagc tgggtcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc      60
tcctgcaagg cttctgggta cacctttacc acctatggta tcagctgggt gcgacaggcc      120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat      180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt      300
ttagtagtac cacctgcctt taattattac tactacgtta tggacgtctg ggggcaaggg      360
accacggtca ccgtctcctc a                                     381

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<210> SEQ ID NO 670
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 670

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

```

-continued

100	105	110	
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser			
115	120	125	

<210> SEQ ID NO 671
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 671

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc	60
atctctctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg	120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac	180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc	240
agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaagggtac acactggccg	300
tacacttttg gccagggggac caagctggag atcaaa	336

<210> SEQ ID NO 672
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 672

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser	
20 25 30	
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser	
35 40 45	
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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 Gly	
85 90 95	
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys	
100 105 110	

<210> SEQ ID NO 673
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

 <400> SEQUENCE: 673

cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc	60
tcctgcaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc	120
cctggacaag ggcttgatg gatgggatgg atcagcggtt acaatggtaa aacaaacgat	180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac	240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt	300
ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg gggccaaggg	360

-continued

accacggtca ccgtctcctc a

381

<210> SEQ ID NO 674
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 674

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
50 55 60

Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr
100 105 110

Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 675
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 675

ggttacacct ttaccaccta tggt

24

<210> SEQ ID NO 676
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 676

Gly Tyr Thr Phe Thr Thr Tyr Gly
1 5

<210> SEQ ID NO 677
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 677

atcagcggtt acaatggtaa aaca

24

<210> SEQ ID NO 678
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 678

Ile Ser Gly Tyr Asn Gly Lys Thr
1 5

<210> SEQ ID NO 679

<211> LENGTH: 60

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 679

tcgagagatc gtttagtagt accacctgcc ctttattatt actactacgt tatggacgtc 60

<210> SEQ ID NO 680

<211> LENGTH: 20

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 680

Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr
1 5 10 15

Val Met Asp Val
20

<210> SEQ ID NO 681

<211> LENGTH: 336

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 681

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60

atctcctgca ggtctagtc aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120

tttcagcaga ggccaggatca atctccaagg cgcctaattt ataagggttc taaccgggac 180

tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240

agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaaggtag acactggccg 300

tacacttttg gccaggggac caagctggag atcaaa 336

<210> SEQ ID NO 682

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 682

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
20 25 30

Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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

-continued

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
 85 90 95

Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> SEQ ID NO 683
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 683

caaagcctcg tatacagtga tggaaacacc tac

33

<210> SEQ ID NO 684
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 684

Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr
 1 5 10

<210> SEQ ID NO 685
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 685

aagggtttct

9

<210> SEQ ID NO 686
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 686

Lys Val Ser
 1

<210> SEQ ID NO 687
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 687

atgcaaggta cacactggcc gtacact

27

<210> SEQ ID NO 688
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 688

Met Gln Gly Thr His Trp Pro Tyr Thr

-continued

1 5

<210> SEQ ID NO 689
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 689

cagggttcagc tgggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc 60
 tcttgcaagg cttctgggta cacctttacc acctatggta tcagttgggt acgacaggcc 120
 cctggacaag ggcttgatgt gatgggatgg atcagcgggtt acaatggtaa aacaaacgat 180
 gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac 240
 atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt 300
 ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg gggccaaggg 360
 accacgggtca ccgctctcctc a 381

<210> SEQ ID NO 690
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 690

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

<210> SEQ ID NO 691
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 691

gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttgagaca gccggcctcc 60
 atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120
 ttccagcaga ggccagggtca atctccaagg cgcctaattt ataaggtttc taaccgggac 180
 tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240
 agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaaggtac acactggccg 300

-continued

tacacttttg gccaggggac caagctggag atcaaa

336

<210> SEQ ID NO 692
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 692

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 Arg Ser Ser Gln Ser Leu Val Tyr Ser
 20 25 30

Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
 35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp 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 Gly
 85 90 95

Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> SEQ ID NO 693
 <211> LENGTH: 381
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 693

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctgggta cacctttacc acctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgggtt acaatggtaa aacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt 300

ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg ggggcaaggg 360

accacggtca ccgtctcctc a 381

<210> SEQ ID NO 694
 <211> LENGTH: 127
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 694

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 Thr Tyr
 20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Tyr Ala Gln Lys Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr

-continued

65	70	75	80	
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys				
	85	90	95	
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr				
	100	105	110	
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser				
	115	120	125	

<210> SEQ ID NO 695
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 695

gatgttgatga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc	60
atctctctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg	120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac	180
tctgggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc	240
agcaggggtgg aggctgagga tgttgggggtt tattactgca tgcaagggtac acactggccg	300
tacacttttg gccaggggac caagctggag atcaaa	336

<210> SEQ ID NO 696
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 696

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly	
1	15
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser	
20	30
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser	
35	45
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro	
50	60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile	
65	80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly	
85	95
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys	
100	110

<210> SEQ ID NO 697
 <211> LENGTH: 384
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 697

caggtgcacc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc	60
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct	120
ccaggaaggg ggctggagtg gatttcatat attagtaatg atggtggtac caaatactat	180

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gtggactctg tggaggggccg attcatcatt tccagggaca acgccaagaa ctcatgtat 240
ctacatatga acagcctcag agccgacgac acggccgtgt attactgtgc gagagatcag 300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa 360
gggaccacgg tcaccgtcgc ctca 384

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<210> SEQ ID NO 698
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 698

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

```

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<210> SEQ ID NO 699
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 699

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ggattcacct tcagtgacca ctac 24

```

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<210> SEQ ID NO 700
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 700

```

```

Gly Phe Thr Phe Ser Asp His Tyr
 1             5

```

```

<210> SEQ ID NO 701
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 701

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```

attagtaatg atggtgtac caaa 24

```

-continued

<210> SEQ ID NO 702
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 702

Ile Ser Asn Asp Gly Gly Thr Lys
 1 5

<210> SEQ ID NO 703
 <211> LENGTH: 63
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 703

gcgagagatc agggatatat tggctacgac tcgtattatt actattccta cggtatggac 60
 gtc 63

<210> SEQ ID NO 704
 <211> LENGTH: 21
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 704

Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser
 1 5 10 15

Tyr Gly Met Asp Val
 20

<210> SEQ ID NO 705
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 705

aaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc 60
 ctctcctgta gggccagtca gagtgtaac aacaaattct tagcctggta ccagcagaaa 120
 tctggccagg ctcccaggct cctcatctat ggtgcaccca gcagggccac tggcatccca 180
 gacaggttca gtggcagtggt gtctgggacc gacttcactc tcaccatcag cggactggag 240
 cctgaagatt ttgaagtgtta ttattgtcaa gtatatggta actcactcac tttcggcgga 300
 gggaccaagg tggagatcaa g 321

<210> SEQ ID NO 706
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 706

Lys Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Pro Leu Phe Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
 20 25 30

-continued

Phe Leu Ala Trp Tyr Gln Gln Lys Ser Gly Gln Ala Pro Arg Leu Leu
 35 40 45

Ile Tyr Gly 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 Gly Leu Glu
 65 70 75 80

Pro Glu Asp Phe Glu Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 707
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 707

cagagtgtta acaacaaatt c

21

<210> SEQ ID NO 708
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 708

Gln Ser Val Asn Asn Lys Phe
 1 5

<210> SEQ ID NO 709
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 709

ggtgcatcc

9

<210> SEQ ID NO 710
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 710

Gly Ala Ser
 1

<210> SEQ ID NO 711
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 711

caagtatatg gtaactcact cact

24

<210> SEQ ID NO 712
 <211> LENGTH: 8

-continued

<212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 712

Gln Val Tyr Gly Asn Ser Leu Thr
 1 5

<210> SEQ ID NO 713
 <211> LENGTH: 384
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 713

cagggtgcagc tgggtggagtc tgggggaggc ttggtcaagc ctggaggggc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct 120
 ccaggggaagg ggctggagtg gatttcatac attagtaatg atggtgggtac caaatactat 180
 gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcatgtat 240
 ctacatatga acagcctcag agccgacgac acggccgtgt attactgtgc gagagatcag 300
 ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa 360
 gggaccacgg tcaccgtctc ctca 384

<210> SEQ ID NO 714
 <211> LENGTH: 128
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 714

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

<210> SEQ ID NO 715
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 715

gaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc 60

-continued

```

ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa 120
tctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag 240
cctgaagatt ttgaagtgtta ttattgtcaa gtatatggta actcactcac ttctggcgga 300
gggaccaagg tggagatcaa a 321

```

```

<210> SEQ ID NO 716
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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```

<400> SEQUENCE: 716

```

```

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

```

```

<210> SEQ ID NO 717
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 717

```

```

cagggtgcagc tgggtggagtc tggggggaggc ttggtcaagc ctggagggtc cctgagactc 60
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct 120
ccaggggaagg ggctggagtg ggtttcatac attagtaatg atggtggtac caaatactac 180
gcagactctg tgaagggccg attcaccatc tccagggaca acgccaagaa ctactgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatcag 300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctgggggcaa 360
gggaccacgg tcaccgtctc ctca 384

