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Sleeman et al.

(54) HIGH AFFINITY HUMAN ANTIBODIES TO PCSK9

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- (51) Int. Cl.

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

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(58) Field of Classification Search

None

See application file for complete search history.

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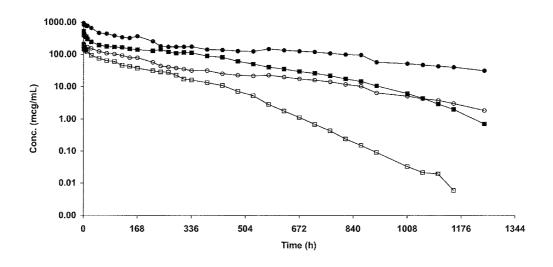
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(57) ABSTRACT

An human antibody or antigen-binding fragment of a human antibody that specifically binds and inhibits human proprotein convertase subtilisin/kexin type 9 (hPCSK9) characterized by the ability to reduce serum LDL cholesterol by 40-80% over a 24, 60 or 90 day period relative to predose levels, with little or no reduction in serum HDL cholesterol and/or with little or no measurable effect on liver function, as determined by ALT and AST measurements.

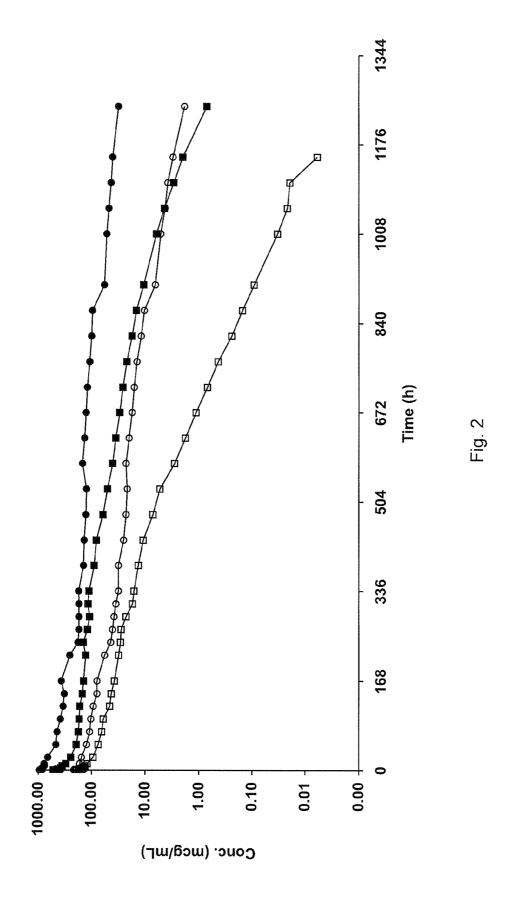
3 Claims, 14 Drawing Sheets

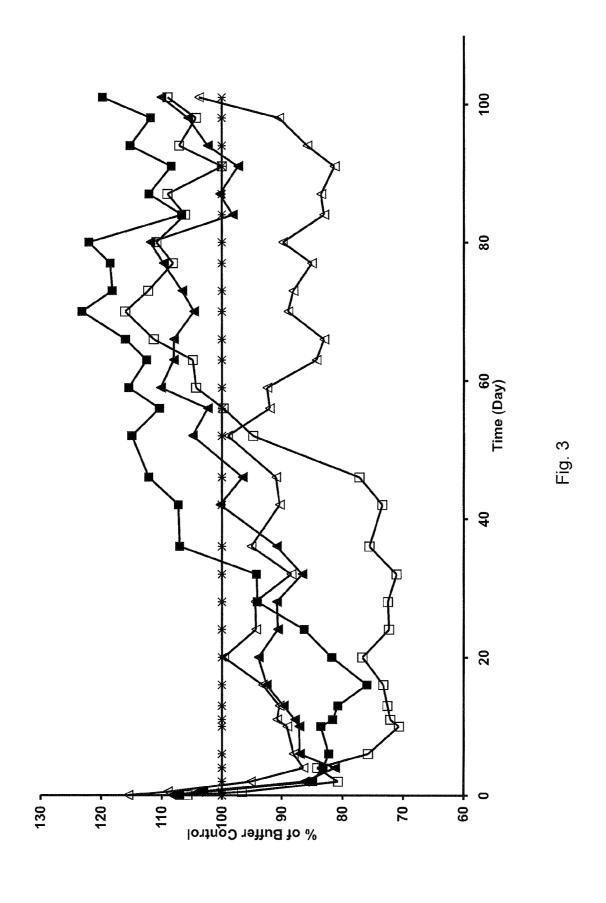


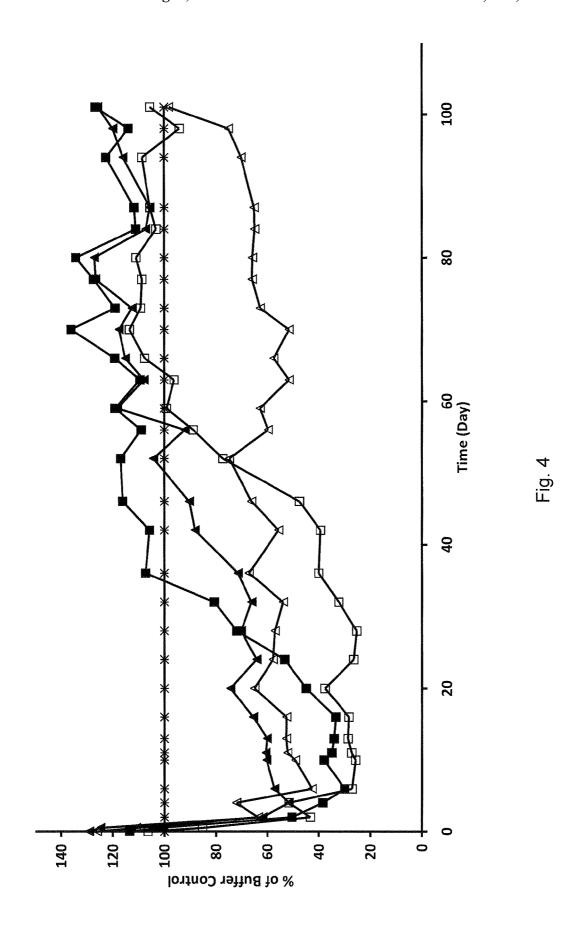
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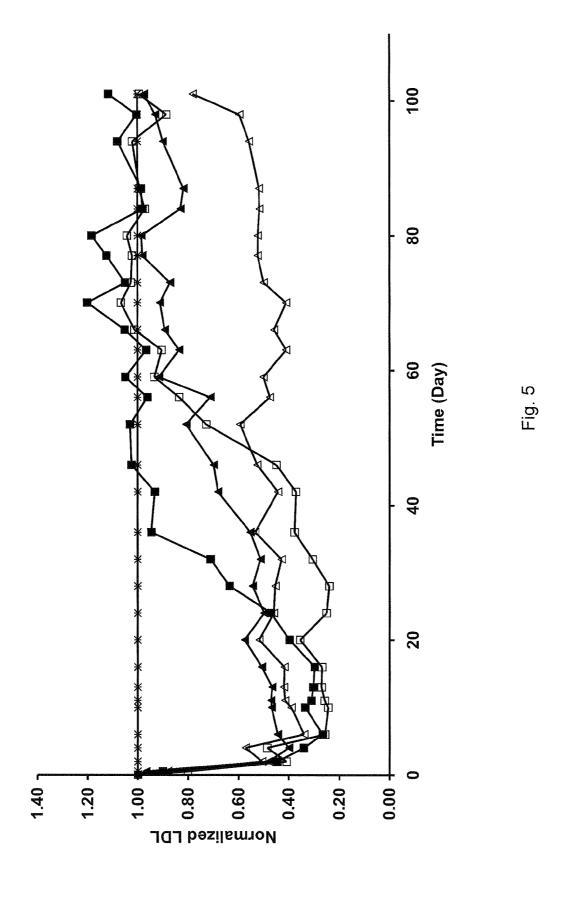
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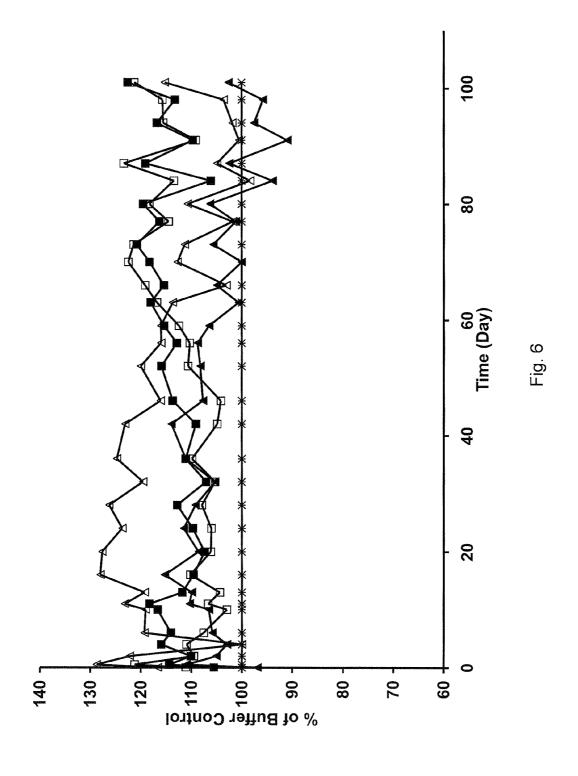
Fig.