```

```

<210> SEQ ID NO 718
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

```

```

<400> SEQUENCE: 718

```

```

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

```

-continued

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Tyr Ile Ser Asn Asp Gly Gly Thr Lys 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser
 100 105 110

Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120 125

<210> SEQ ID NO 719

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 719

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtg ttactgtcaa gtatatggta actcactcac ttctggcgga 300
 gggaccaagg tggagatcaa a 321

<210> SEQ ID NO 720

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 720

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 Ser Val Asn Asn Lys
 20 25 30

Phe 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 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 Val Tyr Gly Asn Ser Leu
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 721

<211> LENGTH: 378

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 721

```

caaatctgc tggatgaatc tggacctgag gtgaaggagc ctggggcctc agtgaaggtc    60
tcttgaagg cttctgggta cacctttacc aactacgcta tcagctgggt gcgacaggtc    120
cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatgggtc cacaaactat    180
gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac    240
atggagctga ggagcctgag atctgacgac acggccatgt attactgtgc gagagggggg    300
gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg ccaagggacc    360
acggtcaccg tctcctca                                     378

```

<210> SEQ ID NO 722

<211> LENGTH: 126

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 722

```

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

```

<210> SEQ ID NO 723

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 723

```

ggttacacct ttaccaacta cgct                                     24

```

<210> SEQ ID NO 724

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 724

```

Gly Tyr Thr Phe Thr Asn Tyr Ala
 1             5

```

<210> SEQ ID NO 725

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 725

gtcagcgctt acaatggtca caca 24

<210> SEQ ID NO 726
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 726

Val Ser Ala Tyr Asn Gly His Thr
1 5

<210> SEQ ID NO 727
<211> LENGTH: 57
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 727

gcgagagggg gtgtagtcgt gccagttgct cccacttct acaacggtat ggacgtc 57

<210> SEQ ID NO 728
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 728

Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
1 5 10 15

Met Asp Val

<210> SEQ ID NO 729
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 729

gatattgtga tgactcagtt tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctctcgca ggtctagtca gagcctctcg catattaatg aatacaacta tttggattgg 120
tacctaaaga agccagggca gtctccacag ctctgatctc atttgggttt taatcggggc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaaactccg 300
tggacgttcg gccaaaggac caagtgga atcaaa 336

<210> SEQ ID NO 730
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 730

Asp Ile Val Met Thr Gln Phe Pro Leu Ser Leu Pro Val Thr Pro Gly

-continued

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

<210> SEQ ID NO 731
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 731

cagagcctcc tgcataataa tgaatacaac tat

33

<210> SEQ ID NO 732
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 732

Gln Ser Leu Leu His Ile Asn Glu Tyr Asn Tyr
1 5 10

<210> SEQ ID NO 733
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 733

ttgggtttt

9

<210> SEQ ID NO 734
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 734

Leu Gly Phe
1

<210> SEQ ID NO 735
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 735

-continued

atgcaagctc ttcaaactcc gtggacg

27

<210> SEQ ID NO 736
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 736

Met Gln Ala Leu Gln Thr Pro Trp Thr
 1 5

<210> SEQ ID NO 737
 <211> LENGTH: 378
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 737

cagggttcagc tgggtgcagtc tggacctgag gtgaaggagc ctggggcctc agtgaaggtc 60
 tcctgcaagg cttctgggta cacctttacc aactacgcta tcagctgggt gcgacaggtc 120
 cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatgggtca caaaaactat 180
 gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac 240
 atggagctga ggagcctgag atctgacgac acggccatgt attactgtgc gagagggggg 300
 gtagtcgtgc cagttgctcc ccactttctac aacggtatgg acgtctgggg ccaagggacc 360
 acggtcaccg tctcctca 378

<210> SEQ ID NO 738
 <211> LENGTH: 126
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 738

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

<210> SEQ ID NO 739
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

-continued

<400> SEQUENCE: 739

```

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc      60
atctcctgca ggtctagtc gagcctcctg catattaatg aatacaacta tttggattgg      120
tacctaaaga agccagggca gtctccacag ctctgatct atttgggttt taatcggggc      180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc      240
agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaaactccg      300
tggacgttcg gccaaaggac caaggtggaa atcaaa                                336

```

<210> SEQ ID NO 740

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 740

```

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 Ile
          20             25             30
Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser
          35             40             45
Pro Gln Leu Leu Ile Tyr Leu Gly Phe 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 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100            105            110

```

<210> SEQ ID NO 741

<211> LENGTH: 378

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 741

```

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc      60
tcctgcaagg cttctgggta cacctttacc aactacgcta tcagctgggt gcgacaggcc      120
cctggacaag ggcttgatg gatgggatgg gtcagcgctt acaatgggtca cacaaactat      180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac      240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaggggggt      300
gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg gcaagggacc      360
acggtcaccg tctcctca                                378

```

<210> SEQ ID NO 742

<211> LENGTH: 126

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 742

-continued

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

<210> SEQ ID NO 743
 <211> LENGTH: 336
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 743

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
 atctctctgca ggtctagtca gagcctctcg catattaatg aatacaacta tttggattgg 120
 tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcggggc 180
 tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
 agcagagtgg aggctgagga tgttgggggt tattactgca tgcaagctct tcaaactccg 300
 tggacgttcg gccaaaggac caaggtggaa atcaaa 336

<210> SEQ ID NO 744
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 744

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 Ile
 20 25 30
 Asn Glu 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 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 745
 <211> LENGTH: 8

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)...(8)
<223> OTHER INFORMATION: Xaa = Any amino acid

<400> SEQUENCE: 745

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> SEQ ID NO 746
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)...(8)
<223> OTHER INFORMATION: Xaa - Any amino acid

<400> SEQUENCE: 746

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> SEQ ID NO 747
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)...(20)
<223> OTHER INFORMATION: Xaa = Any amino acid

<400> SEQUENCE: 747

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa
20

<210> SEQ ID NO 748
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)...(12)
<223> OTHER INFORMATION: Xaa = Any amino acid

<400> SEQUENCE: 748

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

<210> SEQ ID NO 749
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Xaa = Any amino acid

-continued

<400> SEQUENCE: 749

Xaa Xaa Xaa
1

<210> SEQ ID NO 750
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic
 <220> FEATURE:
 <221> NAME/KEY: VARIANT
 <222> LOCATION: (1)...(9)
 <223> OTHER INFORMATION: Xaa = Any amino acid

<400> SEQUENCE: 750

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> SEQ ID NO 751
 <211> LENGTH: 330
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 751

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

-continued

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Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
      260                      265                      270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
      275                      280                      285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
      290                      295                      300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
      305                      310                      315                      320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
      325                      330

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<210> SEQ ID NO 752
<211> LENGTH: 327
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 752

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
  1      5      10      15

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
      35      40      45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
      50      55      60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
      65      70      75      80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
      85      90      95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
      100     105     110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
      115     120     125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
      130     135     140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
      145     150     155     160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
      165     170     175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
      180     185     190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
      195     200     205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
      210     215     220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
      225     230     235     240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
      245     250     255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
      260     265     270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
      275     280     285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser

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290	295	300
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Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
 325

<210> SEQ ID NO 753
 <211> LENGTH: 327
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 753

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

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<210> SEQ ID NO 754
 <211> LENGTH: 2076
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 754