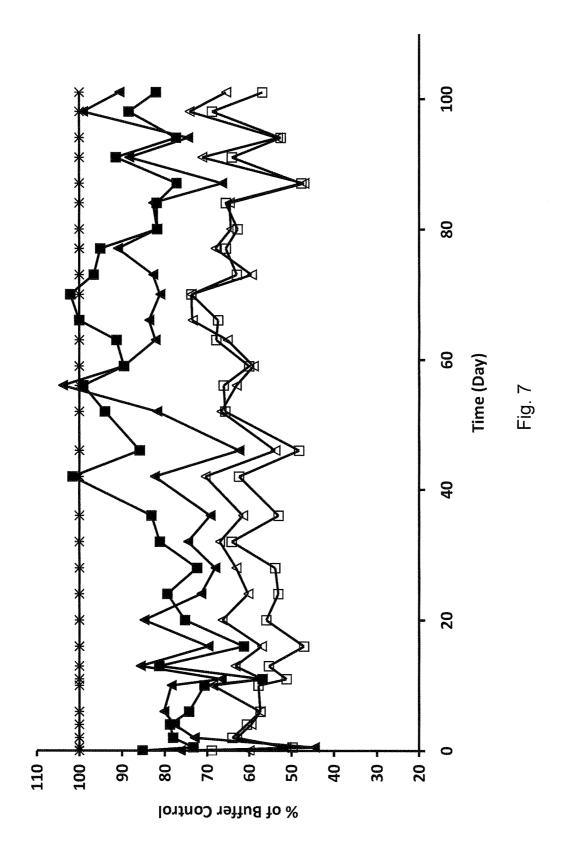


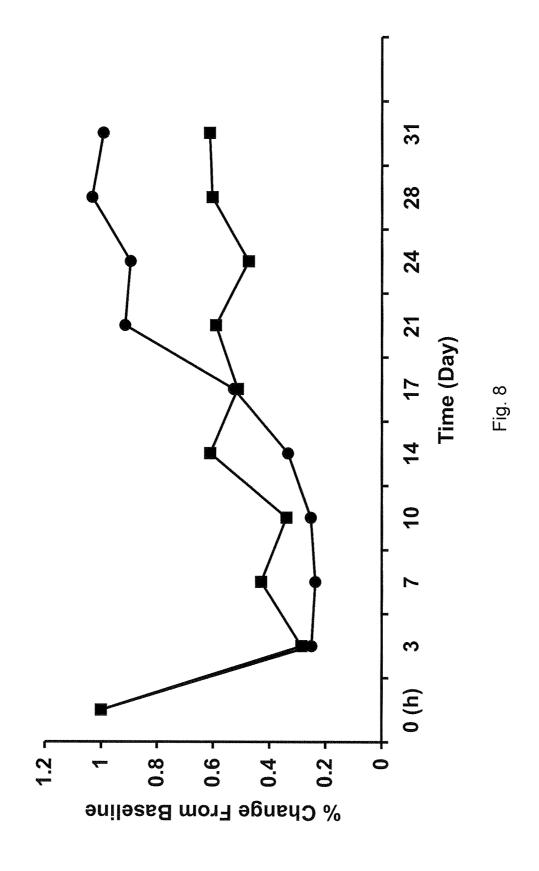


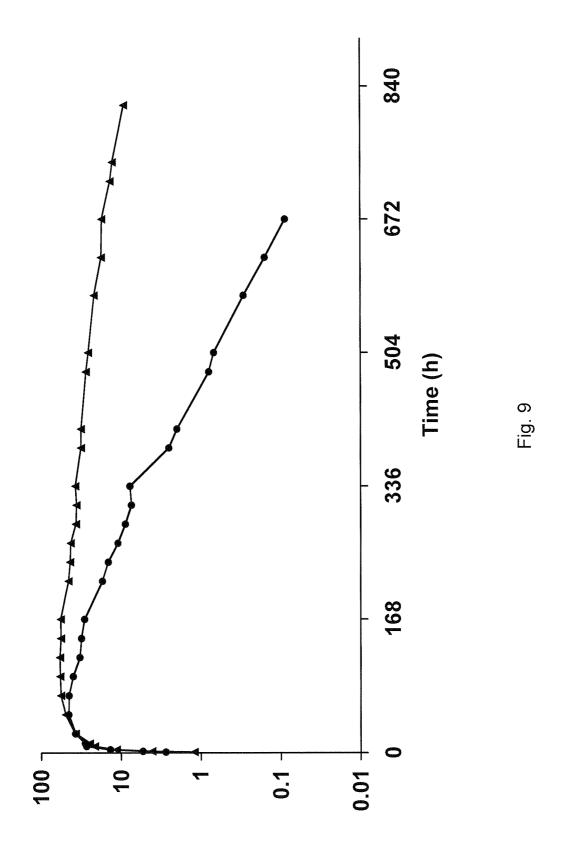












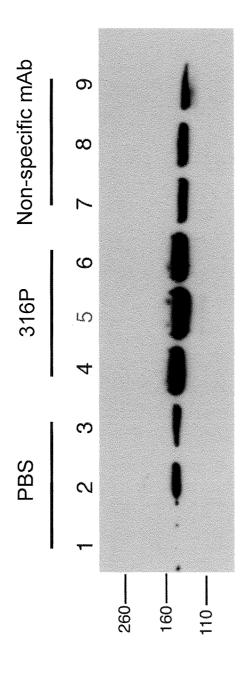
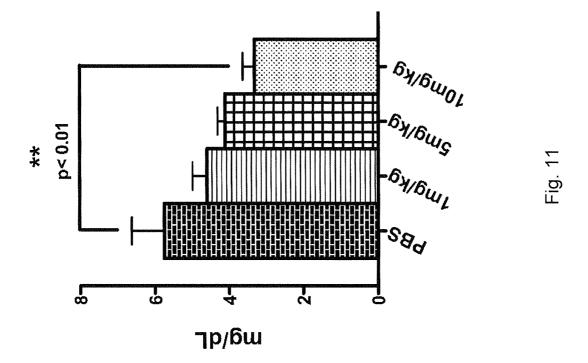
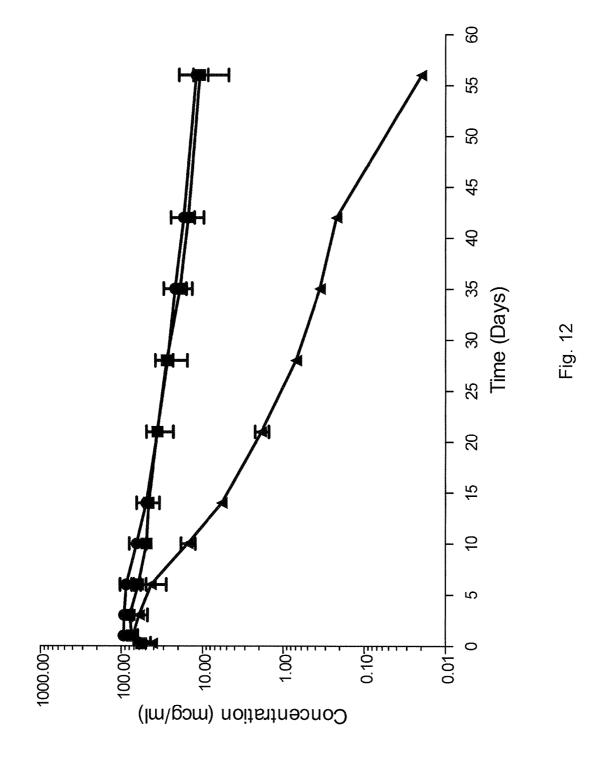
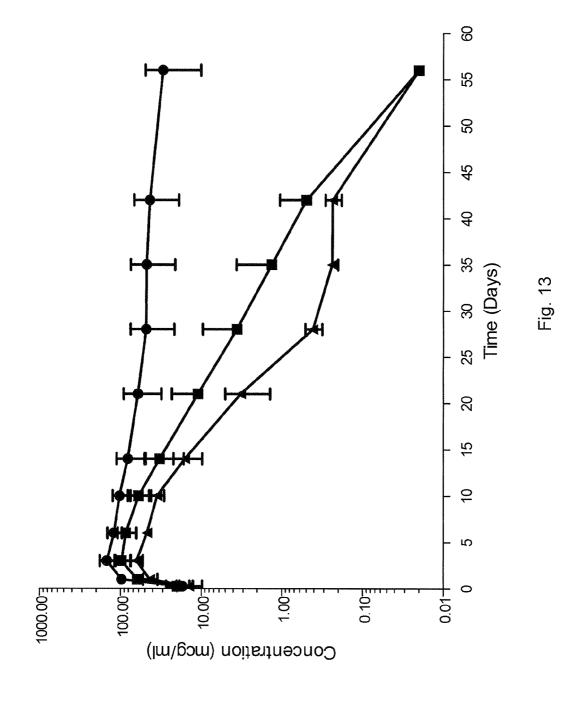
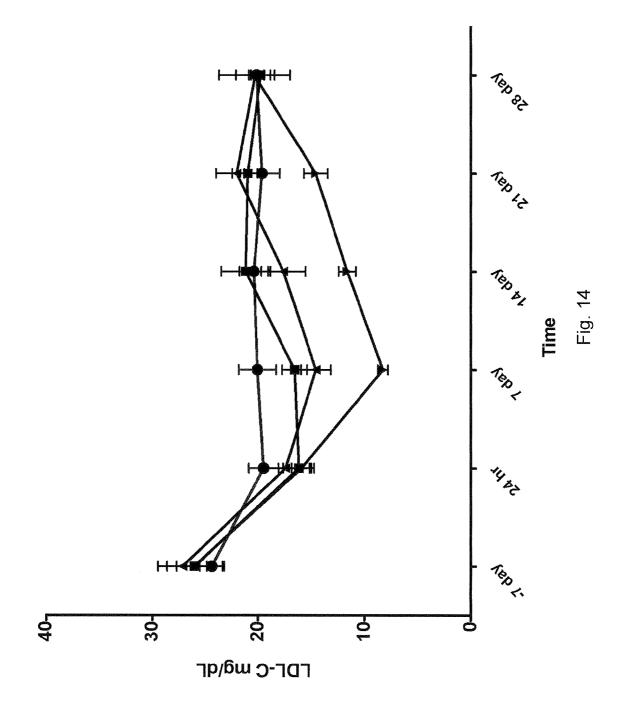


Fig. 1









HIGH AFFINITY HUMAN ANTIBODIES TO PCSK9

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional 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 61/261,776 filed 17 Nov. 2009, 61/249,135 filed 6 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 ²⁰ 9 (PCSK9), and therapeutic methods of using those antibodies.

SEQUENCE LISTING

An ASCII compliant text file of the sequence listing is filed concurrently with the present specification (37 CFR §1.52(e) and 37 CFR §1.821). The contents of the text file are herein incorporated by reference. The text file containing the sequence listing is named "PCSK9_SeqList", was created on ³⁰ 11 Dec. 2009, and contains approximately 418 kilobytes.

STATEMENT OF RELATED ART

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a 35 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 choles- 40 terol 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 45 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. 50 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 60 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

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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.

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 55 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 (e.g., an IgG1 or IgG4 antibody) or may comprise only an antigen-binding portion (e.g., 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, 5 194, 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, 10 674, 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, 15 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 20 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, 25 452, 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% 30 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, 40 142/144, 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, 402/45 404, 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, 50 666/668, 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, 55 258/260, 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 60 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

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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 SEO 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 SEO 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, 35 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 hPCSK9, 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 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 10 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 reduc- 15 tion 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 com- 20 prising 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 25 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) 35 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 40 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; 45 (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 55 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 60 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, 65, 409, 425, 429, 433, 449, 453, 457, 473, 477, 481, 497, 501, 505, 521, 525, 529, 545, 549, 553, 569, 573, 577, 593, 597,

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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 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 50 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, 5 133, 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 10 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 20 binds hPCSK9, comprising a HCDR3 and a LCDR3, wherein HCDR3 comprises an amino acid sequence of the formula X¹-X²-X³-X⁴-X⁵-X⁶-X⁻-X³-X³-X¹0-X¹¹-X¹²-X¹³-X¹⁴-X¹⁵-X¹⁶-X¹¬-X¹³-X¹⁴-X¹⁵-X¹⁶-X¹¬-X¹³-X¹⁰-X²0 (SEQ ID NO:747), wherein X¹ is Ala, X² is Arg or Lys, X³ is Asp, X⁴ is Ser or Ile, X⁵ is Asn or Val, 25 X⁶ is Leu or Trp, X⁻ is Gly or Met, X³ is Asn or Val, X⁰ is Phe or Tyr, X¹⁰ is Asp, X¹¹ is Leu or Met, X¹² is Asp or absent, X¹³ is Tyr or absent, X¹⁴ is Tyr or absent, X¹⁵ is Tyr or absent, X¹⁰ is Asp or absent, and X²⁰ is Val or absent; and LCDR3 comprises an amino acid sequence of the formula X¹-X²-X³-X⁴-X⁵-X⁶-X⁻-X³-X³-X⁰ (SEQ ID NO:750), wherein X¹ is Gln or Met, X² is Gln, X³ is Tyr or Thr, X⁴ is Tyr or Leu, X⁵ is Thr or Gln, X⁶ is Thr, X⁻ is Pro, X³ is Tyr or Leu, and X⁰ is Thr.

In a further embodiment, the antibody or fragment thereof 35 further comprise a HCDR1 sequence of the formula X¹-X²- $X^{3}-X^{4}-X^{5}-X^{6}-X^{7}-X^{8}$ (SEQ ID NO:745), wherein X^{1} is Gly, X² is Phe, X³ is Thr, X⁴ is Phe, X⁵ is Ser or Asn, X⁶ is Ser or Asn, X⁷ is Tyr or His, and X⁸ is Ala or Trp; a HCDR2 sequence of the formula X1-X2-X3-X4-X5-X6-X7-X8 (SEQ ID 40 NO:746), wherein X¹ is Ile, X² is Ser or Asn, X³ is Gly or Gln, X⁴ is Asp or Ser, X⁵ is Gly, X⁶ is Ser or Gly, X⁷ is Thr or Glu, and X⁸ 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} NO:748) wherein X¹ is Gln, X² is Ser, X³ is Val or Leu, X⁴ is 45 Leu, X⁵ is His or Tyr, X⁶ is Arg or Ser, X⁷ is Ser or Asn, X⁸ is Asn or Gly, X⁹ is Asn, X¹⁰ is Arg or Asn, X¹¹ is Asn or Tyr, and X¹² 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 X³ 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 55 by nucleotide sequence segments derived from V_H , D_H and J_H germline sequences, and a light chain variable region (LCVR) encoded by nucleotide sequence segments derived from V_K and J_K germline sequences, wherein the germline 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 65 antigen-binding fragment thereof that binds to a PCSK9 protein of SEQ ID NO:755, wherein the binding of the antibody

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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 e.g., 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, cerovastatin, atorvastatin, simvastatin, pitavastin, 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 5 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 hyper- 20 cholesterolemia 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 25 mg/kg (v); 316P 3 mg/kg (σ); 316P 5 mg/kg (τ). 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 (apolipo $^{30}$ protein 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 35 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 45 5 mg/kg (\square); 300N 5 mg/kg (\bigcirc); 316P 15 mg/kg (ν); 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 (\square); 300N 15 mg/kg ⁵⁰ (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 55 (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 (\square); 300N 15 mg/kg (Δ).
- FIG. 6. Serum HDL cholesterol level as a percentage of 60 change over buffer control. Buffer control (T); 316P 5 mg/kg (v); 300N 5 mg/kg (σ); 316P 15 mg/kg (\square); 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 $mg/kg(\sigma)$; 316P 15 $mg/kg(\square)$; 300N 15 mg/kg (Δ).

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- 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 (\bullet); 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 (ν) 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 (ν) 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

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 25 residues not encoded by human germline immunoglobulin sequences (e.g., 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 30 include mAbs in which CDR sequences derived from the germline of another mammalian species (e.g., 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 (e.g., 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 (e.g., 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; 50 preferably 10^{-11} M; even more preferably 10^{-12} M, as measured by surface plasmon resonance, e.g., BIACORETM or solution-affinity ELISA.

By the term "slow off rate", "Koff" or "kd" is meant an antibody that dissociates from hPCSK9 with a rate constant 55 of 1×10^{-3} s⁻¹ or less, preferably 1×10^{-4} s⁻¹ or less, as determined by surface plasmon resonance, e.g., BIACORETM.

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.

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An "isolated antibody", as used herein, is intended to refer to an antibody that is substantially free of other mAbs having different antigenic specificities (e.g., 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 BIACORETM 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 antibodyantigen 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 (e.g., 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 prop-

erties 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: 5 lysine, arginine, 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, phenylalaninetyrosine, 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 15 having a nonnegative value in the PAM250 log-likelihood

Sequence similarity for polypeptides is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity 20 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 25 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 30 Version 6.1. FASTA (e.g., 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 35 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 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 polypep- 45 tide 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 50 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 55 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). 60 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 65 of IgG2 mAbs; and Q15R, N44S, K52N, V57M, R69K, E79Q, and V82I (by IMGT; Q355R, N384S, K392N,

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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.

(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 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 10 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, 15 752, 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 20 (e.g., 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 25 (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: 30 487-496) (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 35 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 anti- 45 bodies (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 50 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 55 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 60 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 65 epitope within the fragment from about 153 to about 208, from about 200 to about 260, from about 250 to about 300,

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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 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 (~1×10⁻⁹ M to ~410×10⁻⁹ 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 ($\sim 0.7 \times 10^{-9} \mathrm{M}$ to $\sim 36 \times 10^{-9} \mathrm{M}$) 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 following 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 15 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 20 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 25 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 30 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 35 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 (e.g., peptide mutation 45 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 50 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 60 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 65 comprises at least one mutation of a residue at a position selected from the group consisting of 366. In one specific

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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 (e.g., 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 O15R. 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.

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 or antibody frag-

ment 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 5 extent of absorption do not show a significant difference when administered at the same molar dose under similar experimental conditions, either single does or multiple dose. Some antibodies will be considered equivalents or pharmaceutical alternatives if they are equivalent in the extent of their 10 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 medi- 15 cally 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 20 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 25 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 35 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 40 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 termial 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 invention provides therapeutic methods for treating a human patient in need of a composition of the invention. While modifications in lifestyle and conventional drug treatment are often successful in reducing cholesterol levels, not 55 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 famil- 60 ial hypercholesterolemia (hoFH, heFH) is a condition 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 65 LDL-C by inhibiting cholesterol synthesis and upregulating the hepatic LDL receptor, may have little effect in patients

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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.

Specific populations treatable by the therapeutic methods of the invention include patients indicated for LDL apheresis, subjects with PCSK9-activating (GOF) mutations, 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.

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 LIPOFECTINTTM), 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 (e.g., oral mucosa, rectal and intestinal

mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or

The pharmaceutical composition can be also delivered in a vesicle, in particular a liposome (see Langer (1990) Science 5 249:1527-1533; Treat et al. (1989) in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez Berestein and Fidler (eds.), Liss, N.Y., pp. 353-365; Lopez-Berestein, ibid., pp. 317-327; see generally ibid.).

In certain situations, the pharmaceutical composition can 10 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 dissolv- 25 ing, 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 (e.g., propylene glycol, polyethylene glycol), a nonionic surfactant [e.g., polysorbate 80, HCO-50 (polyoxyethylene (50 mol) adduct of hydrogenated castor 35 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 40 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 45 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 dis- 50 carded 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 55 tigrade, and pressure is at or near atmospheric. 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 pharma- 60 ceutical 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), HUMA-LOG MIX 75/25TM pen, HUMALOGTM pen, HUMALIN 65 70/30TM pen (Eli Lilly and Co., Indianapolis, Ind.), NOVOPENTMI, II and III (Novo Nordisk, Copenhagen, Den22

mark), NOVOPEN JUNIORTM (Novo Nordisk, Copenhagen, Denmark), BDTM pen (Becton Dickinson, Franklin Lakes, N.J.), OPTIPENTTM, OPTIPEN PROTM, OPTIPEN STAR-LETTM, and OPTICLIKTTM (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 FLEXPENTM (Novo Nordisk), and the KWIKPENTM (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. The amount of the aforesaid antibody contained is generally about 5 to about 500 mg per dosage form in a unit dose; especially in the form of injection, it is preferred that the aforesaid antibody is contained in about 5 to about 100 mg 20 and in about 10 to about 250 mg for the other dosage forms.

The invention provides therapeutic methods in which the antibody or antibody fragment of the invention is useful to treat hypercholesterolemia associated with a variety of conditions involving hPCSK9. The anti-PCSK9 antibodies or antibody fragments of the invention are particularly useful for the treatment of hypercholesterolemia and the like. Combination therapies may include the anti-PCSK9 antibody of the invention with, for example, one or more of any agent that (1) induces a cellular depletion of cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl (HMG)-coenzyme A (CoA) reductase, such as cerivastatin, atorvastatin, simvastatin, pitavastatin, rosuvastatin, fluvastatin, lovastatin, pravastatin; (2) inhibits cholesterol uptake and or bile acid re-absorption; (3) increase lipoprotein catabolism (such as niacin); and activators of the LXR transcription factor that plays a role in cholesterol elimination such as 22-hydroxycholesterol or fixed combinations such as ezetimibe plus simvastatin; a statin with a bile resin (e.g., cholestyramine, colestipol, colesevelam), a fixed combination of niacin plus a statin (e.g., niacin with lovastatin); or with other lipid lowering agents such as omega-3-fatty acid ethyl esters (for example, oma-

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 Cen-

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, 5 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 U.S. 2007/0280945A1, 10 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-express- 15 ing 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 sequenced. The predicted amino acid sequences of the vari- 25 able 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

	INDEE 1							
	Heavy Cha	ain Variable F	Region	Light Chain Var	riable Region			
Antibody	VH	D	ЈН	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			
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			
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			
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			
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 65 biosensor surface plasmon resonance assay (BIACORETM T100). Each antibody was captured at a flow rate of 4 μl/min

for 90 sec on a goat anti-mouse IgG polyclonal antibody surface created through direct chemical coupling to a BIA-CORETM 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 d/min for 300 sec, and antigenantibody dissociation was monitored for 15 min at either 25° C. or 37° C. $(K_D = pM; T_{1/2} = min)$.

TABLE 2

	25°	25° C.		C.
Antibody	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
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 (BIACORETM 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 BIACORETM chip to form a captured antibody surface. Human PCSK9mmh 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

45		25°	25° C.		C.	
	Antibody	\mathbf{K}_D	T _{1/2}	\mathbf{K}_D	T _{1/2}	
	H1H313P	244	230	780	60	
	H1H314P	3990	65	3560	43	
50	H1H315P	129	151	413	35	
50	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	
55	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 60 described above.