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atgggcaccg tcagctccag gcggtcctgg tggccgctgc cactgctgct gctgctgctg    60
ctgctcctgg gtcccgcggg cgcctgtgag caggaggacg aggacggcga ctacgaggag    120
ctggtgctag ccttgctgtc cgaggaggac ggctggccg aagcaccga gcacggaacc    180
acagccacct tccaccgtg cgccaaggat cgtggagggt tgctggcac ctacgtggtg    240
gtgctgaagg aggagaccca cctctgcag tcagagcgca ctgccgcgg cctgcaggcc    300
caggctgccc gccggggata cctcaccag atcctgcatg tcttccatgg ccttcttcct    360
ggcttctctg tgaagatgag tggcgacctg ctggagctgg ccttgaagtt gccccatgtc    420
gactacatcg aggaggaact ctctgtcttt gccagagca tcccgaggaa cctggagcgg    480
attaccctc caccgtaccg gccgatgaa taccagcccc ccgacggagg cagcctggtg    540
gagggtgtat tcctagacac cagcatacag agtgaccacc gggaaatcga gggcagggtc    600
atggtcaccg acttcagaaa tgtgcccag gaggacggga cccgcttcca cagacaggcc    660
agcaagtgtg acagtcatgg caccacctg gcagggggtg tcagcgccg ggatgccggc    720
gtggccaagg gtgccagcat gcgcagcctg cgcgtgctca actgccaagg gaagggcacg    780
gttagcggca ccctcatagg cctggagttt attcgaaaa gccagctggt ccagcctgtg    840
gggcacttgg tgggtgtgct gcccctggcg ggtgggtaca gccgcgtcct caacgcggcc    900
tgccagcgcc tggcgagggc tggggtcgtg ctggtcaccg ctgccggcaa ctcccgggac    960
gatgctgccc tctactcccc agcctcagct cccgaggtea tcacagttgg ggcaccaat    1020
gccagggacc agccggtgac cctggggact ttggggacca actttggcgg ctgtgtggac    1080
ctctttgccc caggggaggga catcattggt gcctccagcg actgcagcac ctgctttgtg    1140
tcacagagtg ggacatcaca ggctgctgcc cactgtgctg gcattgcagc catgatgctg    1200
tctgccgagc cggagctcac cctggccgag ttgaggcaga gactgatcca cttctctgcc    1260
aaagatgtca tcaatgaggc ctggttcctt gaggaccagc gggtaactgac ccccaacctg    1320
gtggccgccc tgccccccag caccatggg gcaggttggc agctgttttg caggactgtg    1380
tggtcagcac actcggggcc tacacggatg gccacagcca tcgcccgtg cgcgccagat    1440
gaggagctgc tgagctgctc cagtcttctc aggagtgagg agcggcgggg cgagcgcatg    1500
gaggcccaag ggggcaagct ggtctgccgg gcccaaacg cttttggggg tgagggtgtc    1560
tacgccattg ccagggtgct cctgtacccc caggccaact gcagcgtcca cacagctcca    1620
ccagctgagg ccagcatggg gaccctgtgc cactgccacc aacagggcca cgtcctcaca    1680
ggctgcagct cccactggga ggtggaggac cttggcacc acaagccgcc tgtgtgagg    1740
ccacgaggtc agcccaacca gtgctggggc cacaggagg ccagcatcca cgcttctctg    1800
tgccatgccc caggctctga atgcaaagtc aaggagcatg gaatccggc ccctcaggag    1860
caggtgaccg tggcctgcga ggagggtgg accctgactg gctgcagtgc cctccctggg    1920
acctccacg tcctgggggc ctacgccga gacaacacgt gtgtagttag gagccgggac    1980
gtcagcacta caggcagcac cagcgaagag gccgtgacag ccgttgccat ctgctgccgg    2040
agccggcacc tggcgaggc ctcccaggag ctccag    2076

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<210> SEQ ID NO 755
<211> LENGTH: 692
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 755

Met Gly Thr Val Ser Ser Arg Arg Ser Trp Trp Pro Leu Pro Leu Leu
  1          5          10          15

Leu Leu Leu Leu Leu Leu Leu Gly Pro Ala Gly Ala Arg Ala Gln Glu
  20          25          30

Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu
  35          40          45

Glu Asp Gly Leu Ala Glu Ala Pro Glu His Gly Thr Thr Ala Thr Phe
  50          55          60

His Arg Cys Ala Lys Asp Pro Trp Arg Leu Pro Gly Thr Tyr Val Val
  65          70          75          80

Val Leu Lys Glu Glu Thr His Leu Ser Gln Ser Glu Arg Thr Ala Arg
  85          90          95

Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu
  100         105         110

His Val Phe His Gly Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly
  115         120         125

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

Glu Asp Ser Ser Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg
  145         150         155         160

Ile Thr Pro Pro Arg Tyr Arg Ala Asp Glu Tyr Gln Pro Pro Asp Gly
  165         170         175

Gly Ser Leu Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Asp
  180         185         190

His Arg Glu Ile Glu Gly Arg Val Met Val Thr Asp Phe Glu Asn Val
  195         200         205

Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp
  210         215         220

Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly
  225         230         235         240

Val Ala Lys Gly Ala Ser Met Arg Ser Leu Arg Val Leu Asn Cys Gln
  245         250         255

Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg
  260         265         270

Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu Leu Pro
  275         280         285

Leu Ala Gly Gly Tyr Ser Arg Val Leu Asn Ala Ala Cys Gln Arg Leu
  290         295         300

Ala Arg Ala Gly Val Val Leu Val Thr Ala Ala Gly Asn Phe Arg Asp
  305         310         315         320

Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val
  325         330         335

Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly
  340         345         350

Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu Asp Ile
  355         360         365

Ile Gly Ala Ser Ser Asp Cys Ser Thr Cys Phe Val Ser Gln Ser Gly
  370         375         380

Thr Ser Gln Ala Ala Ala His Val Ala Gly Ile Ala Ala Met Met Leu

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385	390	395	400
Ser Ala Glu Pro	Glu Leu Thr Leu Ala	Glu Leu Arg Gln Arg	Leu Ile
	405	410	415
His Phe Ser	Ala Lys Asp Val Ile	Asn Glu Ala Trp Phe	Pro Glu Asp
	420	425	430
Gln Arg Val	Leu Thr Pro Asn Leu Val	Ala Ala Leu Pro	Pro Ser Thr
	435	440	445
His Gly Ala	Gly Trp Gln Leu Phe Cys	Arg Thr Val Trp	Ser Ala His
	450	455	460
Ser Gly Pro	Thr Arg Met Ala Thr	Ala Ile Ala Arg	Cys Ala Pro Asp
465	470	475	480
Glu Glu Leu	Leu Ser Cys Ser Ser	Phe Ser Arg Ser	Gly Lys Arg Arg
	485	490	495
Gly Glu Arg	Met Glu Ala Gln Gly	Gly Lys Leu Val	Cys Arg Ala His
	500	505	510
Asn Ala Phe	Gly Gly Glu Gly Val	Tyr Ala Ile Ala	Arg Cys Cys Leu
	515	520	525
Leu Pro Gln	Ala Asn Cys Ser Val	His Thr Ala Pro	Pro Ala Glu Ala
	530	535	540
Ser Met Gly	Thr Arg Val His Cys	His Gln Gln Gly	His Val Leu Thr
545	550	555	560
Gly Cys Ser	Ser His Trp Glu Val	Glu Asp Leu Gly	Thr His Lys Pro
	565	570	575
Pro Val Leu	Arg Pro Arg Gly Gln	Pro Asn Gln Cys	Val Gly His Arg
	580	585	590
Glu Ala Ser	Ile His Ala Ser Cys	Cys His Ala Pro	Gly Leu Glu Cys
	595	600	605
Lys Val Lys	Glu His Gly Ile Pro	Ala Pro Gln Glu	Gln Val Thr Val
	610	615	620
Ala Cys Glu	Glu Gly Trp Thr Leu	Thr Gly Cys Ser	Ala Leu Pro Gly
625	630	635	640
Thr Ser His	Val Leu Gly Ala Tyr	Ala Val Asp Asn	Thr Cys Val Val
	645	650	655
Arg Ser Arg	Asp Val Ser Thr Thr	Gly Ser Thr Ser	Glu Glu Ala Val
	660	665	670
Thr Ala Val	Ala Ile Cys Cys Arg	Ser Arg His Leu	Ala Gln Ala Ser
	675	680	685
Gln Glu Leu	Gln		
	690		

<210> SEQ ID NO 756

<211> LENGTH: 692

<212> TYPE: PRT

<213> ORGANISM: Macaca mulata

<400> SEQUENCE: 756

Met Gly Thr Val	Ser Ser Arg Arg	Ser Trp Trp Pro	Leu Pro Leu Pro
1	5	10	15
Leu Leu Leu	Leu Leu Leu Gly	Pro Ala Gly Ala	Arg Ala Gln Glu
	20	25	30
Asp Glu Asp	Gly Asp Tyr Glu	Glu Leu Val Leu	Ala Leu Arg Ser Glu
	35	40	45
Glu Asp Gly	Leu Ala Asp Ala	Pro Glu His Gly	Ala Thr Ala Thr Phe
	50	55	60
His Arg Cys	Ala Lys Asp Pro	Trp Arg Leu Pro	Gly Thr Tyr Val Val

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65	70	75	80
Val Leu Lys Glu Glu Thr His Arg Ser Gln Ser Glu Arg Thr Ala Arg	85	90	95
Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu	100	105	110
His Val Phe His His Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly	115	120	125
Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val Asp Tyr Ile Glu	130	135	140
Glu Asp Ser Ser Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg	145	150	155
Ile Thr Pro Ala Arg Tyr Arg Ala Asp Gly Tyr Gln Pro Pro Lys Gly	165	170	175
Gly Ser Leu Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Asp	180	185	190
His Arg Glu Ile Glu Gly Arg Val Met Val Thr Asp Phe Glu Ser Val	195	200	205
Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp	210	215	220
Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly	225	230	235
Val Ala Lys Gly Ala Gly Leu Arg Ser Leu Arg Val Leu Asn Cys Gln	245	250	255
Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg	260	265	270
Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu Leu Pro	275	280	285
Leu Ala Gly Gly Tyr Ser Arg Val Phe Asn Ala Ala Cys Gln Arg Leu	290	295	300
Ala Arg Ala Gly Val Val Leu Val Thr Ala Ala Gly Asn Phe Arg Asp	305	310	315
Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val	325	330	335
Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly	340	345	350
Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu Asp Ile	355	360	365
Ile Gly Ala Ser Ser Asp Cys Ser Thr Cys Phe Val Ser Arg Ser Gly	370	375	380
Thr Ser Gln Ala Ala Ala His Val Ala Gly Ile Ala Ala Met Met Leu	385	390	395
Ser Ala Glu Pro Glu Leu Thr Leu Ala Glu Leu Arg Gln Arg Leu Ile	405	410	415
His Phe Ser Ala Lys Asp Val Ile Asn Glu Ala Trp Phe Pro Glu Asp	420	425	430
Gln Arg Val Leu Thr Pro Asn Leu Val Ala Ala Leu Pro Pro Ser Thr	435	440	445
His Arg Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His	450	455	460
Ser Gly Pro Thr Arg Met Ala Thr Ala Val Ala Arg Cys Ala Gln Asp	465	470	475
Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg	485	490	495

-continued

Gly Glu Arg Ile Glu Ala Gln Gly Gly Lys Arg Val Cys Arg Ala His
 500 505 510
 Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu
 515 520 525
 Leu Pro Gln Val Asn Cys Ser Val His Thr Ala Pro Pro Ala Gly Ala
 530 535 540
 Ser Met Gly Thr Arg Val His Cys His Gln Gln Gly His Val Leu Thr
 545 550 555 560
 Gly Cys Ser Ser His Trp Glu Val Glu Asp Leu Gly Thr His Lys Pro
 565 570 575
 Pro Val Leu Arg Pro Arg Gly Gln Pro Asn Gln Cys Val Gly His Arg
 580 585 590
 Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys
 595 600 605
 Lys Val Lys Glu His Gly Ile Pro Ala Pro Gln Glu Gln Val Ile Val
 610 615 620
 Ala Cys Glu Asp Gly Trp Thr Leu Thr Gly Cys Ser Pro Leu Pro Gly
 625 630 635 640
 Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val
 645 650 655
 Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Lys Glu Ala Val
 660 665 670
 Ala Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Val Gln Ala Ser
 675 680 685
 Gln Glu Leu Gln
 690

<210> SEQ ID NO 757

<211> LENGTH: 694

<212> TYPE: PRT

<213> ORGANISM: Mus muscular

<400> SEQUENCE: 757

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

Pro	Asp	Gly	Ser	Ser	Gln	Val	Glu	Val	Tyr	Leu	Leu	Asp	Thr	Ser	Ile	
			180					185				190				
Gln	Gly	Ala	His	Arg	Glu	Ile	Glu	Gly	Arg	Val	Thr	Ile	Thr	Asp	Phe	
		195					200					205				
Asn	Ser	Val	Pro	Glu	Glu	Asp	Gly	Thr	Arg	Phe	His	Arg	Gln	Ala	Ser	
		210				215					220					
Lys	Cys	Asp	Ser	His	Gly	Thr	His	Leu	Ala	Gly	Val	Val	Ser	Gly	Arg	
		225			230					235					240	
Asp	Ala	Gly	Val	Ala	Lys	Gly	Thr	Ser	Leu	His	Ser	Leu	Arg	Val	Leu	
			245						250					255		
Asn	Cys	Gln	Gly	Lys	Gly	Thr	Val	Ser	Gly	Thr	Leu	Ile	Gly	Leu	Glu	
			260					265					270			
Phe	Ile	Arg	Lys	Ser	Gln	Leu	Ile	Gln	Pro	Ser	Gly	Pro	Leu	Val	Val	
		275					280					285				
Leu	Leu	Pro	Leu	Ala	Gly	Gly	Tyr	Ser	Arg	Ile	Leu	Asn	Ala	Ala	Cys	
		290				295					300					
Arg	His	Leu	Ala	Arg	Thr	Gly	Val	Val	Leu	Val	Ala	Ala	Ala	Gly	Asn	
		305			310					315					320	
Phe	Arg	Asp	Asp	Ala	Cys	Leu	Tyr	Ser	Pro	Ala	Ser	Ala	Pro	Glu	Val	
				325					330					335		
Ile	Thr	Val	Gly	Ala	Thr	Asn	Ala	Gln	Asp	Gln	Pro	Val	Thr	Leu	Gly	
			340					345					350			
Thr	Leu	Gly	Thr	Asn	Phe	Gly	Arg	Cys	Val	Asp	Leu	Phe	Ala	Pro	Gly	
		355					360					365				
Lys	Asp	Ile	Ile	Gly	Ala	Ser	Ser	Asp	Cys	Ser	Thr	Cys	Phe	Met	Ser	
		370				375					380					
Gln	Ser	Gly	Thr	Ser	Gln	Ala	Ala	Ala	His	Val	Ala	Gly	Ile	Val	Ala	
					390					395					400	
Arg	Met	Leu	Ser	Arg	Glu	Pro	Thr	Leu	Thr	Leu	Ala	Glu	Leu	Arg	Gln	
				405					410					415		
Arg	Leu	Ile	His	Phe	Ser	Thr	Lys	Asp	Val	Ile	Asn	Met	Ala	Trp	Phe	
			420					425				430				
Pro	Glu	Asp	Gln	Gln	Val	Leu	Thr	Pro	Asn	Leu	Val	Ala	Thr	Leu	Pro	
		435					440					445				
Pro	Ser	Thr	His	Glu	Thr	Gly	Gly	Gln	Leu	Leu	Cys	Arg	Thr	Val	Trp	
		450				455					460					
Ser	Ala	His	Ser	Gly	Pro	Thr	Arg	Thr	Ala	Thr	Ala	Thr	Ala	Arg	Cys	
					470					475					480	
Ala	Pro	Glu	Glu	Glu	Leu	Leu	Ser	Cys	Ser	Ser	Phe	Ser	Arg	Ser	Gly	
				485					490					495		
Arg	Arg	Arg	Gly	Asp	Trp	Ile	Glu	Ala	Ile	Gly	Gly	Gln	Gln	Val	Cys	
			500					505					510			
Lys	Ala	Leu	Asn	Ala	Phe	Gly										

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Leu Glu Cys Lys Ile Lys Glu His Gly Ile Ser Gly Pro Ser Glu Gln
 610 615 620
 Val Thr Val Ala Cys Glu Ala Gly Trp Thr Leu Thr Gly Cys Asn Val
 625 630 635 640
 Leu Pro Gly Ala Ser Leu Thr Leu Gly Ala Tyr Ser Val Asp Asn Leu
 645 650 655
 Cys Val Ala Arg Val His Asp Thr Ala Arg Ala Asp Arg Thr Ser Gly
 660 665 670
 Glu Ala Thr Val Ala Ala Ala Ile Cys Cys Arg Ser Arg Pro Ser Ala
 675 680 685
 Lys Ala Ser Trp Val Gln
 690

<210> SEQ ID NO 758
 <211> LENGTH: 653
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 758

Glu Phe Arg Cys His Asp Gly Lys Cys Ile Ser Arg Gln Phe Val Cys
 1 5 10 15
 Asp Ser Asp Arg Asp Cys Leu Asp Gly Ser Asp Glu Ala Ser Cys Pro
 20 25 30
 Val Leu Thr Cys Gly Pro Ala Ser Phe Gln Cys Asn Ser Ser Thr Cys
 35 40 45
 Ile Pro Gln Leu Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly
 50 55 60
 Ser Asp Glu Trp Pro Gln Arg Cys Arg Gly Leu Tyr Val Phe Gln Gly
 65 70 75 80
 Asp Ser Ser Pro Cys Ser Ala Phe Glu Phe His Cys Leu Ser Gly Glu
 85 90 95
 Cys Ile His Ser Ser Trp Arg Cys Asp Gly Gly Pro Asp Cys Lys Asp
 100 105 110
 Lys Ser Asp Glu Glu Asn Cys Ala Val Ala Thr Cys Arg Pro Asp Glu
 115 120 125
 Phe Gln Cys Ser Asp Gly Asn Cys Ile His Gly Ser Arg Gln Cys Asp
 130 135 140
 Arg Glu Tyr Asp Cys Lys Asp Met Ser Asp Glu Val Gly Cys Val Asn
 145 150 155 160
 Val Thr Leu Cys Glu Gly Pro Asn Lys Phe Lys Cys His Ser Gly Glu
 165 170 175
 Cys Ile Thr Leu Asp Lys Val Cys Asn Met Ala Arg Asp Cys Arg Asp
 180 185 190
 Trp Ser Asp Glu Pro Ile Lys Glu Cys Gly Thr Asn Glu Cys Leu Asp
 195 200 205
 Asn Asn Gly Gly Cys Ser His Val Cys Asn Asp Leu Lys Ile Gly Tyr
 210 215 220
 Glu Cys Leu Cys Pro Asp Gly Phe Gln Leu Val Ala Gln Arg Arg Cys
 225 230 235 240
 Glu Asp Ile Asp Glu Cys Gln Asp Pro Asp Thr Cys Ser Gln Leu Cys
 245 250 255
 Val Asn Leu Glu Gly Gly Tyr Lys Cys Gln Cys Glu Glu Gly Phe Gln
 260 265 270
 Leu Asp Pro His Thr Lys Ala Cys Lys Ala Val Gly Ser Ile Ala Tyr
 275 280 285