TABLE 4

Antibody	kd (1/s)	T _{1/2} (min)
H1H313P	2.92×10^{-5}	396
H1H318P	3.69×10^{-3}	3

15

45

26 TABLE 6

Antibody	kd (1/s)	T _{1/2} (min)
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 $_{20}$ 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) and H1M300N ("300N") (HCVR/LCVR SEQ ID NO: 218/ 25 226; 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 $^{-30}$ 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 antigenantibody 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

THE C								
2		High hPCSK9 Density Surface					PCSK9 Surface	•
	рН 7	pH 7.4 pH 5.5 pI		pH 7.4pH		5.5		
Antibody	\mathbf{K}_{D}	T _{1/2}	\mathbf{K}_D	T _{1/2}	K_D	T _{1/2}	\mathbf{K}_D	T _{1/2}
316P 300N Control I	191 65 20000	74 507 29	144 1180 ND	83 26 ND	339 310 ND	45 119 ND	188 1380 ND	58 13 ND

The antigen binding properties of 316P and 300N at pH 7.4 or pH 5.5 were determined by a modified BIACORETM assay 50 as described above. Briefly, mAbs were immobilized onto BIACORETM 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), 55 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 60 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 65 observed under the experimental condition) (K_D=pM; $T_{1/2} = min$).

	pH Effect at 25° C.							
		рН	7.4	рН	5.5			
	Antigen	K_D	T _{1/2}	\mathbf{K}_D	T _{1/2}			
			31	6P				
)	hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh	1260 4460 2490 1420 8350 24100	36 10 15 42 8	22 63 166 8 87 349	39 11 13 23 8 5			
			300	ON				
;	hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh hPCSK9-mmh hPCSK9-mmh hPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh mfPCSK9-mmh	1100 NB 1310 2170 NB NB 33100 NB 71000 362000 NB NB	76 NB 46 31 NB NB Cont 14 NB 11 0.2 NB NB NB Cont	1740 NB 7320 67200 NB NB	5 NB 3 0.4 NB NB 31 NB 30 NB NB			
)	hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh	143 3500 191 102 6500 22400	266 11 155 262 3 2	2 33 49 12 ND 106	212 12 56 63 ND 5			

TABLE 7

pH Effect at 37° C.					
	pH 7	7.4 .	pH 5.5		
Antigen	K_D	T _{1/2}	\mathbf{K}_{D}	T _{1/2}	
		316	P		
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	
		Contro	ol 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	
Colb iiiiiii	100	12,	21.	0.5	

pH Effect at 37° C.						
	pH 7	pH 5.5				
Antigen	\mathbf{K}_D	T _{1/2}	K_D	$T_{1/2}$		
maPCSK9-h rPCSK9p-mmh	8830 30200	0.5 1	ND 233	ND 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 20 antibody surface created through direct chemical coupling to a BIACORETM 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 a flowrate of 50 µl/min for 5 min, and the dissociation of 25 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

TABLE 8						
Antibody	\mathbf{K}_D	T _{1/2}				
316P	1780	14				
300N	1060	49				
Control I	23600	25				
Control II	66	216	35			
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-CORETM2000. Tagged (myc-myc-his) human PCSK9, 45 human PCSK1 (hPCSK1) (SEQ ID NO:759), human PCSK7 (hPCSK7) (SEQIDNO: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 $_{50}$ 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, mPCSK9mmh, 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. 60

Example 7

Cross-Reactivity of Anti-hPCSK9 mAbs

Cross-reactivity of anti-hPCSK9 mAbs with mmPCSK9. mfPCSK9, mPCSK9, maPCSK9, or rPCSK9 was determined 28

using BIACORETM3000. Briefly, anti-hPCSK9 mAbs were captured on an anti-hFc surface created through direct chemical coupling to a BIACORETM 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								
	37°	C	25° C.					
Antigen	\mathbf{K}_{D}	T _{1/2}	\mathbf{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				
mPCSK9-mmh	4700	3	2300	11				
maPCSK9-h	19000	1	6810	5				
rPCSK9-mmh	37500	1	14500	2				

TABLE 10

	300N mAb	1		
	37°	C	25° C.	
Antigen	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 m	ıAb		
	37° (C	25° C.	
Antigen	K_D	$T_{1/2}$	\mathbf{K}_D	$\mathrm{T}_{1/2}$
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 m	ıAb		
	37°	С.	25° C.	
Antigen	\mathbf{K}_D	T _{1/2}	\mathbf{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

Control III mAb								
	37° C.		25° C.					
Antigen	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				
maPCSK9-h	780	107	2100	67				
rPCSK9-mmh	NB	NB	33200	2				

pre-mixed with varied amounts of antibody, ranging from 0 to $\sim\!\!50$ 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. IC $_{50}$ 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

	pH 7.2			pH 5.5			
	Plate Coati			ing Surface			
Ab	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	

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 35 domain (amino acids 313-355 of SEQ 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 BIACORETM 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 antibodyantigen 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 antihPCSK9 mAbs to hLDLR-ecto, EGF-A-hFc, or EGF-AB- 50 hFc were determined. Results show that H1H316P and H1M300N blocked the binding of hPCSK9-mmh to hLDLRecto, 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 55 blocked the binding of hPCSK9-mmh to hLDLR EGF-A

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 preequilibrated with varying concentrations of anti-hPCSK9 mAbs. A constant amount of hPCSK9-mmh (500 pM) was

The ability of the mAbs to block hPCSK9 GOF mutant hPCSK9(D374Y)-mmh binding to hLDLR EGF-A domain or hLDLR EGF-AB domain ($\rm IC_{50}$ 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

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

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 describe above using a constant amount of 1 nM of mmh-tagged mmPCSK9 or 1 nM of mPCSK9.

TABLE 16

	1 nM n	nmPCSK9-i	1 nM mPC	SK9-mmh	
	hLDLR-ecto	EGF-A	EGF-AB	EGF-A	EGF-AB
316P 300N	<250 255	<250 256	<250 290	<250 >33000	<250 >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 mPCSK9-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

>10000

<125

223

154

390

316P

300N

Control I

Control II

Control III

mmPCSK9 rPCSK9 mPCSK9 maPCSK9 <250 42880 3704 >100000 >100000 >100000 >100000 >100000 >100000 >100000 <250 11640 8339 2826

>100000

The ability of 316P and Control Ito block hPCSK9 binding 20 to hLDLR was also determined. Briefly, either recombinant hLDLR or hLDLR-EGFA-mFc was immobilized onto BIA-CORETM 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 25 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 40 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) (mPromCat-hC-term-mmh). In addition, hPCSK9 with a point mutation of D374Y (hPCSK9 (D374Y)-mmh) was gener-

Binding specificity of mAbs to test proteins hPCSK9- 60 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 65 detected using HRP-conjugated anti-myc polyclonal antibody (++=OD>1.0; +=OD 0.4-1.0; -=OD<0.4).

TABLE 19

				Chimer	ric Pro	tein	
15	Antibody	hPCSK9	mPCSK9	#1	#2	#3	hPCSK9(D374Y)
	H1M300	++	-	++	+	_	++
	H1M309	++	-	_	_	++	++
	H1M312	++	-	_	_	++	++
20	H1M492	++	_	_	_	-	+
	H1M493	++	-	-	_	++	++
	H1M494	++	-	_	+	++	++
	H1M495	++	-	-	_	++	++
2.5	H1M496	++	-	-	_	++	++
25	H1M497	++	-	-	++	+	++
	H1M498	++	-	_	-	+	++
	H1M499	++	-	-	_	++	++
	H1M500	++	-	++	-	-	++
30	H1M502	++	-	-	-	++	++
50	H1M503	++	-	_	++	-	++
	H1M504	++	-	-	-	-	+
	H1M505	++	-	++	+	-	++
	H1M508	++	-	-	-	++	++
35	H1H318P	++	-	++	-	-	++
	H1H334P	++	-	++	-	-	++
	H1H316P	++	++	++	++	++	++
	H1H320P	++	-	_	++	-	++
	Control I	++	-	-	-	++	++
40							

Binding specificity of 316P, 300N and control antihPCSK9 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	++ ++ ++ ++	++ - ++	++ - ++ ++	++ ++ ++ ++	++ ++ ++ ++
rPCSK9-mmh Chimeric Protein #1 Chimeric Protein #2 Chimeric Protein #3 hPCSK9 (D374Y)	++ ++ ++ ++ ++	- ++ ++ + +	- - - ++ ++	++ ++ ++ ++	+ ++ ++ ++ ++

Similar results for selected mAbs were obtained by BIA-CORETM 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.

		_	Chimeric Protein					
Antibody	hPCSK9	mPCSK9	#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 10 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 15 each well followed by 1 hr incubation at RT. 316P (1 µg/ml) was added and incubated for another hour at RT. Plate-bound 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 anti-body specific for chimeric protein #1.

Example 10

BIACORETM-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

		Second mAb								
First 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 60 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 65 medium. Data are expressed as IC_{50} values for each experiment (IC_{50} =antibody concentration at which increases LDL

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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 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)-	2.1	1.1	>50	0.7	0.6
mmh					
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 H1M300N 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 H1M300N 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 Treatment 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 30 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 35 by specific procedures (e.g., 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 40 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 45 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 50 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 55 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. 60 Whenever possible, blood was collected via a single draw and then divided appropriately.

PK Study. Blood samples (1.5 ml) were collected at predose, 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 65 (SST). Specimen storage serum is transferred to 2 vials and stored at -60° C. or below.

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Serum samples were analyzed using an optimized ELISA (enzyme-linked immunosorbant 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).

TABLE 25

	3	16P	300N			
PK Parameter	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} (µg/ml)	184	527	226	1223		
$T_{1/2}(h)$	83	184	215	366		

Serum Chemistry. Blood samples were collected at predose, 12 hr, 48 hr, and subsequently once every 48 hr, for clinical chemistry analysis, in particular lipid profiles (i.e. 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 (TCho); 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 (~35%, FIG. 3). A robust decrease of ~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 (~10-15% reduction) and LDL-C (~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 func-

tion as determined by ALT and AST measurements. All animals receiving an anti-PCSK9 antibody in the study exhibited a rapid suppression If LDL-C and total cholesterol.

A similar LDL-C lowering effect of 316P and 300N was also observed in cynomolgous 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 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 46	84 63
$\mathrm{C}_{max}\left(\mu\mathrm{g/ml} ight) \ \mathrm{T}_{1/2}\left(\mathrm{h} ight)$	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 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 i.p.) 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 (predict) 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 1,316P, 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 µg/ml for C57BL/6 mice and 55-196 µg/ml for hPCSK9 heterozygous mice. At Day 56, Control I mAb levels were about 12 µg/ml and 300N levels were about 11 µg/ml whereas 316P levels were about less than 0.02 μg/ml in C57BL/6 mice. At Day 56 in hPCSK9 heterozygous mice, Control I mAb levels were about 29 µg/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 μ 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×10⁻⁹; $T_{1/2}$ =min; WT=wildtype).

TABLE 27

	316P		300N		Control I		Control II		Control III	
	\mathbf{K}_{D}	T _{1/2}	K_D	T _{1/2}	\mathbf{K}_{D}	T _{1/2}	\mathbf{K}_{D}	T _{1/2}	\mathbf{K}_D	T _{1/2}
WT P70 A	1.00 1.42		0.69 1.68		30.6 19.0					

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TABLE 27-continued

	316	P	300)N_	Cont	trol I	Cont	rol II	Cont	rol III
	${\bf K}_D$	T _{1/2}	\mathbf{K}_D	T _{1/2}	\mathbf{K}_D	T _{1/2}	${\bf K}_D$	T _{1/2}	K_D	T _{1/2}
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 $\rm K_D$ of $\rm 1\times10^{-9}$ M to $\rm 410\times10^{-9}$ M; and $\rm T_{12}$ shortened about 30-fold, from 37 to 1 min, indicating that 316P binds an epitope on hPCSK9 comprising D238 of hPCSK9 (SEQ ID 30 NO:755). Additionally, BIACORETM assays show that 316P binding affinity and $\rm T_{1/2}$ were reduced about 5- to 10-fold when a residue at 153, 159 or 343 was mutated. Specifically, $\rm K_D$ was reduced from about $\rm 1\times10^{-9}$ M to between about 5-8×10⁻⁹ M when any one of S153, E159 or D343 were 35 mutated; while $\rm T_{1/2}$ 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 $\rm K_D$ of from about $\rm 0.7\times10^{-9}$ M to about $\rm 36\times10^{-9}$ M 40 and a shorter $\rm T_{1/2}$ 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 BIA-CORETM assays show that 300N binding affinity and $\rm T_{1/2}$ were reduced between 2- to >10-fold when a residue at 147 or 380 was mutated. Specifically, $\rm K_D$ was reduced from about $\rm 0.69\times10^{-9}$ M to between about 2-9×10⁻⁹ M when any of S147 or V380 were mutated; while $\rm T_{12}$ 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) 55 (from ~0.1×10⁻⁹ to ~4.5×10⁻⁹), 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 ~0.6×10⁻⁹ to ~5.9×10⁻⁹, 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 variant 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 anti-body (-=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 deliv-

ered 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 sassessed 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.

60

120

180

240

300

351

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<210> SEQ ID NO 6
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 6
Ile Gly Ser Thr Gly Asp Thr
<210> SEQ ID NO 7
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 7
gtaagagagg ggtgggaggt accetttgac tac
                                                                        33
<210> SEQ ID NO 8
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 8
Val Arg Glu Gly Trp Glu Val Pro Phe Asp Tyr
<210> SEQ ID NO 9
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 9
gacatccaga tgacccagtc tccagccacc ctgtctgtgt ctccagggga aagagccgcc
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ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca ccagaaacct
                                                                       120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
                                                                       180
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aggttcagtg gcattgggtc tgggacagag ttcactctca ttatcagcag cctgcagtct
gaagattttg cattttattt ctgtcagcag tataataact ggcctccatt cactttcggc
cctgggacca aggtggagat caaacga
<210> SEQ ID NO 10
<211> LENGTH: 109
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 10
Asp Ile Gln Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
                                    10
Glu Arg Ala Ala Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
Leu Ala Trp Tyr His Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
                            40
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
                        55
Ile Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Ser
                   70
Glu Asp Phe Ala Phe Tyr Phe Cys Gln Gln Tyr Asn Asn Trp Pro Pro
Phe Thr Phe Gly Pro Gly Thr Lys Val Glu Ile Lys Arg
<210> SEQ ID NO 11
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 11
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cagagtgtta gcagcaac
<210> SEQ ID NO 12
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 12
Gln Ser Val Ser Ser Asn
<210> SEQ ID NO 13
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 13
ggtgcatcc
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<210> SEQ ID NO 14
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 14
Gly Ala Ser
<210> SEQ ID NO 15
<211> LENGTH: 30
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 15
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cagcagtata ataactggcc tccattcact
<210> SEO ID NO 16
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 16
Gln Gln Tyr Asn Asn Trp Pro Pro Phe Thr
<210> SEQ ID NO 17
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 17
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt tactctaagt agttacgaca tgcactgggt ccgccaatct
acaggaaaag gtctggagtg ggtctcagct attggttcta ccggtgacac atactatcca
ggctccgtga agggccgatt caccatcacc agagaaaaag ccaagaactc cgtgtatctt
                                                                      240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgtaag agaggggtgg
gaggtaccct ttgactactg gggccaggga accctggtca ccgtctcctc a
<210> SEQ ID NO 18
<211> LENGTH: 117
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 18
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1
                                    1.0
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Ser Thr Gly Lys Gly Leu Glu Trp Val
        35
                            40
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
                        55
Gly Arg Phe Thr Ile Thr Arg Glu Lys Ala Lys Asn Ser Val Tyr Leu
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Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val Arg Glu Gly Trp Glu Val Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu 105 Val Thr Val Ser Ser <210> SEQ ID NO 19 <211> LENGTH: 324 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 19 qaaataqtqa tqacqcaqtc tccaqccacc ctqtctqtqt ctccaqqqqa aaqaqccqcc 60 ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca ccagaaacct 120 ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180 aggttcagtg gcattgggtc tgggacagag ttcactctca ttatcagcag cctgcagtct 240 gaagattttg cattttattt ctgtcagcag tataataact ggcctccatt cactttcggc 300 cctgggacca aagtggatat caaa 324 <210> SEQ ID NO 20 <211> LENGTH: 108 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 20 Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Arg Ala Ala Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala Trp Tyr His Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ile Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Ser Glu Asp Phe Ala Phe Tyr Phe Cys Gln Gln Tyr Asn Asn Trp Pro Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys 100 <210> SEO ID NO 21 <211> LENGTH: 351 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 21 gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc 60 teetgtgeag eetetggatt taetetaagt agttaegaea tgeactgggt eegeeaaget acaggaaaag gtctggagtg ggtctcagct attggttcta ccggtgacac atactatcca 180 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt