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Leu Phe Phe Thr Asn Arg His Glu Val Arg Lys Met Thr Leu Asp Arg
 290                295                300

Ser Glu Tyr Thr Ser Leu Ile Pro Asn Leu Arg Asn Val Val Ala Leu
305                310                315                320

Asp Thr Glu Val Ala Ser Asn Arg Ile Tyr Trp Ser Asp Leu Ser Gln
                325                330                335

Arg Met Ile Cys Ser Thr Gln Leu Asp Arg Ala His Gly Val Ser Ser
                340                345                350

Tyr Asp Thr Val Ile Ser Arg Asp Ile Gln Ala Pro Asp Gly Leu Ala
                355                360                365

Val Asp Trp Ile His Ser Asn Ile Tyr Trp Thr Asp Ser Val Leu Gly
                370                375                380

Thr Val Ser Val Ala Asp Thr Lys Gly Val Lys Arg Lys Thr Leu Phe
385                390                395                400

Arg Glu Asn Gly Ser Lys Pro Arg Ala Ile Val Val Asp Pro Val His
                405                410                415

Gly Phe Met Tyr Trp Thr Asp Trp Gly Thr Pro Ala Lys Ile Lys Lys
                420                425                430

Gly Gly Leu Asn Gly Val Asp Ile Tyr Ser Leu Val Thr Glu Asn Ile
                435                440                445

Gln Trp Pro Asn Gly Ile Thr Leu Asp Leu Leu Ser Gly Arg Leu Tyr
                450                455                460

Trp Val Asp Ser Lys Leu His Ser Ile Ser Ser Ile Asp Val Asn Gly
465                470                475                480

Gly Asn Arg Lys Thr Ile Leu Glu Asp Glu Lys Arg Leu Ala His Pro
                485                490                495

Phe Ser Leu Ala Val Phe Glu Asp Lys Val Phe Trp Thr Asp Ile Ile
                500                505                510

Asn Glu Ala Ile Phe Ser Ala Asn Arg Leu Thr Gly Ser Asp Val Asn
                515                520                525

Leu Leu Ala Glu Asn Leu Leu Ser Pro Glu Asp Met Val Leu Phe His
                530                535                540

Asn Leu Thr Gln Pro Arg Gly Val Asn Trp Cys Glu Arg Thr Thr Leu
545                550                555                560

Ser Asn Gly Gly Cys Gln Tyr Leu Cys Leu Pro Ala Pro Gln Ile Asn
                565                570                575

Pro His Ser Pro Lys Phe Thr Cys Ala Cys Pro Asp Gly Met Leu Leu
                580                585                590

Ala Arg Asp Met Arg Ser Cys Leu Thr Glu Ala Glu Ala Val Ala
                595                600                605

Thr Gln Glu Thr Ser Thr Val Arg Leu Lys Val Ser Ser Thr Ala Val
                610                615                620

Arg Thr Gln His Thr Thr Thr Arg Pro Val Pro Asp Thr Ser Arg Leu
625                630                635                640

Pro Gly Ala Thr Pro Gly Leu Thr Thr Val Glu Ile Val
                645                650

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<210> SEQ ID NO 759

<211> LENGTH: 753

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 759

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Met Glu Arg Arg Ala Trp Ser Leu Gln Cys Thr Ala Phe Val Leu Phe
 1                5                10                15

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Cys Ala Trp Cys Ala Leu Asn Ser Ala Lys Ala Lys Arg Gln Phe Val
 20 25 30
 Asn Glu Trp Ala Ala Glu Ile Pro Gly Gly Pro Glu Ala Ala Ser Ala
 35 40 45
 Ile Ala Glu Glu Leu Gly Tyr Asp Leu Leu Gly Gln Ile Gly Ser Leu
 50 55 60
 Glu Asn His Tyr Leu Phe Lys His Lys Asn His Pro Arg Arg Ser Arg
 65 70 75 80
 Arg Ser Ala Phe His Ile Thr Lys Arg Leu Ser Asp Asp Asp Arg Val
 85 90 95
 Ile Trp Ala Glu Gln Gln Tyr Glu Lys Glu Arg Ser Lys Arg Ser Ala
 100 105 110
 Leu Arg Asp Ser Ala Leu Asn Leu Phe Asn Asp Pro Met Trp Asn Gln
 115 120 125
 Gln Trp Tyr Leu Gln Asp Thr Arg Met Thr Ala Ala Leu Pro Lys Leu
 130 135 140
 Asp Leu His Val Ile Pro Val Trp Gln Lys Gly Ile Thr Gly Lys Gly
 145 150 155 160
 Val Val Ile Thr Val Leu Asp Asp Gly Leu Glu Trp Asn His Thr Asp
 165 170 175
 Ile Tyr Ala Asn Tyr Asp Pro Glu Ala Ser Tyr Asp Phe Asn Asp Asn
 180 185 190
 Asp His Asp Pro Phe Pro Arg Tyr Asp Pro Thr Asn Glu Asn Lys His
 195 200 205
 Gly Thr Arg Cys Ala Gly Glu Ile Ala Met Gln Ala Asn Asn His Lys
 210 215 220
 Cys Gly Val Gly Val Ala Tyr Asn Ser Lys Val Gly Gly Ile Arg Met
 225 230 235 240
 Leu Asp Gly Ile Val Thr Asp Ala Ile Glu Ala Ser Ser Ile Gly Phe
 245 250 255
 Asn Pro Gly His Val Asp Ile Tyr Ser Ala Ser Trp Gly Pro Asn Asp
 260 265 270
 Asp Gly Lys Thr Val Glu Gly Pro Gly Arg Leu Ala Gln Lys Ala Phe
 275 280 285
 Glu Tyr Gly Val Lys Gln Gly Arg Gln Gly Lys Gly Ser Ile Phe Val
 290 295 300
 Trp Ala Ser Gly Asn Gly Gly Arg Gln Gly Asp Asn Cys Asp Cys Asp
 305 310 315 320
 Gly Tyr Thr Asp Ser Ile Tyr Thr Ile Ser Ile Ser Ser Ala Ser Gln
 325 330 335
 Gln Gly Leu Ser Pro Trp Tyr Ala Glu Lys Cys Ser Ser Thr Leu Ala
 340 345 350
 Thr Ser Tyr Ser Ser Gly Asp Tyr Thr Asp Gln Arg Ile Thr Ser Ala
 355 360 365
 Asp Leu His Asn Asp Cys Thr Glu Thr His Thr Gly Thr Ser Ala Ser
 370 375 380
 Ala Pro Leu Ala Ala Gly Ile Phe Ala Leu Ala Leu Glu Ala Asn Pro
 385 390 395 400
 Asn Leu Thr Trp Arg Asp Met Gln His Leu Val Val Trp Thr Ser Glu
 405 410 415
 Tyr Asp Pro Leu Ala Asn Asn Pro Gly Trp Lys Lys Asn Gly Ala Gly
 420 425 430
 Leu Met Val Asn Ser Arg Phe Gly Phe Gly Leu Leu Asn Ala Lys Ala

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435					440					445					
Leu	Val	Asp	Leu	Ala	Asp	Pro	Arg	Thr	Trp	Arg	Ser	Val	Pro	Glu	Lys
450					455					460					
Lys	Glu	Cys	Val	Val	Lys	Asp	Asn	Asp	Phe	Glu	Pro	Arg	Ala	Leu	Lys
465					470					475					480
Ala	Asn	Gly	Glu	Val	Ile	Ile	Glu	Ile	Pro	Thr	Arg	Ala	Cys	Glu	Gly
			485						490					495	
Gln	Glu	Asn	Ala	Ile	Lys	Ser	Leu	Glu	His	Val	Gln	Phe	Glu	Ala	Thr
			500						505				510		
Ile	Glu	Tyr	Ser	Arg	Arg	Gly	Asp	Leu	His	Val	Thr	Leu	Thr	Ser	Ala
		515					520					525			
Ala	Gly	Thr	Ser	Thr	Val	Leu	Leu	Ala	Glu	Arg	Glu	Arg	Asp	Thr	Ser
	530					535					540				
Pro	Asn	Gly	Phe	Lys	Asn	Trp	Asp	Phe	Met	Ser	Val	His	Thr	Trp	Gly
545					550					555					560
Glu	Asn	Pro	Ile	Gly	Thr	Trp	Thr	Leu	Arg	Ile	Thr	Asp	Met	Ser	Gly
			565						570					575	
Arg	Ile	Gln	Asn	Glu	Gly	Arg	Ile	Val	Asn	Trp	Lys	Leu	Ile	Leu	His
			580					585					590		
Gly	Thr	Ser	Ser	Gln	Pro	Glu	His	Met	Lys	Gln	Pro	Arg	Val	Tyr	Thr
		595					600					605			
Ser	Tyr	Asn	Thr	Val	Gln	Asn	Asp	Arg	Arg	Gly	Val	Glu	Lys	Met	Val
	610					615					620				
Asp	Pro	Gly	Glu	Glu	Gln	Pro	Thr	Gln	Glu	Asn	Pro	Lys	Glu	Asn	Thr
625					630					635					640
Leu	Val	Ser	Lys	Ser	Pro	Ser	Ser	Ser	Ser	Val	Gly	Gly	Arg	Arg	Asp
			645						650					655	
Glu	Leu	Glu	Glu	Gly	Ala	Pro	Ser	Gln	Ala	Met	Leu	Arg	Leu	Leu	Gln
			660					665					670		
Ser	Ala	Phe	Ser	Lys	Asn	Ser	Pro	Pro	Lys	Gln	Ser	Pro	Lys	Lys	Ser
	675						680					685			
Pro	Ser	Ala	Lys	Leu	Asn	Ile	Pro	Tyr	Glu	Asn	Phe	Tyr	Glu	Ala	Leu
	690					695					700				
Glu	Lys	Leu	Asn	Lys	Pro	Ser	Gln	Leu	Lys	Asp	Ser	Glu	Asp	Ser	Leu
705					710					715					720
Tyr	Asn	Asp	Tyr	Val	Asp	Val	Phe	Tyr	Asn	Thr	Lys	Pro	Tyr	Lys	His
			725					730					735		
Arg	Asp	Asp	Arg	Leu	Leu	Gln	Ala	Leu	Val	Asp	Ile	Leu	Asn	Glu	Glu
			740					745					750		

Asn

<210> SEQ ID NO 760

<211> LENGTH: 785

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 760

Met	Pro	Lys	Gly	Arg	Gln	Lys	Val	Pro	His	Leu	Asp	Ala	Pro	Leu	Gly
1				5					10					15	
Leu	Pro	Thr	Cys	Leu	Trp	Leu	Glu	Leu	Ala	Gly	Leu	Phe	Leu	Leu	Val
			20						25				30		
Pro	Trp	Val	Met	Gly	Leu	Ala	Gly	Thr	Gly	Gly	Pro	Asp	Gly	Gln	Gly
		35					40					45			
Thr	Gly	Gly	Pro	Ser	Trp	Ala	Val	His	Leu	Glu	Ser	Leu	Glu	Gly	Asp
	50					55					60				

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Gly Glu Glu Glu Thr Leu Glu Gln Gln Ala Asp Ala Leu Ala Gln Ala
 65 70 75 80
 Ala Gly Leu Val Asn Ala Gly Arg Ile Gly Glu Leu Gln Gly His Tyr
 85 90 95
 Leu Phe Val Gln Pro Ala Gly His Arg Pro Ala Leu Glu Val Glu Ala
 100 105 110
 Ile Arg Gln Gln Val Glu Ala Val Leu Ala Gly His Glu Ala Val Arg
 115 120 125
 Trp His Ser Glu Gln Arg Leu Leu Arg Arg Ala Lys Arg Ser Val His
 130 135 140
 Phe Asn Asp Pro Lys Tyr Pro Gln Gln Trp His Leu Asn Asn Arg Arg
 145 150 155 160
 Ser Pro Gly Arg Asp Ile Asn Val Thr Gly Val Trp Glu Arg Asn Val
 165 170 175
 Thr Gly Arg Gly Val Thr Val Val Val Val Asp Asp Gly Val Glu His
 180 185 190
 Thr Ile Gln Asp Ile Ala Pro Asn Tyr Ser Pro Glu Gly Ser Tyr Asp
 195 200 205
 Leu Asn Ser Asn Asp Pro Asp Pro Met Pro His Pro Asp Val Glu Asn
 210 215 220
 Gly Asn His His Gly Thr Arg Cys Ala Gly Glu Ile Ala Ala Val Pro
 225 230 235 240
 Asn Asn Ser Phe Cys Ala Val Gly Val Ala Tyr Gly Ser Arg Ile Ala
 245 250 255
 Gly Ile Arg Val Leu Asp Gly Pro Leu Thr Asp Ser Met Glu Ala Val
 260 265 270
 Ala Phe Asn Lys His Tyr Gln Ile Asn Asp Ile Tyr Ser Cys Ser Trp
 275 280 285
 Gly Pro Asp Asp Asp Gly Lys Thr Val Asp Gly Pro His Gln Leu Gly
 290 295 300
 Lys Ala Ala Leu Gln His Gly Val Ile Ala Gly Arg Gln Gly Phe Gly
 305 310 315 320
 Ser Ile Phe Val Val Ala Ser Gly Asn Gly Gly Gln His Asn Asp Asn
 325 330 335
 Cys Asn Tyr Asp Gly Tyr Ala Asn Ser Ile Tyr Thr Val Thr Ile Gly
 340 345 350
 Ala Val Asp Glu Glu Gly Arg Met Pro Phe Tyr Ala Glu Glu Cys Ala
 355 360 365
 Ser Met Leu Ala Val Thr Phe Ser Gly Gly Asp Lys Met Leu Arg Ser
 370 375 380
 Ile Val Thr Thr Asp Trp Asp Leu Gln Lys Gly Thr Gly Cys Thr Glu
 385 390 395 400
 Gly His Thr Gly Thr Ser Ala Ala Ala Pro Leu Ala Ala Gly Met Ile
 405 410 415
 Ala Leu Met Leu Gln Val Arg Pro Cys Leu Thr Trp Arg Asp Val Gln
 420 425 430
 His Ile Ile Val Phe Thr Ala Thr Arg Tyr Glu Asp Arg Arg Ala Glu
 435 440 445
 Trp Val Thr Asn Glu Ala Gly Phe Ser His Ser His Gln His Gly Phe
 450 455 460
 Gly Leu Leu Asn Ala Trp Arg Leu Val Asn Ala Ala Lys Ile Trp Thr
 465 470 475 480
 Ser Val Pro Tyr Leu Ala Ser Tyr Val Ser Pro Val Leu Lys Glu Asn

-continued

485					490					495					
Lys	Ala	Ile	Pro	Gln	Ser	Pro	Arg	Ser	Leu	Glu	Val	Leu	Trp	Asn	Val
			500					505					510		
Ser	Arg	Met	Asp	Leu	Glu	Met	Ser	Gly	Leu	Lys	Thr	Leu	Glu	His	Val
		515					520					525			
Ala	Val	Thr	Val	Ser	Ile	Thr	His	Pro	Arg	Arg	Gly	Ser	Leu	Glu	Leu
		530					535					540			
Lys	Leu	Phe	Cys	Pro	Ser	Gly	Met	Met	Ser	Leu	Ile	Gly	Ala	Pro	Arg
		545					550					555			560
Ser	Met	Asp	Ser	Asp	Pro	Asn	Gly	Phe	Asn	Asp	Trp	Thr	Phe	Ser	Thr
			565						570					575	
Val	Arg	Cys	Trp	Gly	Glu	Arg	Ala	Arg	Gly	Thr	Tyr	Arg	Leu	Val	Ile
			580					585					590		
Arg	Asp	Val	Gly	Asp	Glu	Ser	Phe	Gln	Val	Gly	Ile	Leu	Arg	Gln	Trp
		595					600					605			
Gln	Leu	Thr	Leu	Tyr	Gly	Ser	Val	Trp	Ser	Ala	Val	Asp	Ile	Arg	Asp
		610					615					620			
Arg	Gln	Arg	Leu	Leu	Glu	Ser	Ala	Met	Ser	Gly	Lys	Tyr	Leu	His	Asp
		625					630					635			640
Asp	Phe	Ala	Leu	Pro	Cys	Pro	Pro	Gly	Leu	Lys	Ile	Pro	Glu	Glu	Asp
			645						650					655	
Gly	Tyr	Thr	Ile	Thr	Pro	Asn	Thr	Leu	Lys	Thr	Leu	Val	Leu	Val	Gly
			660					665					670		
Cys	Phe	Thr	Val	Phe	Trp	Thr	Val	Tyr	Tyr	Met	Leu	Glu	Val	Tyr	Leu
		675					680					685			
Ser	Gln	Arg	Asn	Val	Ala	Ser	Asn	Gln	Val	Cys	Arg	Ser	Gly	Pro	Cys
		690					695					700			
His	Trp	Pro	His	Arg	Ser	Arg	Lys	Ala	Lys	Glu	Glu	Gly	Thr	Glu	Leu
		705					710					715			720
Glu	Ser	Val	Pro	Leu	Cys	Ser	Ser	Lys	Asp	Pro	Asp	Glu	Val	Glu	Thr
			725						730					735	
Glu	Ser	Arg	Gly	Pro	Pro	Thr	Thr	Ser	Asp	Leu	Leu	Ala	Pro	Asp	Leu
			740					745					750		
Leu	Glu	Gln	Gly	Asp	Trp	Ser	Leu	Ser	Gln	Asn	Lys	Ser	Ala	Leu	Asp
		755					760					765			
Cys	Pro	His	Gln	His	Leu	Asp	Val	Pro	His	Gly	Lys	Glu	Glu	Gln	Ile
		770					775					780			
Cys															
785															