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caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgtaag agaggggtgg gaggtaccct ttgactactg gggccaggga accctggtca ccgtctcctc a <210> SEQ ID NO 22 <211> LENGTH: 117 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 22 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr 25 Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val 40 Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys 55 Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu 70 Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val Arg Glu Gly Trp Glu Val Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu 105 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 ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240 gaagattttg cagtttatta ctgtcagcag tataataact ggcctccatt cactttcggc 300 cctgggacca aagtggatat 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 1.0 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn 25 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile 40 Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly

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55 Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys <210> SEQ ID NO 25 <211> LENGTH: 342 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 25 caggtgcagc tggtgcagtc tgggggaggc gtggtccagc ctggggaggtc cctgagactc 60 teetgtgeag egtetggatt eacetteagt agetatggea tgeactgggt eegeeagget 120 ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatacattat 180 ggagactccg tgagggccg aatcatcata tccagagaca attccgagaa cacgttgtat 240 ctggaaatga acagcctgag agccgaggac acggcaatgt actattgtgc gagagagaag 300 ggtttagact 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 Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Phe Ile Gly Phe Asp Gly Ser Asn Ile His Tyr Gly Asp Ser Val Arg Gly Arg Ile Ile Ile Ser Arg Asp Asn Ser Glu Asn Thr Leu Tyr Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys Ala Arg Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Thr Val Thr Val 100 105 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

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<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
<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
                                                                       2.4
<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
<210> SEQ ID NO 31
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 31
                                                                       21
gcgagagaga agggtttaga c
<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
<210> SEQ ID NO 33
<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 33
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                                                                       60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
                                                                      120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
                                                                      180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
                                                                      240
gatgattttg caacttatta ctgccaacag tataatagtt attacacttt tggccagggg
                                                                      300
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accaaggtgg aaatcaaacg a
                                                                      321
<210> SEQ ID NO 34
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 34
Ala Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Tyr Thr
               85
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100
<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
<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
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Lys Ala Ser
<210> SEQ ID NO 39
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 39
                                                                       24
caacaqtata ataqttatta cact
<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> SEOUENCE: 41
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
                                                                       60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct
                                                                      120
ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatacattat
ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat
ctggaaatga acagcctgag agccgaggac acggcaatgt actattgtgc gagagagaag
ggtttagact ggggccaggg aaccetggte accgteteet ca
<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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                            40
Ala Phe Ile Gly Phe Asp Gly Ser Asn Ile His Tyr Gly Asp Ser Val
Arg Gly Arg Ile Ile Ile Ser Arg Asp Asn Ser Glu Asn Thr Leu Tyr
                    70
Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys
Ala Arg Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Leu Val Thr Val
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            100
                                105
                                                    110
Ser Ser
<210> SEQ ID NO 43
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 43
qacatccaqa tqacccaqtc tccttccacc ctqtctqcat ctqtaqqaqa caqaqtcacc
                                                                      60
                                                                     120
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
                                                                     240
gatgattttg caacttatta ctgccaacag tataatagtt attacacttt tggccagggg
                                                                     300
                                                                     318
accaagctgg agatcaaa
<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
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                            40
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Tyr Thr
Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
           100
<210> SEQ ID NO 45
<211> LENGTH: 342
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 45
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
                                                                      60
teetgtgeag cetetggatt cacetteagt agetatggea tgeactgggt cegecagget
                                                                     120
ccaggcaagg ggctggagtg ggtggcagtt ataggatttg atggaagtaa tatatactat
                                                                     180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat
                                                                     240
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ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagagaag

ggtttagact ggggccaggg aaccctggtc accgtctcct ca

300

342

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<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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                           40
Ala Val Ile Gly Phe Asp Gly Ser Asn Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Leu Val Thr Val
                               105
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 tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tataatagtt attacacttt tggccagggg
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
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                           40
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Tyr Thr
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Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys <210> SEQ ID NO 49 <211> LENGTH: 342 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 49 caggtgcagc tgcaggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60 tectqtqcaq eqtetqqatt cacettcaqt aqetatqqca tqcactqqqt ceqecaqqet 120 ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatatattat 180 ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat 240 ctggaaatga acagcctgag agccgaggac acggcagtgt attattgtgc gagagagaag 300 ggtttagact ggggccaggg aaccetggte actgteteet 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 Val Val Gln Pro Gly Arg 10 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Phe Ile Gly Phe Asp Gly Ser Asn Ile Tyr Tyr Gly Asp Ser Val Arg Gly Arg Ile Ile Ile Ser Arg Asp Asn Ser Glu Asn Thr Leu Tyr Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Leu Val Thr Val 105 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

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Gly Phe Thr Phe Ser Ser Tyr Gly
<210> SEQ ID NO 53
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 53
                                                                        24
ataggatttg atggaagtaa tata
<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
<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
<210> SEQ ID NO 57
<211> LENGTH: 342
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 57
gccatccaga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc
                                                                        60
atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagtt
                                                                       120
tggtatcagc agaaaccagg acagceteet aagttgetee tttactggge etetaceegg
                                                                       180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc
                                                                       240
atcagcagcc tgcaggctga agatgtggca aattattact gtcaccaata ttacagtatt
                                                                       300
ccgtggacgt tcggccaagg gaccaaggtg gagatcaaac ga
                                                                       342
<210> SEQ ID NO 58
```

<210> SEQ 1D NO 58

-continued <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 Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Phe His Thr Ser Asn Asn Lys Asn Tyr Leu Val Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Asn Tyr Tyr Cys His Gln Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile 100 105 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 <210> SEQ ID NO 61 <211> LENGTH: 9 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 61 9 tgggcctct <210> SEQ ID NO 62 <211> LENGTH: 3 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic

Trp Ala Ser

<400> SEQUENCE: 62

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<210> SEQ ID NO 63
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 63
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
<210> SEQ ID NO 65
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 65
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
                                                                     60
teetgtgeag egtetggatt eacetteagt agetatggea tgeactgggt eegeeagget
                                                                    120
ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatatattat
ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat
                                                                     240
ctggaaatga acagcctgag agccgaggac acggcagtgt attattgtgc gagagagaag
ggtttagact ggggccaggg aaccetggte accgteteet 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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                           40
Ala Phe Ile Gly Phe Asp Gly Ser Asn Ile Tyr Tyr Gly Asp Ser Val
Arg Gly Arg Ile Ile Ile Ser Arg Asp Asn Ser Glu Asn Thr Leu Tyr
Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Leu Val Thr Val
                               105
```

Ser Ser

-continued

```
<210> SEQ ID NO 67
<211> LENGTH: 339
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 67
gacategtga tgacceagte tecagactee etggetgtgt etetgggega gagggeeace
                                                                      60
atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagtt
                                                                     120
tqqtatcaqc aqaaaccaqq acaqcctcct aaqttqctcc tttactqqqc ctctacccqq
                                                                     180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc
                                                                     240
atcagcagcc tgcaggctga agatgtggca aattattact gtcaccaata ttacagtatt
                                                                     300
                                                                     339
ccgtggacgt tcggccaagg gaccaaggtg gaaatcaaa
<210> SEO ID NO 68
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 68
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
                                    10
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Phe His Thr
Ser Asn Asn Lys Asn Tyr Leu Val Trp Tyr Gln Gln Lys Pro Gly Gln
Pro Pro Lys Leu Leu Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Asn Tyr Tyr Cys His Gln
Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
                               105
Lys
<210> SEQ ID NO 69
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 69
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
                                                                      60
teetgtgeag cetetggatt cacetteagt agetatggea tgeactgggt cegecagget
                                                                     120
ccaggcaagg ggctggagtg ggtggcagtt ataggatttg atggaagtaa tatatactat
                                                                     180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat
                                                                     240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagagaag
                                                                     300
ggtttagact ggggccaggg aaccetggte accgteteet ca
                                                                     342
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<210> SEQ ID NO 70 <211> LENGTH: 114

-continued

<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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Gly Phe Asp Gly Ser Asn Ile Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Lys Gly Leu Asp Trp Gly Gln Gly Thr Leu Val Thr Val 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 atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagct tggtaccagc agaaaccagg acagceteet aagetgetea tttactggge etetaceegg gaatcogggg toootgacog attoagtggc agogggtotg ggacagattt cactotcaco atcagcagcc tgcaggctga agatgtggca gtttattact gtcaccaata ttacagtatt ccgtggacgt tcggccaagg gaccaaggtg gaaatcaaa <210> SEQ ID NO 72 <211> LENGTH: 113 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 72 Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly 10 Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Phe His Thr 25 Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gl
n Ala Glu Asp Val Ala Val Tyr Tyr Cys His Gl
n $\,$ 90

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Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
<210> SEQ ID NO 73
<211> LENGTH: 354
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 73
gaagtgcagc tggtgcagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt cacctttaac aactatgcca tgaactgggt ccgccaggct
                                                                      120
ccaggaaagg gactggactg ggtctcaact attagtggta gcggtggtac tacaaactac
                                                                      180
gcagactccg tgaagggccg tttcattatt tcccgagaca gttccaaaca cacgctgtat
                                                                      240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct
                                                                      300
aactggggaa atttcgatct ctggggccgt 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
                                  10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asn Tyr
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp Val
Ser Thr Ile Ser Gly Ser Gly Gly Thr Thr Asn Tyr Ala Asp Ser Val
Lys Gly Arg Phe Ile Ile Ser Arg Asp Ser Ser Lys His Thr Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Lys Asp Ser Asn Trp Gly Asn Phe Asp Leu Trp Gly Arg Gly Thr
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
                                                                       24
ggattcacct ttaacaacta tgcc
<210> SEO ID NO 76
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 76
Gly Phe Thr Phe Asn Asn Tyr Ala
<210> SEQ ID NO 77
<211> LENGTH: 24
<212> TYPE: DNA
<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
<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
<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 tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc
                                                                        60
atcaactgca agtccagcca gagtgtttta tacaggtcca acaataggaa cttcttaggt
                                                                       120
tggtaccagc agaaaccagg gcagcctcct aatctactca tttactgggc atctacccgg
                                                                       180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc
                                                                       240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcaacaata ttatactact
                                                                       300
ccgtacactt ttggccaggg gaccaaggtg gaaatcaaac ga
                                                                       342
```

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<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
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Arg
Ser Asn Asn Arg Asn Phe Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln
Pro Pro Asn Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val_{50}
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
Tyr Tyr Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
           100
                               105
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
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 84
Gln Ser Val Leu Tyr Arg Ser Asn Asn Arg Asn Phe
<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
<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
caacaatatt atactactcc gtacact
<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
                - 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 tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt cacctttaac aactatgcca tgaactgggt ccgccaggct
ccaggaaagg gactggactg ggtctcaact attagtggta gcggtggtac tacaaactac
gcagactccg tgaagggccg tttcattatt tcccgagaca gttccaaaca cacgctgtat
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct
aactggggaa atttcgatct ctggggccgt ggcaccctgg tcactgtctc ctca
<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
                                    10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asn Tyr
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp Val
Ser Thr Ile Ser Gly Ser Gly Gly Thr Thr Asn Tyr Ala Asp Ser Val
Lys Gly Arg Phe Ile Ile Ser Arg Asp Ser Ser Lys His Thr Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Lys Asp Ser Asn Trp Gly Asn Phe Asp Leu Trp Gly Arg Gly Thr
Leu Val Thr Val Ser Ser
```

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<210> SEQ ID NO 91

<211> LENGTH: 339

115

<212> TYPE: DNA

<213 > ORGANISM: Artificial Sequence

<220> FEATURE:

<223 > OTHER INFORMATION: Synthetic

<400> SEQUENCE: 91

gacategtga tgacceagte tecagaetee etggetgtgt etetgggega gagggeeace 60 atcaactqca aqtccaqcca qaqtqtttta tacaqqtcca acaataqqaa cttcttaqqt 120 tggtaccage agaaaccagg geagesteet aatstactea tttactggge atstaccegg 180 gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240 atcagcagcc tgcaggctga agatgtggca gtttattact gtcaacaata ttatactact 300 339 ccgtacactt ttggccaggg gaccaagctg gagatcaaa

<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

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Arg 25

Ser Asn Asn Arg Asn Phe Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln

Pro Pro Asn Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val

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

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln

Tyr Tyr Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile

Lys

<210> SEQ ID NO 93

<211> LENGTH: 354

<212> TYPE: DNA

<213 > ORGANISM: Artificial Sequence

<220> FEATURE:

<223 > OTHER INFORMATION: Synthetic

<400> SEOUENCE: 93

gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc 60 teetgtgeag cetetggatt cacetttaac aactatgeea tgagetgggt cegecagget 120 ccagggaagg ggctggagtg ggtctcagct attagtggta gcggtggtac tacatactac 180 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240 ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct 300 aactggggaa atttcgatct ctggggccgt ggcaccctgg tcactgtctc ctca 354

-continued

<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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asn Tyr 25 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 40 Ser Ala Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val 55 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Asp Ser Asn Trp Gly Asn Phe Asp Leu Trp Gly Arg Gly Thr 100 105 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 gacategtga tgacceagte tecagactee etggetgtgt etetgggega gagggeeace atcaactgca agtccagcca gagtgtttta tacaggtcca acaataggaa cttcttagct tggtaccage agaaaccagg acagecteet aagetgetea tttactggge atetaccegg gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240 atcaqcaqcc tqcaqqctqa aqatqtqqca qtttattact qtcaacaata ttatactact 339 ccqtacactt ttqqccaqqq qaccaaqctq qaqatcaaa <210> SEQ ID NO 96 <211> LENGTH: 113 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 96 Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly 5 1.0 Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Arg Ser Asn Asn Arg Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln 40 Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 70

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Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
Tyr Tyr Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
                       105
Lys
<210> SEQ ID NO 97
<211> LENGTH: 351
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 97
caggtgcagc tggtgcagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
                                                                     120
tcctqtqcaq tctctqqatt caccctcaqt aqctacqata tqcactqqqt ccqccaacct
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 ccgtctcctc 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
                                    10
Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Thr Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Pro Thr Gly Lys Gly Leu Glu Trp Val
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
Arg Glu Gly Trp Asp Val Pro Phe Asp Phe Trp Gly Gln Gly Thr Leu
           100
                               105
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
ggattcaccc tcagtagcta cgat
                                                                      24
<210> SEQ ID NO 100
<211> LENGTH: 8
<212> TYPE: PRT
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 100
Gly Phe Thr Leu Ser Ser Tyr Asp
<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
<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 accetttgac 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
<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 tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc
                                                                        60
atcacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca
                                                                       120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tacaaagtgg ggtcccatca
                                                                       180
cggttcagcg gcagtggatc tggcacagat ttcactctca ccatcagcag cctgcagcct
                                                                       240
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa
                                                                       300
gggaccaagg tggagatcaa acga
                                                                       324
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<210> SEQ ID NO 106
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 106
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Arg Asn Asp
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                           40
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
                       55
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Tyr Asn Tyr Pro Trp
               85
                                   90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
           100
<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
<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
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Ala Ala Ser

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1
<210> SEQ ID NO 111
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<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
                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
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                       60
tcctgtgcag tctctggatt caccctcagt agctacgata tgcactgggt ccgccaacct
acaggaaaag gtctggagtg ggtctcagct attggttcta ctggtgacac atactatcca
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggatgg
gacgtaccct ttgacttctg gggccaggga accctggtca ccgtctcctc a
<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
Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Thr Leu Ser Ser Tyr
                                25
Asp Met His Trp Val Arg Gln Pro Thr Gly Lys Gly Leu Glu Trp Val
                           40
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
                        55
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
                    70
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
                                    90
Arg Glu Gly Trp Asp Val Pro Phe Asp Phe Trp Gly Gln Gly Thr Leu
                                105
```