<210> SEQ ID NO 761

<211> LENGTH: 692

<212> TYPE: PRT

<213> ORGANISM: Macaca fascicularis

<400> SEQUENCE: 761

Met	Gly	Thr	Val	Ser	Ser	Arg	Arg	Ser	Trp	Trp	Pro	Leu	Pro	Leu	Pro
1				5					10					15	
Leu	Leu	Leu	Leu	Leu	Leu	Leu	Gly	Pro	Ala	Gly	Ala	Arg	Ala	Gln	Glu
			20					25					30		
Asp	Glu	Asp	Gly	Asp	Tyr	Glu	Glu	Leu	Val	Leu	Ala	Leu	Arg	Ser	Glu
		35						40					45		
Glu	Asp	Gly	Leu	Ala	Asp	Ala	Pro	Glu	His	Gly	Ala	Thr	Ala	Thr	Phe
	50				55						60				
His	Arg	Cys	Ala	Lys	Asp	Pro	Trp	Arg	Leu	Pro	Gly	Thr	Tyr	Val	Val

-continued

65	70	75	80
Val Leu Lys Glu Glu Thr His Arg Ser Gln Ser Glu Arg Thr Ala Arg	85	90	95
Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu	100	105	110
His Val Phe His His Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly	115	120	125
Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val Asp Tyr Ile Glu	130	135	140
Glu Asp Ser Ser Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg	145	150	155
Ile Thr Pro Ala Arg Tyr Arg Ala Asp Gly Tyr Gln Pro Pro Lys Gly	165	170	175
Gly Ser Leu Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Asp	180	185	190
His Arg Glu Ile Glu Gly Arg Val Met Val Thr Asp Phe Glu Ser Val	195	200	205
Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp	210	215	220
Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly	225	230	235
Val Ala Lys Gly Ala Gly Leu Arg Ser Leu Arg Val Leu Asn Cys Gln	245	250	255
Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg	260	265	270
Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu Leu Pro	275	280	285
Leu Ala Gly Gly Tyr Ser Arg Val Phe Asn Ala Ala Cys Gln Arg Leu	290	295	300
Ala Arg Ala Gly Val Val Leu Val Thr Ala Ala Gly Asn Phe Arg Asp	305	310	315
Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val	325	330	335
Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly	340	345	350
Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu Asp Ile	355	360	365
Ile Gly Ala Ser Ser Asp Cys Ser Thr Cys Phe Val Ser Arg Ser Gly	370	375	380
Thr Ser Gln Ala Ala Ala His Val Ala Gly Ile Ala Ala Met Met Leu	385	390	395
Ser Ala Glu Pro Glu Leu Thr Leu Ala Glu Leu Arg Gln Arg Leu Ile	405	410	415
His Phe Ser Ala Lys Asp Val Ile Asn Glu Ala Trp Phe Pro Glu Asp	420	425	430
Gln Arg Val Leu Thr Pro Asn Leu Val Ala Ala Leu Pro Pro Ser Thr	435	440	445
His Arg Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His	450	455	460
Ser Gly Pro Thr Arg Met Ala Thr Ala Val Ala Arg Cys Ala Gln Asp	465	470	475
Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg	485	490	495

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Gly Glu Arg Ile Glu Ala Gln Gly Gly Lys Arg Val Cys Arg Ala His
 500 505 510
 Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu
 515 520 525
 Leu Pro Gln Val Asn Cys Ser Val His Thr Ala Pro Pro Ala Gly Ala
 530 535 540
 Ser Met Gly Thr Arg Val His Cys His Gln Gln Gly His Val Leu Thr
 545 550 555 560
 Gly Cys Ser Ser His Trp Glu Val Glu Asp Leu Gly Thr His Lys Pro
 565 570 575
 Pro Val Leu Arg Pro Arg Gly Gln Pro Asn Gln Cys Val Gly His Arg
 580 585 590
 Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys
 595 600 605
 Lys Val Lys Glu His Gly Ile Pro Ala Pro Gln Glu Gln Val Ile Val
 610 615 620
 Ala Cys Glu Asp Gly Trp Thr Leu Thr Gly Cys Ser Ala Leu Pro Gly
 625 630 635 640
 Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val
 645 650 655
 Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Glu Glu Ala Val
 660 665 670
 Ala Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Val Gln Ala Ser
 675 680 685
 Gln Glu Leu Gln
 690

<210> SEQ ID NO 762

<211> LENGTH: 698

<212> TYPE: PRT

<213> ORGANISM: Mesocricetus auratus

<400> SEQUENCE: 762

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

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Arg	Lys	Val	Pro	Ser	Gly	Ser	Gly	Gln	Val	Glu	Val	Tyr	Leu	Leu	Asp	
			180					185					190			
Thr	Ser	Ile	Gln	Ser	Asp	His	Arg	Glu	Ile	Glu	Gly	Arg	Val	Thr	Val	
	195						200					205				
Thr	Asp	Phe	Asn	Ser	Val	Pro	Glu	Glu	Asp	Gly	Thr	Arg	Phe	His	Arg	
	210					215					220					
Gln	Ala	Ser	Lys	Cys	Asp	Ser	His	Gly	Thr	His	Leu	Ala	Gly	Val	Val	
225					230					235					240	
Ser	Gly	Arg	Asp	Ala	Gly	Val	Ala	Lys	Gly	Thr	Ile	Leu	His	Gly	Leu	
				245					250					255		
Arg	Val	Leu	Asn	Cys	Gln	Gly	Lys	Gly	Ile	Val	Ser	Gly	Ile	Leu	Thr	
			260					265					270			
Gly	Leu	Glu	Phe	Ile	Trp	Lys	Ser	Gln	Leu	Met	Gln	Pro	Ser	Gly	Pro	
	275						280					285				
Gln	Val	Val	Leu	Leu	Pro	Leu	Ala	Gly	Arg	Tyr	Ser	Arg	Val	Leu	Asn	
	290					295					300					
Thr	Ala	Cys	Gln	His	Leu	Ala	Arg	Thr	Gly	Val	Val	Leu	Val	Ala	Ala	
305					310					315					320	
Ala	Gly	Asn	Phe	Arg	Asp	Asp	Ala	Cys	Leu	Tyr	Ser	Pro	Ala	Ser	Ala	
				325					330					335		
Pro	Glu	Val	Ile	Thr	Val	Gly	Ala	Thr	Asp	Val	Gln	Asp	Gln	Pro	Val	
			340					345					350			
Thr	Leu	Gly	Thr	Leu	Gly	Thr	Asn	Phe	Gly	Arg	Cys	Val	Asp	Leu	Phe	
	355						360					365				
Ala	Pro	Gly	Lys	Asp	Ile	Ile	Gly	Ala	Ser	Ser	Asp	Cys	Ser	Ala	Cys	
	370					375					380					
Phe	Met	Ser	Gln	Ser	Gly	Thr	Ser	Gln	Ala	Ala	Ala	His	Val	Ala	Gly	
385					390					395					400	
Ile	Val	Ala	Met	Met	Leu	Thr	Leu	Glu	Pro	Glu	Leu	Thr	Leu	Thr	Glu	
				405					410					415		
Leu	Arg	Gln	Arg	Leu	Ile	His	Phe	Ser	Thr	Lys	Asp	Ala	Ile	Asn	Met	
			420					425					430			
Ala	Trp	Phe	Pro	Glu	Asp	Gln	Arg	Val	Leu	Thr	Pro	Asn	Leu	Val	Ala	
		435					440					445				
Thr	Leu	Pro	Pro	Ser	Thr	His	Gly	Thr	Gly	Gly	Gln	Leu	Leu	Cys	Arg	
	450					455					460					
Thr	Val	Trp	Ser	Ala	His	Ser	Gly	Pro	Thr	Arg	Ala	Ala	Thr	Ala	Thr	
465					470					475					480	
Ala	Arg	Cys	Ala	Pro	Gly	Glu	Glu	Leu	Leu	Ser	Cys	Ser	Ser	Phe	Ser	
				485					490					495		
Arg	Ser	Gly	Arg	Arg	Arg	Gly	Asp	Arg	Ile	Glu	Ala	Ala	Gly	Thr	Gln	
			500					505					510			
Gln	Val	Cys	Lys	Ala	Leu	Asn	Ala	Phe	Gly	Gly	Glu	Gly	Val	Tyr	Ala	
		515					520					525				
Val	Ala	Arg	Cys	Cys	Leu	Leu	Pro	Arg	Ala	Asn	Cys	Ser	Ile	His	Thr	
	530					535					540					
Thr	Pro	Ala	Ala	Arg	Thr	Ser	Leu	Glu	Thr	His	Ala	His	Cys	His	Gln	
545					550					555					560	
Lys	Asp	His	Val	Leu	Thr	Gly	Cys	Ser	Leu	His	Trp	Glu	Val	Glu	Gly	
				565					570					575		
Ile	Gly	Val	Gln	Pro	Leu	Ala	Val	Leu	Arg	Ser	Arg	His	Gln	Pro	Gly	
			580				585						590			
Gln	Cys	Thr	Gly	His	Arg	Glu	Ala	Ser	Val	His	Ala	Ser	Cys	Cys	His	
	595						600					605				

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Ala Pro Gly Leu Glu Cys Lys Ile Lys Glu His Gly Ile Ser Gly Pro
610 615 620

Ala Glu Gln Val Thr Val Ala Cys Glu Ala Gly Trp Thr Leu Thr Gly
625 630 635 640

Cys Asn Val Leu Pro Gly Ala Phe Ile Thr Leu Gly Ala Tyr Ala Val
645 650 655

Asp Asn Thr Cys Val Ala Arg Ser Arg Val Thr Asp Thr Ala Gly Arg
660 665 670

Thr Gly Glu Glu Ala Thr Val Ala Ala Ala Ile Cys Cys Arg Asn Arg
675 680 685

Pro Ser Ala Lys Ala Ser Trp Val His Gln
690 695

<210> SEQ ID NO 763

<211> LENGTH: 691

<212> TYPE: PRT

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 763

Met Gly Ile Arg Cys Ser Thr Trp Leu Arg Trp Pro Leu Ser Pro Gln
1 5 10 15

Leu Leu Leu Leu Leu Leu Cys Pro Thr Gly Ser Arg Ala Gln Asp
20 25 30

Glu Asp Gly Asp Tyr Glu Glu Leu Met Leu Ala Leu Pro Ser Gln Glu
35 40 45

Asp Ser Leu Val Asp Glu Ala Ser His Val Ala Thr Ala Thr Phe Arg
50 55 60

Arg Cys Ser Lys Glu Ala Trp Arg Leu Pro Gly Thr Tyr Val Val Val
65 70 75 80

Leu Met Glu Glu Thr Gln Arg Leu Gln Val Glu Gln Thr Ala His Arg
85 90 95

Leu Gln Thr Trp Ala Ala Arg Arg Gly Tyr Val Ile Lys Val Leu His
100 105 110

Val Phe Tyr Asp Leu Phe Pro Gly Phe Leu Val Lys Met Ser Ser Asp
115 120 125

Leu Leu Gly Leu Ala Leu Lys Leu Pro His Val Glu Tyr Ile Glu Glu
130 135 140

Asp Ser Leu Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg Ile
145 150 155 160

Ile Pro Ala Trp Gln Gln Thr Glu Glu Asp Ser Ser Pro Asp Gly Ser
165 170 175

Ser Gln Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Gly His
180 185 190

Arg Glu Ile Glu Gly Arg Val Thr Ile Thr Asp Phe Asn Ser Val Pro
195 200 205

Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp Ser
210 215 220

His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly Val
225 230 235 240

Ala Lys Gly Thr Ser Leu His Ser Leu Arg Val Leu Asn Cys Gln Gly
245 250 255

Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg Lys
260 265 270

Ser Gln Leu Ile Gln Pro Ser Gly Pro Leu Val Val Leu Leu Pro Leu
275 280 285

-continued

Ala Gly Gly Tyr Ser Arg Ile Leu Asn Thr Ala Cys Gln Arg Leu Ala	
290 295 300	
Arg Thr Gly Val Val Leu Val Ala Ala Ala Gly Asn Phe Arg Asp Asp	
305 310 315 320	
Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val Gly	
325 330 335	
Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly Thr	
340 345 350	
Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Lys Asp Ile Ile	
355 360 365	
Gly Ala Ser Ser Asp Cys Ser Thr Cys Tyr Met Ser Gln Ser Gly Thr	
370 375 380	
Ser Gln Ala Ala Ala His Val Ala Gly Ile Val Ala Met Met Leu Asn	
385 390 395 400	
Arg Asp Pro Ala Leu Thr Leu Ala Glu Leu Arg Gln Arg Leu Ile Leu	
405 410 415	
Phe Ser Thr Lys Asp Val Ile Asn Met Ala Trp Phe Pro Glu Asp Gln	
420 425 430	
Arg Val Leu Thr Pro Asn Arg Val Ala Thr Leu Pro Pro Ser Thr Gln	
435 440 445	
Glu Thr Gly Gly Gln Leu Leu Cys Arg Thr Val Trp Ser Ala His Ser	
450 455 460	
Gly Pro Thr Arg Thr Ala Thr Ala Thr Ala Arg Cys Ala Pro Glu Glu	
465 470 475 480	
Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Arg Arg Arg Gly	
485 490 495	
Asp Arg Ile Glu Ala Ile Gly Gly Gln Gln Val Cys Lys Ala Leu Asn	
500 505 510	
Ala Phe Gly Gly Glu Gly Val Tyr Ala Val Ala Arg Cys Cys Leu Leu	
515 520 525	
Pro Arg Val Asn Cys Ser Ile His Asn Thr Pro Ala Ala Arg Ala Gly	
530 535 540	
Pro Gln Thr Pro Val His Cys His Gln Lys Asp His Val Leu Thr Gly	
545 550 555 560	
Cys Ser Phe His Trp Glu Val Glu Asn Leu Arg Ala Gln Gln Gln Pro	
565 570 575	
Leu Leu Arg Ser Arg His Gln Pro Gly Gln Cys Val Gly His Gln Glu	
580 585 590	
Ala Ser Val His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys Lys	
595 600 605	
Ile Lys Glu His Gly Ile Ala Gly Pro Ala Glu Gln Val Thr Val Ala	
610 615 620	
Cys Glu Ala Gly Trp Thr Leu Thr Gly Cys Asn Val Leu Pro Gly Ala	
625 630 635 640	
Ser Leu Pro Leu Gly Ala Tyr Ser Val Asp Asn Val Cys Val Ala Arg	
645 650 655	
Ile Arg Asp Ala Gly Arg Ala Asp Arg Thr Ser Glu Glu Ala Thr Val	
660 665 670	
Ala Ala Ala Ile Cys Cys Arg Ser Arg Pro Ser Ala Lys Ala Ser Trp	
675 680 685	
Val His Gln	
690	

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What is claimed is:

1. A method for treating hypercholesterolemia comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising an antibody or antigen-binding fragment thereof which specifically binds hPCSK9, wherein the antibody or antigen-binding fragment comprises the heavy and light chain CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs:90/92 and 218/226.

2. The method of claim 1, wherein the antibody or antigen-binding fragment comprises heavy and light chain CDR amino acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232.

3. The method of claim 2, wherein the antibody or antigen-binding fragment comprises an HCVR having the amino acid sequence of SEQ ID NO:218 and an LCVR having the amino acid sequence of SEQ ID NO:226.

4. The method of claim 1, wherein the antibody or antigen-binding fragment comprises heavy and light chain CDR amino acid sequences having SEQ ID NOs:76, 78, 80, 84, 86 and 88.

5. The method of claim 4, wherein the antibody or antigen-binding fragment comprises an HCVR having the amino acid sequence of SEQ ID NO:90 and an LCVR having the amino acid sequence of SEQ ID NO:92.

6. The method of claim 1, wherein the antibody or antigen-binding fragment binds to the same epitope on hPCSK9 as an antibody comprising heavy and light chain CDR amino acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232; or SEQ ID NOs: 76, 78, 80, 84, 86 and 88.

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7. The method of claim 1, wherein the antibody or antigen-binding fragment competes for binding to hPCSK9 with an antibody comprising heavy and light chain CDR amino acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232; or SEQ ID NOs: 76, 78, 80, 84, 86 and 88.

8. The method of claim 1, wherein the patient is on a therapeutic statin regimen at the time of or just prior to administration of the pharmaceutical composition.

9. The method of claim 8, wherein the therapeutic statin regimen comprises a statin selected from the group consisting of cerivastatin, atorvastatin, simvastatin, pitavastatin, rosuvastatin, fluvastatin, lovastatin and pravastatin.

10. The method of claim 9, wherein the statin is atorvastatin.

11. The method of claim 1, wherein the pharmaceutical composition comprises between 25 mg to 200 mg of the antibody or antigen-binding fragment thereof.

12. The method of claim 11, wherein the pharmaceutical composition comprises 50 mg of the antibody or antigen-binding fragment thereof.

13. The method of claim 11, wherein the pharmaceutical composition comprises 100 mg of the antibody or antigen-binding fragment thereof.

14. The method of claim 11, wherein the pharmaceutical composition comprises 150 mg of the antibody or antigen-binding fragment thereof.

15. The method of claim 1, wherein the patient has heterozygous Familial Hypercholesterolemia (heFH).

16. The method of claim 1, wherein the patient has a form of hypercholesterolemia that is not Familial Hypercholesterolemia (nonFH).

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