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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
<400> SEQUENCE: 115
gccatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc
                                                                        60
atcacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca
                                                                       120
qqqaaaqccc ctaaqctcct qatctatqct qcatccaqtt tacaaaqtqq qqtcccatca
                                                                       180
cqqttcaqcq qcaqtqqatc tqqcacaqat ttcactctca ccatcaqcaq cctqcaqcct
                                                                       240
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa
                                                                       300
                                                                       321
gggaccaagg tggaaatcaa a
<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
                                     10
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Arg Asn Asp
                                25
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Tyr Asn Tyr Pro Trp
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 117
<211> LENGTH: 351
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 117
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                        60
teetgtgeag cetetggatt cacceteagt agetacgata tgeactgggt cegecaaget
                                                                       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 ccgtctcctc a
                                                                       351
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<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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
Arg Glu Gly Trp Asp Val Pro Phe Asp Phe Trp Gly Gln Gly Thr Leu
                                105
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 tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca
gggaaagccc ctaagctcct gatctatgct gcatccagtt tacaaagtgg ggtcccatca
aggttcagcg gcagtggatc tggcacagat ttcactctca ccatcagcag cctgcagcct
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa
gggaccaagg tggaaatcaa a
<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
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Arg Asn Asp
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                           40
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Tyr Asn Tyr Pro Trp
```

2.4

101 102

-continued Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 <210> SEQ ID NO 121 <211> LENGTH: 384 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 121 caggtgcagc tgcaggagtc ggggccagga ctggtgaagc cttcggagac cctgtccctc 120 acctqcactq tctctqqqqa ctccatcaat acttactact qqaqctqqtt ccqqcaqccc ccagggaagg 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 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Asn Thr Tyr 25 Tyr Trp Ser Trp Phe Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Ile Asp Thr Pro Arg Asn Gln Phe Ser Leu Lys Leu Ile Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Arg Ile Thr Met Ile Arg Gly Val Thr Leu Tyr Tyr Tyr Ser 105 Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 115 <210> SEQ ID NO 123 <211> LENGTH: 24 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 123

ggggactcca tcaatactta ctac

<210> SEQ ID NO 124

<211> LENGTH: 8 <212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 124
Gly Asp Ser Ile Asn Thr Tyr Tyr
<210> SEQ ID NO 125
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 125
                                                                        21
atctattata gtggaaccac c
<210> SEO 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
<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
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
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> SEOUENCE: 129
gacatccaga tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc
                                                                        60
atcacttgct gggccagtca ggacattagc agttatttag cctggtatca gcaaaaacca
                                                                       120
gggatagece ctaageteet gatetatget geatecaett tgcaaagtgg ggteeeatea
                                                                       180
aggttcggcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct
                                                                       240
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```
gaagattttg caacttatta ctgtcaacag cttaatagtt accctcggac gttcggccaa
gggaccaagg tggaaatcaa acga
<210> SEQ ID NO 130
<211> LENGTH: 108
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<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
                                    10
Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Asp Ile Ser Ser Tyr
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Ile Ala Pro Lys Leu Leu Ile
                           40
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Gly Gly
                       55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                    70
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Arg
               85
                                    90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
           100
<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
<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
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<400> SEQUENCE: 134
Ala Ala Ser
<210> SEQ ID NO 135
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 135
                                                                       27
caacagetta atagttacce teggacg
<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
<210> SEQ ID NO 137
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 137
caggtgcagc tgcaggagtc ggggccagga ctggtgaagc cttcggagac cctgtccctc
acctgcactg tctctgggga ctccatcaat acttactact ggagctggtt ccggcagccc
ccagggaagg gactggagtg gattgggtat atctattata gtggaaccac caactacaac
controcted agagingagt carratated atagacange chaggaacca gitteteening
aagctgatct ctgtgaccgc agcggacacg gccgtgtatt actgtgcgag agagaggatt
                                                                      300
actatqattc qqqqaqttac cctctactat tactcctacq qtatqqacqt ctqqqqccaa
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> SEOUENCE: 138
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
                5
                                   1.0
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Asn Thr Tyr
                                25
Tyr Trp Ser Trp Phe Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
                            40
Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
                        55
Ser Arg Val Thr Ile Ser Ile Asp Thr Pro Arg Asn Gln Phe Ser Leu
```

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Lys Leu Ile Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Arg Ile Thr Met Ile Arg Gly Val Thr Leu Tyr Tyr Ser Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <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 gggccagtca ggacattagc agttatttag cctggtatca gcaaaaacca 120 gggatagccc ctaagctcct gatctatgct gcatccactt tgcaaagtgg ggtcccatca 180 aggtteggeg geagtggate tgggacagaa tteaetetea eaateageag eetgeageet 240 gaagattttg caacttatta ctgtcaacag cttaatagtt 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 Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Asp Ile Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Ile Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Gly Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 <210> SEO ID NO 141 <211> LENGTH: 384 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 141 caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60 acctgcactg tctctgggga ctccatcaat acttactact ggagctggat ccggcagccc ccagggaagg gactggagtg gattgggtat atctattata gtggaaccac caactacaac 180 ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg

-continued aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcgag agagaggatt actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa gggaccacgg tcaccgtctc ctca <210> SEQ ID NO 142 <211> LENGTH: 128 <212> TYPE: PRT <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 10 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Asn Thr Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Arg Ile Thr Met Ile Arg Gly Val Thr Leu Tyr Tyr Ser 105 Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <210> SEQ ID NO 143 <211> LENGTH: 321 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 143 gacatecaga tgacecagte tecatectee etgtetgeat etgtaggaga cagagteace atcacttqcc qqqcaaqtca qqacattaqc aqttatttaq qctqqtatca qcaqaaacca gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180 agqttcaqcq qcaqtqqatc tqqqacaqaa ttcactctca caatcaqcaq cctqcaqcct 240 gaagattttg caacttatta ctgtcaacag cttaatagtt accctcggac gttcggccaa 300 321 gggaccaagg tggaaatcaa a <210> SEO 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 10

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr 25

120

180

240

360

378

113 114

-continued

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys <210> SEQ ID NO 145 <211> LENGTH: 378 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 145 caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc tcctqcaaqq cttctqqtta cacctttacc aactatqqta tcaqctqqqt qcqacaqqcc cctggacaag gacttgagtt aatgggatgg attagtggtt acaatggtaa cacaaactat gcacaagaac tccaggccag agtcaccatg accacagaca catccacgag cacagcctac atggagctga ggaacctgag atctgacgac acggccgtat attactgtgc gagagataga gtcgttgtag cagctgctaa ttactacttt tattctatgg acgtctgggg ccaagggacc acggtcaccg tctcctca <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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Met Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Glu Leu Gln Ala Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Arg Val Val Val Ala Ala Ala Asn Tyr Tyr Phe Tyr Ser 100 105 Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <210> SEQ ID NO 147 <211> LENGTH: 24 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 147

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ggttacacct ttaccaacta tggt
                                                                         24
<210> SEQ ID NO 148
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 148
Gly Tyr Thr Phe Thr Asn Tyr Gly
<210> SEQ ID NO 149
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 149
                                                                         2.4
attagtggtt acaatggtaa caca
<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
<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
<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
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 tgacccagtc tccactctcc ctgtccgtca cccttggaca gccggcctcc
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-continued atotootgoa ggtotagtoa aagootogta tacagtgatg gagacacota ottgaattgg tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgctttcac actgaaaatc ageggggtgg aggeegagga tgttggggtt tactactgea tgeaagetae acaetggeet cggacgttcg gccaagggac caaggtggaa atcaaacga 339 <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 1.0 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser 25 Asp Gly Asp Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser 40 Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Lys Ile Ser Gly Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 105 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 caaageeteg tatacagtga tggagacace tac 33 <210> SEQ ID NO 156 <211> LENGTH: 11 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 156 Gln Ser Leu Val Tyr Ser Asp Gly Asp Thr Tyr 5 <210> SEQ ID NO 157 <211> LENGTH: 9 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic

aaggtttct 9

<400> SEQUENCE: 157

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<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
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<223 > OTHER INFORMATION: Synthetic
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Met Gln Ala Thr His Trp Pro Arg Thr
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teetgeaagg ettetggtta cacetttace aactatggta teagetgggt gegacaggee
cctggacaag gacttgagtt aatgggatgg attagtggtt acaatggtaa cacaaactat
                                                                        180
gcacaagaac tccaggccag agtcaccatg accacagaca catccacgag cacagcctac
                                                                        240
atggagctga ggaacctgag atctgacgac acggccgtat attactgtgc gagagataga
                                                                        300
gtegttgtag cagetgetaa ttactaettt tattetatgg aegtetgggg ccaagggace
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acggtcaccg tctcctca
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<212> TYPE: PRT
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Met
                           40
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-continued

Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Glu Leu Gln Ala Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Arg Val Val Val Ala Ala Ala Asn Tyr Tyr Phe Tyr Ser Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <210> SEQ ID NO 163 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 163 gatgttgtga tgactcagtc tccactctcc ctgtccgtca cccttggaca gccggcctcc 60 atctcctgca ggtctagtca aagcctcgta tacagtgatg gagacaccta cttgaattgg 120 tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180 tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgctttcac actgaaaatc 240 ageggggtgg aggeegagga tgttggggtt tactactgea tgeaagetae acaetggeet 300 cggacgttcg gccaagggac caaggtggaa 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 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asp Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Lys Ile Ser Gly Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala 90 Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 105 <210> SEO ID NO 165 <211> LENGTH: 378 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 165

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Gln Pro Ala	Ser Ile Ser Cys . 20	Arg Ser Ser Gln 25	Ser Leu Val Tyr Ser 30							
Asp Gly Asp 35	•	Trp Phe Gln Gln	Arg Pro Gly Gln Ser 45							
Pro Arg Arg 50	Leu Ile Tyr Lys 55	Val Ser Asn Arg	Asp Ser Gly Val Pro							
Asp Arg Phe	Ser Gly Ser Gly 70	Ser Gly Thr Asp 75	Phe Thr Leu Lys Ile 80							
Ser Arg Val	Glu Ala Glu Asp 85	Val Gly Val Tyr 90	Tyr Cys Met Gln Ala 95							
Thr His Trp	Pro Arg Thr Phe	Gly Gln Gly Thr 105	Lys Val Glu Ile Lys 110							
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				120						
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tacageceat c	tctgaagag caggct	cacc atcaccaagg	acacctccaa aaaccaggtg	240						
gtccttacaa t	gaccaacat ggaccc	tgtg gacacagcca	catattactg tgcacacagg	300						
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gtcaccgtct c	ctca			375						
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Thr Leu Thr	Leu Thr Cys Thr 20	Phe Ser Gly Phe 25	Ser Leu Ile Thr Ser 30							
Gly Val Gly 35		Arg Gln Pro Pro 40	Gly Lys Ala Leu Glu 45							
Trp Leu Ala 50	Leu Ile Tyr Trp 55	Asn Gly Asp Lys	Arg Tyr Ser Pro Ser 60							
Leu Lys Ser 65	Arg Leu Thr Ile 70	Thr Lys Asp Thr 75	Ser Lys Asn Gln Val 80							
Val Leu Thr	Met Thr Asn Met . 85	Asp Pro Val Asp 90	Thr Ala Thr Tyr Tyr 95							
Cys Ala His	Arg Ile Thr Glu 100	Thr Ser Tyr Tyr 105	Phe Tyr Tyr Gly Met 110							
Asp Val Trp 115	Gly Gln Gly Thr	Thr Val Thr Val 120	Ser Ser 125							

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<212> TYPE: PRT
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<212> TYPE: DNA
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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Ile Tyr Trp Asn Gly Asp Lys
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<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
Val
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<211> LENGTH: 339
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic
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tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactccg
                                                                      300
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ctcactttcg gcggagggac caaggtggaa atcaaacga
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<211> LENGTH: 113
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 178
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                                    10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
                                25
His Gly Tyr Asp Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
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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<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 180
Gln Ser Leu Leu His Ser His Gly Tyr Asp Tyr
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<212> TYPE: DNA
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
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<210> SEO ID NO 183
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 183
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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Met Gln Ala Leu Gln Thr Pro Leu Thr
1
                 5
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<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
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acctgcacct tctctggatt ctcactcatc actagtggag tgggtgtggg ctggattcgt
                                                                       120
cagececeg gaaaggeest ggagtggett geacteattt attggaatgg tgataagege
                                                                       180
tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg
                                                                       240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacagg
                                                                       300
ataactgaaa ctagttacta cttctactac ggtatggacg tctggggcca agggaccacg
                                                                       360
gtcaccgtct cctca
                                                                       375
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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Gly	Val	Gly 35	Val	Gly	Trp	Ile	Arg 40	Gln	Pro	Pro	Gly	Lys 45	Ala	Leu	Glu	
Trp	Leu 50	Ala	Leu	Ile	Tyr	Trp 55	Asn	Gly	Asp	Lys	Arg 60	Tyr	Ser	Pro	Ser	
Leu 65	ГЛа	Ser	Arg	Leu	Thr 70	Ile	Thr	Lys	Asp	Thr 75	Ser	Lys	Asn	Gln	Val 80	
Val	Leu	Thr	Met	Thr 85	Asn	Met	Asp	Pro	Val 90	Asp	Thr	Ala	Thr	Tyr 95	Tyr	
CAa	Ala	His	Arg 100	Ile	Thr	Glu	Thr	Ser 105	Tyr	Tyr	Phe	Tyr	Tyr 110	Gly	Met	
Asp	Val	Trp 115	Gly	Gln	Gly	Thr	Thr 120	Val	Thr	Val	Ser	Ser 125				
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atctcctgca ggtctagtca gagcctcctg catagtcatg gatacgacta tttggattgg 12											120					
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 1											180					
teeggggtee etgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaate 24											240					
agca	agagt	egg a	aggct	gag	ga tọ	gttg	gggtt	tat	ttact	gca	tgc	aagc	tct a	acaa	actccg	300
ctca	actt	cg q	gegga	aggg	ac ca	aaggi	tgga	gato	caaa							336
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1	110	741		5	0111	501		Lou	10	200		741		15	017	
Glu	Pro	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25	Ser	Gln	Ser	Leu	Leu 30	His	Ser	
His	Gly	Tyr 35	Asp	Tyr	Leu	Asp	Trp 40	Tyr	Leu	Gln	Lys	Pro 45	Gly	Gln	Ser	
Pro	Gln 50	Leu	Leu	Ile	Tyr	Leu 55	Gly	Ser	Asn	Arg	Ala 60	Ser	Gly	Val	Pro	
Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe	Thr	Leu	Lys	Ile 80	
Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Val	Gly	Val 90	Tyr	Tyr	Cys	Met	Gln 95	Ala	
Leu	Gln	Thr	Pro 100	Leu	Thr	Phe	Gly	Gly 105	Gly	Thr	Lys	Val	Glu 110	Ile	Lys	
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<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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cagececcag gaaaggeett ggagtggett geacteattt attggaatgg tgataagege
                                                                     180
tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg
                                                                     240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacagg
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ataactgaaa ctagttacta cttctactac ggtatggacg tctggggcca agggaccacg
                                                                     360
                                                                     375
qtcaccqtct cctca
<210> SEO TD NO 190
<211> LENGTH: 125
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 190
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Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ile Thr Ser
Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
Trp Leu Ala Leu Ile Tyr Trp Asn Gly Asp Lys Arg Tyr Ser Pro Ser
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
Cys Ala His Arg Ile Thr Glu Thr Ser Tyr Tyr Phe Tyr Tyr Gly Met
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
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<211> LENGTH: 336
<212> TYPE: DNA
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<220> FEATURE:
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atctcctgca ggtctagtca gagcctcctg catagtcatg gatacgacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactccg
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ctcactttcg gcggagggac caaggtggag atcaaa
                                                                     336
<210> SEQ ID NO 192
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<211> LENGTH: 112

<212> TYPE: PRT

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		THER		ORMA'	rion:	: Syr	nthet	ic								
< 400) > S	EQUEI	ICE:	192												
Asp 1	Ile	Val	Met	Thr 5	Gln	Ser	Pro	Leu	Ser 10	Leu	Pro	Val	Thr	Pro 15	Gly	
Glu	Pro	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25	Ser	Gln	Ser	Leu	Leu 30	His	Ser	
His	Gly	Tyr 35	Asp	Tyr	Leu	Asp	Trp 40	Tyr	Leu	Gln	Lys	Pro 45	Gly	Gln	Ser	
Pro	Gln 50	Leu	Leu	Ile	Tyr	Leu 55	Gly	Ser	Asn	Arg	Ala 60	Ser	Gly	Val	Pro	
Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe	Thr	Leu	Lys	Ile 80	
Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Val	Gly	Val 90	Tyr	Tyr	Cys	Met	Gln 95	Ala	
Leu	Gln	Thr	Pro 100	Leu	Thr	Phe	Gly	Gly 105	Gly	Thr	Lys	Val	Glu 110	Ile	ГÀа	
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caqa	atca	cct t	gaaq	qqaqt	c to	ggte	ctact	cto	gatas	aaac	ccto	cacac	qac (cctca	acgctg	60
_						-							_		atccgt	120
cago	ccc	cag q	gaaaq	ggcc	et ge	gagto	ggatt	gca	actca	attt	atte	ggaat	tc 1	tgata	aagcgc	180
taca	agcc	cat o	ctctç	gaaga	ag ca	agget	caco	c ato	cacca	aagg	acad	cctc	caa a	aaaco	caggta	240
gtco	ctta	caa t	gaco	caaca	at go	gacco	ctgtg	g gad	cacaç	gcca	cata	atta	ctg 1	tgcad	cacaga	300
cato	gaca	gct (egte	ctact	a ct	tcta	actac	ggt	atg	gacg	tata	gggg	cca a	aggga	atcacg	360
gtca	accg	tct (cctca	ā												375
<211 <212 <213 <220	L > L 2 > T 3 > O 0 > F	EQ II ENGTI YPE: RGANI EATUI THER	H: 12 PRT ISM: RE:	25 Art:												
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Gln 1	Ile	Thr	Leu	5 5	Glu	Ser	Gly	Pro	Thr 10	Leu	Val	Lys	Pro	Ser 15	Gln	
Thr	Leu	Thr	Leu 20	Thr	CÀa	Thr	Phe	Ser 25	Gly	Phe	Ser	Leu	Ser 30	Thr	Ser	
Gly	Val	Gly 35	Val	Gly	Trp	Ile	Arg 40	Gln	Pro	Pro	Gly	Lys 45	Ala	Leu	Glu	
Trp	Leu 50	Ala	Leu	Ile	Tyr	Trp 55	Asn	Ser	Asp	Lys	Arg 60	Tyr	Ser	Pro	Ser	
Leu 65	Lys	Ser	Arg	Leu	Thr 70	Ile	Thr	Lys	Asp	Thr 75	Ser	Lys	Asn	Gln	Val 80	
Val	Leu	Thr	Met	Thr 85	Asn	Met	Asp	Pro	Val 90	Asp	Thr	Ala	Thr	Tyr 95	Tyr	
CAa	Ala	His	Arg	His	Asp	Ser	Ser	Ser	Tyr	Tyr	Phe	Tyr	Tyr	Gly	Met	

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105
Asp Val Trp Gly Gln Gly Ile Thr Val Thr Val Ser Ser
<210> SEQ ID NO 195
<211> LENGTH: 30
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 195
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<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
                5
<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
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<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
<210> SEQ ID NO 199
<211> LENGTH: 51
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 199
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gcacacagac atgacagete gtectaetae ttetaetaeg gtatggaegt e
<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
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Val
<210> SEQ ID NO 201
<211> LENGTH: 339
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 201
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atctcctqca qqtctaqtca qaqcctcctc cataqtcatq qatacaacta tttqqattqq
                                                                      120
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttc taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcggt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttgggatt tattactgca tgcaagctct acagactcct
                                                                      300
ctcactttcg gcggagggac 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
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
                               25
His Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
Arq
<210> SEQ ID NO 203
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 203
cagageetee tecatagtea tggatacaae 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
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Gln Ser Leu Leu His Ser His Gly Tyr Asn Tyr

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10
<210> SEQ ID NO 205
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 205
ttqqqttct
                                                                         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
<210> SEQ ID NO 207
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 207
atgcaagete tacagactee teteact
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<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
<210> SEQ ID NO 209
<211> LENGTH: 375
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 209
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acctgcacct tctctgggtt ctcactcagc actagtggag tgggtgtggg ctggatccgt
                                                                       120
cagececcag gaaaggeest ggagtggett geacteattt attggaatte tgataagege
                                                                       180
tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggta
                                                                       240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga
                                                                       300
catgacaget egtectaeta ettetaetae ggtatggaeg tetggggeea agggaeeaeg
                                                                       360
gtcaccgtct cctca
                                                                       375
<210> SEQ ID NO 210
<211> LENGTH: 125
<212> TYPE: PRT
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<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 Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Ala Leu Ile Tyr Trp Asn Ser 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 Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr 90 Cys Ala His Arg His Asp Ser Ser Ser Tyr Tyr Phe Tyr Tyr Gly Met 105 Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <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 atotoctgca ggtctagtca gagcctcctc catagtcatg gatacaacta tttggattgg tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttc taatcgggcc tccggggtcc ctgacaggtt cagtggcggt ggatcaggca cagattttac actgaaaatc agcagagtgg aggctgagga tgttgggatt tattactgca tgcaagctct acagactcct ctcactttcg gcggagggac caaggtggag atcaaa <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 10 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 25 His Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 55 Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala 90

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Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
          100
<210> SEQ ID NO 213
<211> LENGTH: 375
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 213
cagatcacct tgaaggagtc tggtcctacg ctggtgaaac ccacacagac cctcacgctg
                                                                      60
acctgcacct tctctgggtt ctcactcagc actagtggag tgggtgtggg ctggatccgt
                                                                     120
cagececcag gaaaggeest ggagtggett geacteattt attggaatte tgataagege
                                                                     180
tacaqcccat ctctqaaqaq caqqctcacc atcaccaaqq acacctccaa aaaccaqqtq
                                                                     240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga
                                                                     300
catgacaget egtectacta ettetactae ggtatggaeg tetggggeea agggaeeaeg
                                                                     360
gtcaccgtct 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
                                 10
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
Trp Leu Ala Leu Ile Tyr Trp Asn Ser Asp Lys Arg Tyr Ser Pro Ser
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
Cys Ala His Arg His Asp Ser Ser Ser Tyr Tyr Phe Tyr Tyr Gly Met
                               105
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<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 gagcctcctc catagtcatg gatacaacta tttggattgg
                                                                     120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
                                                                     180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                     240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acagactcct
```

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ctcactttcg gcggagggac caaggtggag atcaaa
                                                                      336
<210> SEQ ID NO 216
<211> LENGTH: 112
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 216
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
His Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
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
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 217
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 217
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tcctgtgcag cctctggatt cacctttagt agtcactgga tgaagtgggt ccgccaggct
ccaqqqaaqq qqctqqaqtq qqtqqccaac ataaaccaaq atqqaaqtqa qaaatactat
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgttt
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt
gtactaatgg tctatgatat ggactactac tactacggta tggacgtctg gggccaaggg
                                                                      360
                                                                      381
accacqqtca ccqtctcctc a
<210> SEQ ID NO 218
<211> LENGTH: 127
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 218
Glu Met Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
                                25
Trp Met Lys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                         40
Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
                        55
```

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
        70
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 219
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 219
                                                                      24
ggattcacct ttagtagtca ctgg
<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
<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
<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:
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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 224
Ala Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr
Gly Met Asp Val
<210> SEQ ID NO 225
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 225
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                                                                      60
                                                                     120
atotoctgca ggtotagtca gagootoctg catagtaatg gaaacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
                                                                     180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                     240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaaactct acaaactccg
                                                                     300
ctcactttcg gcggagggac caaggtggag 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
                        10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
Asn Gly Asn Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr
                                   90
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
           100
                               105
<210> SEQ ID NO 227
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 227
cagageetee tgeatagtaa tggaaacaac tat
                                                                      33
<210> SEQ ID NO 228
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<211> LENGTH: 11 <212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

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gtactaatgg totatgatat ggactactac tactacggta tggacgtctg gggccaaggg

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accaeggica eegieteete a
                                                                     381
<210> SEQ ID NO 234
<211> LENGTH: 127
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 234
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
Trp Met Lys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                           40
Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
                       55
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
                   70
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr
                                105
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<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
atctcctgca ggtctagtca gagcctcctg catagtaatg gaaacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaaactct acaaactccg
                                                                     336
ctcactttcg gcggagggac caaggtggag atcaaa
<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
                                    10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
                               25
Asn Gly Asn Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
                          40
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
                       55
```

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Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys <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 tggtggagtc tgggggaggc ttggtccagc ctggggggtc cctgagactc 60 teetgtgeag cetetggatt cacetttagt agteactgga tgagetgggt cegecagget 120 ccagggaagg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat 180 qtqqactctq tqaaqqqccq attcaccatc tccaqaqaca acqccaaqaa ctcactqtat 240 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt 300 gtactaatgg tctatgatat ggactactac tactacggta tggacgtctg ggggcaaggg 360 accacggtca 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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr Tyr 100 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 239 <211> LENGTH: 336 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 239 gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60 atctcctqca qqtctaqtca qaqcctcctq cataqtaatq qaaacaacta tttqqattqq

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tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc agcagagtgg aggctgagga tgttggggtt tattactgca tgcaaactct acaaactccg ctcactttcg gcggagggac caaggtggag atcaaa <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 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Asn Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr 90 Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys <210> SEQ ID NO 241 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 241 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc teetgtgeag tetetggatt eacetteagt agetatggea tgeactgggt eegecagget 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 360 381 accacqqtca ccqtctcctc a <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 10 Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Thr Phe Ser Ser Tyr 25

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Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
Ala Ala Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Val Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Lys Thr Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Asn Cys
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr
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Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                            120
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 243
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<211> LENGTH: 8
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 244
Gly Phe Thr Phe Ser Ser Tyr Gly
<210> SEQ ID NO 245
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 245
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<210> SEQ ID NO 246
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 246
Ile Ser Tyr Asp Gly Ser Asn Lys
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<210> SEQ ID NO 247
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 248
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Gly Met Asp Val
<210> SEQ ID NO 249
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 249
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tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttt taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
ctcactttcg gcggagggac caaggtggag atcaga
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<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
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Arg
           100
                                105
<210> SEQ ID NO 251
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 251
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cagageetee tgeatagtaa tggatacaae tat

60

120

180

240

300

336

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<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 252
Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
<210> SEQ ID NO 253
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 253
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<211> LENGTH: 3
<212> TYPE: PRT
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<220> FEATURE:
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Leu Gly Phe
<210> SEQ ID NO 255
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 255
atgcaagete tacaaactee teteact
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<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
                 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
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teetgtgeag tetetggatt cacetteagt agetatggea tgeactgggt cegecagget
                                                                       120
ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat
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25

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Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 <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 tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60 teetgtgeag cetetggatt caeetteagt agetatggea tgeaetgggt eegeeagget 120 ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180 240 gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaaatatt 300 gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg ggggcaaggg 360 accaeggica eegieteete 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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr 105 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEO ID NO 263 <211> LENGTH: 336 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 266

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Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Thr Phe Ser Ser Tyr
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
Ala Ala Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Val Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Lys Thr Leu Tyr
                70
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Asn Cys
               85
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr
                              105
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 267
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 268
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<210> SEQ ID NO 269
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<210> SEQ ID NO 271
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 272
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Gly Met Asp Val
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<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttt taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
ctcactttcg gcggagggac 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
                                   10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
                               25
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro
                        55
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
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                                    90
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Arg
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<211> LENGTH: 33
<212> TYPE: DNA
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<213> ORGANISM: Artificial Sequence

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<211> LENGTH: 11
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 276
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<210> SEQ ID NO 277
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 277
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<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
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<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
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<210> SEQ ID NO 281
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 281
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<400> SEQUENCE: 284

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Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 105 <210> SEQ ID NO 285 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 285 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60 tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120 ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaaatatt gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg ggggcaaggg 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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 25 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 40 Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val $50 \\ 0 \\ 0 \\ 0$ Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr 105 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

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<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 ctgcccgtca cccctggaga gccggcctcc 60 atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc 180 tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240 agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct 300 336 ctcactttcg gcggagggac caaggtggag atcaaa <210> SEQ ID NO 288 <211> LENGTH: 112 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 288 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly 10 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 25 Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys <210> SEQ ID NO 289 <211> LENGTH: 372 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 289 cagatcacct tgaaggagtc tggtcctacg ctggtaaaac ccacacagac cctcacgctg 60 acctgcacct tetetgggtt ctcactcage getagtggag tgggtgtggg etggtteegt 120 cageceecag gaaaggeest ggagtggett geacteattt attggaatga tgataagegt 180 tacageceat etetaaagaa eageeteace ateaceaagg acaceteeaa aaaceaggtg 240 gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga 300 atacatctat ggtcctactt ctactacggt atggacgtct ggggccaagg gaccacggtc 360 accgtctcct ca 372

<210> SEQ ID NO 290 <211> LENGTH: 124 <212> TYPE: PRT

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<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
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Ala Ser
Gly Val Gly Val Gly Trp Phe Arg Gln Pro Pro Gly Lys Ala Leu Glu
Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser 50 \, 60 \,
Leu Lys Asn Ser Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
Cys Ala His Arg Ile His Leu Trp Ser Tyr Phe Tyr Tyr Gly Met Asp
                               105
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<210> SEQ ID NO 291
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 291
gggttctcac tcagcgctag tggagtgggt
                                                                       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
<210> SEQ ID NO 293
<211> LENGTH: 21
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 293
                                                                       21
atttattgga atgatgataa g
<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
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<210> SEQ ID NO 295
<211> LENGTH: 48
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 295
gcacacagaa tacatctatg gtcctacttc 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
                                    10
<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
atotootgca ggtotagtca gactotootg catagtaatg gatacaacta tttcgattgg
                                                                       120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacagatt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                       240
agcagagtgg aggctgagga tgttggaatt tattactgca tgcaagctct acaaactcct
                                                                       336
ctcactttcg gcggagggac caaggtggag atcaga
<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
                                   10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr Leu Leu His Ser
                                25
Asn Gly Tyr Asn Tyr Phe Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
                            40
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Arg
            100
                                105
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<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 299
cagactetee tgcatagtaa tggatacaac tat
                                                                          33
<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
                 5
<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
<210> SEQ ID NO 303
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 303
                                                                          27
atgcaagete tacaaactee teteact
<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
                 5
<210> SEQ ID NO 305
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 305
cagateacet tgaaggagte tggteetacg etggtaaaac ceacacagae eetcacgetg
acctgcacct tctctgggtt ctcactcagc gctagtggag tgggtgtggg ctggttccgt
cagececcag gaaaggeest ggagtggett geacteattt attggaatga tgataagegt
tacageceat etetaaagaa eageeteace ateaceaagg acaceteeaa aaaceaggtg
                                                                     240
qtccttacaa tqaccaacat qqaccctqtq qacacaqcca catattactq tqcacacaqa
atacatctat ggtcctactt ctactacggt atggacgtct ggggccaagg gaccacggtc
                                                                     360
                                                                     372
acceteteet ca
<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
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Ala Ser
                                25
Gly Val Gly Val Gly Trp Phe Arg Gln Pro Pro Gly Lys Ala Leu Glu
Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser
Leu Lys Asn Ser Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                                    90
Cys Ala His Arg Ile His Leu Trp Ser Tyr Phe Tyr Tyr Gly Met Asp
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<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 ggtctagtca gactctcctg catagtaatg gatacaacta tttcgattgg
                                                                     120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
                                                                     180
teeggggtee etgacagatt eagtggeagt ggateaggea eagattttae aetgaaaate
                                                                     240
agcagagtgg aggctgagga tgttggaatt tattactgca tgcaagctct acaaactcct
                                                                     300
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                     336
<210> SEO ID NO 308
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 308 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr Leu Leu His Ser Asn Gly Tyr Asn Tyr Phe Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 105 <210> SEQ ID NO 309 <211> LENGTH: 372 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 309 cagateacet tgaaggagte tggteetaeg etggtgaaac ceacacagae ceteaegetg acctgcacct tetetgggtt ctcactcage getagtggag tgggtgtggg etggateegt cagececcag gaaaggeest ggagtggett geacteattt attggaatga tgataagege tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga atacatctat ggtcctactt ctactacggt atggacgtct gggggcaagg gaccacggtc 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 Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Ala Ser Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Ala Leu Ile Tyr Trp Asn Asp Asp Lys Arg Tyr Ser Pro Ser Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr 90 Cys Ala His Arg Ile His Leu Trp Ser Tyr Phe Tyr Tyr Gly Met Asp 105 Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

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120

115

<210> SEQ ID NO 311 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 311 gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60 atctcctqca qqtctaqtca qactctcctq cataqtaatq qatacaacta tttqqattqq 120 tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180 tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240 agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct 300 ctcactttcg gcggagggac caaggtggag atcaaa 336 <210> SEQ ID NO 312 <211> LENGTH: 112 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 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 25 Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys <210> SEQ ID NO 313 <211> LENGTH: 381 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 313 caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctgggggcctc agtgaaggtc 60 teetgeaagg ettetggtta cacetttaec acetatggta teagttgggt acgacaggee 120 cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat 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

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<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
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
                            40
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
                   70
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Ser Tyr Tyr
                               105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
       115
                           120
<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
<210> SEQ ID NO 317
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 317
atcagcggtt acaatggtaa aaca
                                                                       24
<210> SEQ ID NO 318
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 318

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Ile Ser Gly Tyr Asn Gly Lys Thr
               5
<210> SEQ ID NO 319
<211> LENGTH: 60
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 319
togagagato gtttagtagt accacotgoo ottaattatt ootactaogt tatggaogto
                                                                       60
<210> SEQ ID NO 320
<211> LENGTH: 20
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 320
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Ser Tyr Tyr
                                    1.0
Val Met Asp Val
            2.0
<210> SEQ ID NO 321
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 321
gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
tctcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
tetggggtee cagacagatt cageggeagt gggteaggea etgattteae aetgaaaate
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
tacacttttq qccaqqqqac caaqctqqaq 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
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
                                25
Asp Gly Asn Thr Tyr Leu Asn Trp Ser Gln Gln Arg Pro Gly Gln Ser
                            40
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
```

```
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
                                 105
<210> SEQ ID NO 323
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 323
                                                                          33
caaagcctcg tatacagtga tggaaacacc tac
<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
<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
<210> SEQ ID NO 327
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 327
                                                                          27
atgcaaggta cacactggcc gtacact
<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
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<210> SEQ ID NO 329
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 329
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc
                                                                      60
teetgeaagg ettetggtta cacetttace acetatggta teagttgggt acgaeaggee
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
                                                                     180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
                                                                     240
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
                                                                     300
ttaqtaqtac cacctqccct taattattcc tactacqtta tqqacqtctq qqqccaaqqq
                                                                     360
accacggtca ccgtctcctc 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
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
                        55
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Ser Tyr Tyr
                              105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<210> SEQ ID NO 331
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 331
gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc
                                                                      60
atotoctgca ggtotagtca aagootogta tacagtgatg gaaacacota ottgaattgg
                                                                     120
tctcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
                                                                     180
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
                                                                     240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
                                                                     300
tacacttttg gccaggggac caagctggag atcaaa
                                                                     336
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<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 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr Leu Asn Trp Ser Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105 <210> SEQ ID NO 333 <211> LENGTH: 381 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 333 caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc teetgeaagg ettetggtta eacetttace acetatggta teagetgggt gegacaggee cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt ttagtagtac cacctgccct taattattcc tactacgtta tggacgtctg ggggcaaggg accaeggica eegicteete a <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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 40 Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Tyr Ala Gln Lys Leu Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys

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Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Ser Tyr Tyr Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 335 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 335 gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60 atctcctqca qqtctaqtca aaqcctcqta tacaqtqatq qaaacaccta cttqaattqq 120 tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180 tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240 agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac 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 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105 <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 tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc 60 tcctgtgcag cctctggatt caccttcagt agctatagca tggactgggt ccgccaggct 120 ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac 180 gcagactetg tgaagggeeg atteaceate tecagagaea eegecaagaa eteactgtat 240 ctgcaaatga acagcctgag agacgaggac acggctgttt attactgtgc gagagagggc

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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
<400> SEQUENCE: 338
Glu Val Gl<br/>n Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly 1<br/> \phantom{0} 10 \phantom{0} 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
Ser Met Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
Ser Ser Ile Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
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
Ala Arg Glu Gly Ser Ser Arg Leu Phe Asp Tyr Trp Gly Gln Gly Thr
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
<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
<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
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<220> FEATURE:

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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 342
Ile Ser Ser Ser Ser Tyr Ile
<210> SEQ ID NO 343
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 343
                                                                      33
gcgagagag gcagtagcag actttttgac tac
<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
             5
<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 tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagagacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaggtgg agtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
gaggattttg caacttatta ctgccaacag tataatagtt attggtacac ttttggccag
gggaccaagc tggagatcaa a
<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
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Gly Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                   70
                                        75
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Trp Tyr
```

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Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
<210> SEQ ID NO 347
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 347
                                                                        18
cagagtatta gtagctgg
<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
<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
<210> SEQ ID NO 351
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 351
                                                                        27
caacagtata atagttattg gtacact
<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
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<210> SEQ ID NO 353
<211> LENGTH: 354
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 353
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc
                                                                      60
tectatagaa cetetagatt cacetteagt agetatagea tagactaggt cegecagget
                                                                     120
                                                                     180
ccaqqqaaqq qqctqqaqtq qqtctcatcc attaqtaqta qtaqtaqtta catatactac
geagactetg tgaagggeeg atteaceate teeagagaca eegeeaagaa eteactgtat
                                                                     240
ctgcaaatga acagcctgag agacgaggac acggctgttt attactgtgc gagagagggc
                                                                     300
                                                                     354
agtagcagac tttttgacta ctggggccag ggaaccctgg tcaccgtctc ctca
<210> SEO 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
                                    10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
Ser Met Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                            40
Ser Ser Ile Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ala Lys Asn Ser Leu Tyr
Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Glu Gly Ser Ser Arg Leu Phe Asp Tyr Trp Gly Gln Gly Thr
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> SEOUENCE: 355
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagagacca
                                                                     120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaggtgg agtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
                                                                     240
gaggattttg caacttatta ctgccaacag tataatagtt attggtacac ttttggccag
                                                                     300
gggaccaagc tggagatcaa a
                                                                     321
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<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 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Glu Gly Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 7.0 75 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Trp Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 <210> SEQ ID NO 357 <211> LENGTH: 354 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 357 gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagagggc agtagcagac tttttgacta ctggggccaa 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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr 70 75 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

Ala Arg Glu Gly Ser Ser Arg Leu Phe Asp Tyr Trp Gly Gln Gly Thr

-continued 100 105 110 Leu Val Thr Val Ser Ser <210> SEQ ID NO 359 <211> LENGTH: 321 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 359 gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60 atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca 120 gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca 180 aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240 gatgattttg caacttatta ctgccaacag tataatagtt attggtacac ttttggccag 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 10 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Trp Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys <210> SEQ ID NO 361 <211> LENGTH: 384 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 361 caggtgcacc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc 60 tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct 120 ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat 180

gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat

ctacatatga acagecteag agecgaegae aeggeegtgt attactgtge gagagateag

ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa

240

300

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```
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
<400> SEQUENCE: 362
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His 20 \hspace{1.5cm} 25 \hspace{1.5cm} 30 \hspace{1.5cm}
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
                           40
Ser Tyr Ile Ser Asn Asp Gly Gly Thr Lys Tyr Tyr Val Asp Ser Val
                      55
Glu Gly Arg Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
Leu His Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Ser
                               105
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
                           120
<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
                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
                                                                       24
attagtaatg atggtggtac caaa
<210> SEQ ID NO 366
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 366
Ile Ser Asn Asp Gly Gly Thr Lys
<210> SEQ ID NO 367
<211> LENGTH: 63
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 367
gegagagate agggatatat tggctaegae tegtattatt actatteeta eggtatggae
                                                                       60
atc
                                                                       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 Ser
                                    10
Tyr Gly Met Asp Val
<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
ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
totggccagg otoccaggot cotcatotat ggtgcatoca gcagggccac tggcatocca
gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag
                                                                      240
cctgaagatt ttgaagtgta ttattgtcaa gtatatggta actcactcac tctcggcgga
                                                                      300
                                                                      321
gggaccaagg tggagatcaa g
<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
                                    10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
            20
                                25
Phe Leu Ala Trp Tyr Gln Gln Lys Ser Gly Gln Ala Pro Arg Leu Leu
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
```

```
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Glu
                   70
Pro Glu Asp Phe Glu Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu
Thr Leu Gly Gly Gly Thr Lys Val Glu Ile Lys
<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
<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
<210> SEQ ID NO 375
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 375
                                                                        24
caagtatatg gtaactcact cact
<210> SEQ ID NO 376
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 376
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Gln Val Tyr Gly Asn Ser Leu Thr
<210> SEQ ID NO 377
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 377
                                                                         60
caqqtqcaqc tqqtqqaqtc tqqqqqaqqc ttqqtcaaqc ctqqaqqqtc cctqaqactc
teetgtgeag cetetggatt cacetteagt gaccactaca tgagetggat cegecagget
                                                                        120
ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat
                                                                        180
gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat
                                                                        240
ctacatatga acagceteag ageegaegae aeggeegtgt attactgtge gagagateag
                                                                        300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa
                                                                        360
                                                                        384
gggaccacgg tcaccgtctc ctca
<210> SEO 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
                                     10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
Ser Tyr Ile Ser Asn Asp Gly Gly Thr Lys Tyr Tyr Val Asp Ser Val
Glu Gly Arg Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
Leu His Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser 100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEO ID NO 379
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 379
gaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc
                                                                         60
ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
                                                                        120
tetggecagg eteccagget ecteatetat ggtgeateca geagggecae tggeatecea
                                                                        180
gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag
```

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```
cctgaagatt ttgaagtgta ttattgtcaa gtatatggta actcactcac tctcggcgga
gggaccaagg tggagatcaa a
<210> SEQ ID NO 380
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 380
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Pro Leu Phe Pro Gly
                                   10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
Phe Leu Ala Trp Tyr Gln Gln Lys Ser Gly Gln Ala Pro Arg Leu Leu
                           40
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
                       55
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Glu
                   70
Pro Glu Asp Phe Glu Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu
                                    90
Thr Leu Gly Gly Gly Thr Lys Val Glu Ile Lys
           100
<210> SEQ ID NO 381
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 381
caggtgcagc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc
teetgtgeag eetetggatt eacetteagt gaccactaca tgagetggat eegecagget
ccagggaagg ggctggagtg ggtttcatac attagtaatg atggtggtac caaatactac
                                                                     180
gcagactctg tgaagggccg attcaccatc tccagggaca acgccaagaa ctcactgtat
                                                                     240
                                                                     300
ctqcaaatqa acaqcctqaq aqccqaqqac acqqccqtqt attactqtqc qaqaqatcaq
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctgggggcaa
                                                                     360
                                                                     384
gggaccacgg tcaccgtctc ctca
<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
                                    10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                            40
Ser Tyr Ile Ser Asn Asp Gly Gly Thr Lys Tyr Tyr Ala Asp Ser Val
```

55

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <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 ctctcctqca qqqccaqtca qaqtqttaac aacaaattct taqcctqqta ccaqcaqaaa 120 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240 cctgaagatt ttgcagtgta ttactgtcaa gtatatggta actcactcac tttcggcgga 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 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu 75 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 <210> SEQ ID NO 385 <211> LENGTH: 360 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 385 gaggtgcaga aggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc 60 teetgtacag cetetggatt cacetteagt acttataaca tgaattgggt cegecagget

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```
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
<210> SEQ ID NO 386
<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
                                   10
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
                                25
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                            40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
                    70
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
            100
                                105
Gly Thr Leu Val Thr Val Ser Ser
<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
<210> SEQ ID NO 389
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 389
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24

attaggagta gtagtaatta cata

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<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
<210> SEQ ID NO 391
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 391
                                                                      39
gcgagagatg gcagcagttg gtacgactac tctgactac
<210> SEQ ID NO 392
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 392
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
1
                5
<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 tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acagatacca
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
                                                                     240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
                                                                     300
                                                                     321
gggaccaagg tggaaatcaa a
<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
                                    10
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
                            40
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
    50
                 55
```

```
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
<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
<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
<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
<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
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241 242

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gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60 atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acagatacca 120 gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180 aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240 qatqattttq caacttatta ctqccaacaq tatattaqtt attctcqqac qttcqqccaa 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
<400> SEQUENCE: 404
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
               85
                                   90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
<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 tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt caccttcagt acttataaca tgaactgggt ccgccaggct
ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
ageagttggt acgactactc tgactactgg ggccaaggaa ccctggtcac cgtctcctca
<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
                                 10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
                               25
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
                       55
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
```

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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
Gly Thr Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 407
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 407
qacatccaqa tqacccaqtc tccttccacc ctqtctqcat ctqtaqqaqa caqaqtcacc
                                                                      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
                                                                     120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
                                                                     180
aggttcagcg 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
                5
                                   10
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                                       75
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
               85
                                   90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
<210> SEQ ID NO 409
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 409
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
                                                                      60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct
                                                                     120
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
                                                                     180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat
                                                                     240
```

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ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
<210> SEQ ID NO 410
<211> LENGTH: 120
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<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
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
                               25
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                         40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
                   70
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                                    90
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
Gly Thr Leu Val Thr Val Ser Ser
       115
<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
<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
<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
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<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 414
Ile Arg Ser Ser Ser Asn Tyr Ile
<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> SEOUENCE: 416
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
<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 tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acagatacca
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
gggaccaagg tggaaatcaa a
<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
                                  10
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
                                25
Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
                        55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
                 70
```

```
 \hbox{Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg } \\
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100
<210> SEQ ID NO 419
<211> LENGTH: 18
<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
<211> EBROTH: 5
<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
<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
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<210> SEQ ID NO 425 <211> LENGTH: 360 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 425 gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc 60 tectqtacaq cetetqqatt cacetteaqt aettataaca tqaattqqqt ceqecaqqet 120 ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catactac 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 426 <211> LENGTH: 120 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 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 25 Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 115 <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 tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60 atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acagatacca 120 gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca 180 aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct 240 gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa 300 321

gggaccaagg tggaaatcaa a

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<210> SEQ ID NO 428
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 428
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
                               25
Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
                                  90
               85
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 tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc
teetgtgeag cetetggatt eacetteagt aettataaca tgaactgggt eegecagget
ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
agcagttggt acgactactc tgactactgg ggccaaggaa ccctggtcac cgtctcctca
<210> SEQ ID NO 430
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 430
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
                                   10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
                              25
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                           40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
```

```
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
                               105
Gly Thr Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 431
<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 431
gacatecaga tgacecagte teettecace etgtetgeat etgtaggaga cagagteace
                                                                      60
atcacttqcc qqqccaqtca qaqtattaqt aqctqqttqq cctqqtatca qcaqaaacca
                                                                     120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag 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> SEOUENCE: 432
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
                                25
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
<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 tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
                                                                      60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct
                                                                     120
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
                                                                     180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagag ttcactgtat
                                                                     240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
```

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agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
<210> SEQ ID NO 434
<211> LENGTH: 120
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 434
Glu Val Gl<br/>n Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly 1<br/> \phantom{0} 10 \phantom{0} 15
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                            40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
                       55
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Ser Leu Tyr
                    70
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
            100
                                 105
Gly Thr Leu Val Thr Val Ser Ser
      115
<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
                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
                                                                         24
attaggagta gtagtaatta cata
<210> SEQ ID NO 438
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 438
Ile Arg Ser Ser Ser Asn Tyr Ile
<210> SEQ ID NO 439
<211> LENGTH: 39
<212> TYPE: DNA
<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
<210> SEQ ID NO 441
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 441
gacatecaga tgacecagte teetteeace etgtetgeat etgtaggaga cagagteace
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acaggtacca
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
gggaccaagg tggaaatcaa a
<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
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
                                25
Leu Ala Trp Tyr Gln Gln Val Pro Gly Lys Ala Pro Lys Leu Leu Ile
                            40
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
                    70
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
                                    90
```

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Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100
<210> SEQ ID NO 443
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<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
<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
<210> SEQ ID NO 447
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 447
                                                                          27
caacagtata ttagttattc tcggacg
<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
```

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<210> SEQ ID NO 449
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 449
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
                                                                      60
teetgtacag cetetggatt cacetteagt aettataaca tgaattgggt eegeeagget
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
                                                                     180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagag ttcactgtat
                                                                     240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
                                                                     300
ageagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
                                                                     360
<210> SEQ ID NO 450
<211> LENGTH: 120
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 450
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
                                    10
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
           2.0
                               25
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                          40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Ser Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
Gly Thr Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 451
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 451
qacatccaga tqacccaqtc tccttccacc ctqtctqcat ctqtaqqaqa caqaqtcacc
                                                                      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acaggtacca
                                                                     120
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
                                                                     240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
                                                                     300
gggaccaagg tggaaatcaa a
                                                                      321
```

<210> SEQ ID NO 452 <211> LENGTH: 107

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<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 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Val Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 <210> SEO ID NO 453 <211> LENGTH: 360 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 453 gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc 60 teetgtgeag cetetggatt cacetteagt aettataaca tgaactgggt eegeeagget ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca <210> SEQ ID NO 454 <211> LENGTH: 120 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 454 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr 25 Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 40 Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 90 Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln 105

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Gly Thr Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 455
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 455
qacatccaqa tqacccaqtc tccttccacc ctqtctqcat ctqtaqqaqa caqaqtcacc
                                                                      60
                                                                     120
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
                                                                     240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
                                                                     300
                                                                     321
gggaccaagg tggaaatcaa a
<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
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
                            40
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
<210> SEQ ID NO 457
<211> LENGTH: 360
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 457
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
                                                                      60
teetgtacag cetetggatt cacetteagt acttataaca tgaattgggt cegecagget
                                                                     120
ccagggaagg 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
```

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<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
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                           40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
                  70
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
                               105
Gly Thr Leu Val Thr Val Ser Ser
       115
<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
<210> SEQ ID NO 461
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 461
                                                                       24
attaggagta gtagtaatta cata
<210> SEQ ID NO 462
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 462

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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
<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> SEOUENCE: 464
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
                5
<210> SEO ID NO 465
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 465
gacatecaga tgacecagte teetteeace etgtetgeat etgtaggaga cagagteace
                                                                      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acagatacca
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
                                                                     321
gggaccaagg tggaaatcaa a
<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
                                   10
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
                                25
Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
                           40
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
                        55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
```

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<210> SEQ ID NO 467
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 467
                                                                      18
cagagtatta gtagctgg
<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
<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
<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> SEOUENCE: 472
5
<210> SEQ ID NO 473
<211> LENGTH: 360
<212> TYPE: DNA
```

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 473
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
teetgtacag cetetggatt cacetteagt aettataaca tgaattgggt eegecagget
                                                                     120
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
                                                                     180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ttcactgtat
                                                                     240
                                                                     300
ctqcaaatqa acaqcctqaq aqccqatqac acqqctqtqt attactqtqc qaqaqatqqc
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
                                                                     360
<210> SEQ ID NO 474
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 474
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Thr Tyr
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                            40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
Gly Thr Leu Val Thr Val Ser Ser
<210> SEQ ID NO 475
<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 475
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                      60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca acagatacca
                                                                     120
gggaaagccc ctaaactcct gatctataag gcgtctagtt tagaaaatgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
                                                                     240
gatgattttg 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:
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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 476
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
<210> SEQ ID NO 477
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 477
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc
                                                                         60
teetgtgeag cetetggatt cacetteagt aettataaca tgaactgggt eegeeagget
ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
agcagttggt acgactactc tgactactgg ggccaaggaa ccctggtcac cgtctcctca
<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 Gl<br/>n Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly 1<br/> \phantom{0} 10 \phantom{0} 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                             40
Ser Ser Ile Arg Ser Ser Ser Asn Tyr Ile Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
                    70
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln
            100
                                 105
Gly Thr Leu Val Thr Val Ser Ser
      115
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<210> SEQ ID NO 479
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 479
gacatecaga tgacecagte teettecace etgtetgeat etgtaggaga cagagteace
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
                                                                     120
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
                                                                     240
qatqattttq caacttatta ctqccaacaq tatattaqtt attctcqqac qttcqqccaa
                                                                     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
<400> SEQUENCE: 480
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
                        55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 481
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 481
gaggtgcaac tagtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
teetgtgtag tetetggatt eacetteggt gaetaegaea tgeaetgggt eegteaaget
                                                                     120
acaggaagag gtctggagtg ggtctcaggt attgctcctg 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

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 482
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
Ser Leu Arg Leu Ser Cys Val Val Ser Gly Phe Thr Phe Gly Asp Tyr
Asp Met His Trp Val Arg Gln Ala Thr Gly Arg Gly Leu Glu Trp Val
                          40
Ser Gly Ile Ala Pro Ala Gly Asp Thr Ser Tyr Thr Gly Ser Val Lys
                       55
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu His Leu
Gln Met Asn Ser Leu Thr Thr Gly Asp Thr Ala Ile Tyr Tyr Cys Ala
Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr Trp Gly Gln Gly Thr
           100
                               105
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
<210> SEQ ID NO 485
<211> LENGTH: 21
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 485
                                                                       21
attgctcctg ctggtgacac a
<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
```

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<210> SEQ ID NO 487
<211> LENGTH: 36
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 487
gctagagagg atatagcagt gcctggtttt 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
<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 gagtgttagc agcaacttag cctggtacca gcagaaacct
                                                                       120
ggccaggctc ccagactcct catctatggt gcatccacga gggccactgg cttcccagcc
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct
                                                                       240
gaagattttg cagtttatta ctgtcagcag tataataagt ggcctccgtt cactttcggc
cctgggacca aagtggattt 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
                 5
                                    10
Glu Arg Gly Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
                                 25
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
                            40
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Phe Pro Ala Arg Phe Ser Gly
                        55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
                    70
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Lys Trp Pro Pro
                                     90
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Phe Lys
            100
                                 105
```

```
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 491
cagagtgtta gcagcaac
                                                                            18
<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
<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
<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
<210> SEQ ID NO 497
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 497 60 gaggtgcaac tagtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc teetgtgtag tetetggatt eacetteggt gaetaegaea tgeactgggt eegteaaget acaggaagag gtctggagtg ggtctcaggt attgctcctg ctggtgacac atcctataca ggctccgtga agggccgatt caccatctcc agagagaatg ccaagaactc cttgcatctt 240 caaatgaaca gcctgacaac cggggacacg gctatatatt attgtgctag agaggatata gcagtgcctg 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> SEOUENCE: 498 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Val Val Ser Gly Phe Thr Phe Gly Asp Tyr Asp Met His Trp Val Arg Gln Ala Thr Gly Arg Gly Leu Glu Trp Val Ser Gly Ile Ala Pro Ala Gly Asp Thr Ser Tyr Thr Gly Ser Val Lys 55 Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu His Leu Gln Met Asn Ser Leu Thr Thr Gly Asp Thr Ala Ile Tyr Tyr Cys Ala Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser <210> SEQ ID NO 499 <211> LENGTH: 324 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 499 qaaataqtqa tqacqcaqtc tccaqccacc ctqtctqtqt ctccaqqqqa acqaqqcacc 60 ctctcctqca qqqccaqtca qaqtqttaqc aqcaacttaq cctqqtacca qcaqaaacct 120 ggccaggctc ccagactcct catctatggt gcatccacga gggccactgg cttcccagcc 180 aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240 gaagattttg cagtttatta ctgtcagcag tataataagt ggcctccgtt cactttcggc 300 cctgggacca aagtggatat 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

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Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
Glu Arg Gly Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Phe Pro Ala Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Lys Trp Pro Pro
                                   90
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
           100
<210> SEQ ID NO 501
<211> LENGTH: 354
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 501
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
teetgtgeag cetetggatt eacetteggt gactaegaea tgeactgggt eegeeaaget
acaggaaaag gtctggagtg ggtctcagct attgctcctg ctggtgacac atactatcca
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgctag agaggatata
gcagtgcctg gttttgatta ctggggccaa ggaaccctgg tcaccgtctc ctca
<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
                                   10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asp Tyr
                              25
Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
                           40
Ser Ala Ile Ala Pro Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
                       55
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
               85
                                   90
Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr Trp Gly Gln Gly Thr
           100
                               105
Leu Val Thr Val Ser Ser
       115
```

```
<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
cteteetgea gggeeagtea gagtgttage ageaacttag cetggtacca geagaaacet
                                                                      120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
                                                                      180
                                                                      240
agqttcaqtq qcaqtqqqtc tqqqacaqaq ttcactctca ccatcaqcaq cctqcaqtct
gaagattttg cagtttatta ctgtcagcag tataataagt ggcctccgtt cactttcggc
                                                                      300
                                                                      324
cctgggacca aagtggatat caaa
<210> SEO ID NO 504
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 504
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
                                    10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
                    70
                                        75
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Lys Trp Pro Pro
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
<210> SEQ ID NO 505
<211> LENGTH: 378
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 505
caaattctgc tggtgcaatc tggacctgag gtgaaggagc ctgggggcctc agtgaaggtc
                                                                      60
tcctgcaagg cttctggtta cacctttacc aactacgcta tcagctgggt gcgacaggtc
                                                                      120
cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat
                                                                      180
gcacatgaag tocagggcag agtcaccatg accacagaca catccacgac cacagcctac
                                                                      240
atggagetga ggageetgag atetgaegae aeggeeatgt attaetgtge gagagggggt
                                                                      300
gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg ccaagggacc
                                                                      360
                                                                      378
acggtcaccg tctcctca
<210> SEQ ID NO 506
<211> LENGTH: 126
<212> TYPE: PRT
```

<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 506
Gln Ile Leu Leu Val Gln Ser Gly Pro Glu Val Lys Glu Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
Ala Ile Ser Trp Val Arg Gln Val Pro Gly Gln Gly Leu Glu Trp Met
Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala His Glu Val
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys
Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
                               105
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                            120
<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
<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 acaatggtca 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
```

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```
<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 ccccacttct acaacggtat ggacgtc
<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
                5
                                  10
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
atctcctgca ggtctagtca gagcctcctg catattaatg aatacaacta tttggattgg
tacctaaaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaactccg
tggacgttag gccaagggac caaggtggaa atcaaa
<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
                                    10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ile
Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Trp Thr Leu Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
                                105
```

```
<210> SEQ ID NO 515
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 515
cagageetee tgeatattaa tgaatacaae tat
<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 As<br/>n Glu Tyr As<br/>n Tyr \,
              5
1
<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
<210> SEQ ID NO 519
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 519
                                                                           27
atqcaaqctc ttcaaactcc qtqqacq
<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:
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<223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 521 caggttcagc tggtgcagtc tggacctgag gtgaaggagc ctgggggcctc agtgaaggtc teetgeaagg ettetggtta cacetttace aactaegeta teagetgggt gegacaggte cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat 180 gcacatgaag tocagggcag agtcaccatg accacagaca catccacgac cacagcctac 240 atqqaqctqa qqaqcctqaq atctqacqac acqqccatqt attactqtqc qaqaqqqqqt 300 360 qtaqtcqtqc caqttqctcc ccacttctac aacqqtatqq acqtctqqqq ccaaqqqacc 378 acggtcaccg tctcctca <210> SEQ ID NO 522 <211> LENGTH: 126 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 522 Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Glu Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Ala Ile Ser Trp Val Arg Gln Val Pro Gly Gln Gly Leu Glu Trp Met 40 Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala His Glu Val Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 523 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 523 qatattqtqa tqactcaqtc tccactctcc ctqcccqtca cccctqqaqa qccqqcctcc 60 atctcctgca ggtctagtca gagcctcctg catattaatg aatacaacta tttggattgg 120 tacctaaaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc 180 tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240 agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaactccg 300 tggacgttag gccaagggac caaggtggaa atcaaa 336 <210> SEQ ID NO 524 <211> LENGTH: 112 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 524 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ile Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Trp Thr Leu Gly Gln Gly Thr Lys Val Glu Ile Lys 100 105 <210> SEQ ID NO 525 <211> LENGTH: 378 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 525 caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctgggggcctc agtgaaggtc 60 teetgeaagg ettetggtta cacetttace aactaegeta teagetgggt gegacaggee cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaggggt gtagtegtge cagttgetee ceaettetae aaeggtatgg aegtetgggg geaagggaee acggtcaccg tctcctca <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 10 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr 25 Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 40 Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala Gln Lys Leu 55 Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr 70 Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys 90 Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly 100 105

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Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                            120
<210> SEQ ID NO 527
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 527
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                       60
atctcctgca ggtctagtca gagcctcctg catattaatg aatacaacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct tcaaactccg
                                                                      300
tggacgttcg gccaagggac 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
                                    10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ile
                                25
Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                                105
<210> SEQ ID NO 529
<211> LENGTH: 351
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 529
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                       60
tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca
                                                                      120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca
                                                                      180
ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaaactc cttctatctt
                                                                      240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata
                                                                      300
agaacaccct atgattattg gggccaggga gcccgggtca ccgtctcctc a
                                                                      351
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<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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Thr Gly Ser Val Met
Gly Arg Phe Thr Ile Ser Arg Asp Ala Ala Lys Asn Ser Phe Tyr Leu
Glu Met Asn Ser Leu Arg Val Gly Asp Thr Ala Val Tyr Tyr Cys Ala
Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Ala Arg
                                105
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
<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 ctggtgacac 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
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Ile Gly Ser Thr Gly Asp Thr

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<210> SEQ ID NO 535
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<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> SEOUENCE: 536
Ala Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr
                5
<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
ctctcctgca gggccagtca gagtgttagc agcaatgtag cctggtacca gcagaaacct
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
cctgggacca aagtggatat caaa
<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
                                    10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
                                25
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
                           40
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
                        55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
                    70
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro
                                    90
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100
                                105
```

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<210> SEQ ID NO 539
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 539
                                                                          18
cagagtgtta gcagcaat
<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
<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
<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
<210> SEQ ID NO 545
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 545 gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca 180 ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaaactc cttctatctt gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata 300 351 agaacaccct atgattattg gggccaggga accctggtca ccgtctcctc a <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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr 25 Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Thr Gly Ser Val Met Gly Arg Phe Thr Ile Ser Arg Asp Ala Ala Lys Asn Ser Phe Tyr Leu Glu Met Asn Ser Leu Arg Val Gly Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Thr Leu 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 gagtgttagc agcaatgtag cctggtacca gcagaaacct 120 ggccaggete ccaggeteet catetatggt geatecacea gggccaetgg tateccagee 180 aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct 240 gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc 300 cctgggacca aagtggatat caaa 324 <210> SEO ID NO 548 <211> LENGTH: 108 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

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<400> SEQUENCE: 548
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
          100
<210> SEQ ID NO 549
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 549
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagct
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactatcca
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggaata
agaacaccct atgattattg gggccaagga accctggtca ccgtctcctc a
<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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
                           40
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
                       55
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Thr Leu
          100
                              105
Val Thr Val Ser Ser
```

115

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<210> SEQ ID NO 551
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 551
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc
                                                                      60
ctctcctgca gggccagtca gagtgttagc agcaatttag cctggtacca gcagaaacct
                                                                     120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
                                                                     180
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct
                                                                     240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
                                                                     300
                                                                     324
cctqqqacca aaqtqqatat caaa
<210> SEO 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
                                    10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
<210> SEQ ID NO 553
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 553
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
teetgtgeag eetetggatt eaceetaagt agetaegaea tgeactgggt eegeeaagea
                                                                     120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca
                                                                     180
ggeteegtga tgggeegatt caccatetee agagaegetg ceaaaaacte ettetatett
                                                                     240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata
                                                                     300
agaacaccct atgattattg gggccaggga gcccgggtca ccgtctcctc a
                                                                     351
<210> SEQ ID NO 554
<211> LENGTH: 117
<212> TYPE: PRT
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<213> ORGANISM: Artificial Sequence

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<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
Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Thr Gly Ser Val Met
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
 \hbox{Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Ala Arg } \\
                               105
           100
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
<210> SEQ ID NO 557
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 557
                                                                      21
attggcagta ctggtgacac a
<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
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<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
<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
             5
<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
ctctcctgca gggccagtca gagtgttagc agcaatgtag cctggtacca gcagaaacct
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
cctgggacca aagtggatat caaa
<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
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
                           40
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
                       55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro
                                    90
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
           100
<210> SEQ ID NO 563
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<210 > SEQ ID NO 563 <211 > LENGTH: 18

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 563
                                                                           18
cagagtgtta gcagcaat
<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
<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
<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
                  5
<210> SEQ ID NO 569
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
                               25
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro
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                                   90
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagct
                                                                     120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactatcca
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggaata
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<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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
Ser Ala Ile Gly Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
                       55
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
                   70
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Thr Leu
           100
                               105
Val Thr Val Ser Ser
      115
<210> SEQ ID NO 575
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<211> LENGTH: 324

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<212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 575 gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc ctctcctgca gggccagtca gagtgttagc agcaatttag cctggtacca gcagaaacct qqccaqqctc ccaqqctcct catctatqqt qcatccacca qqqccactqq tatcccaqcc aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240 gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc 300 324 cctqqqacca aaqtqqatat caaa <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 5 10 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn 25 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys <210> SEQ ID NO 577 <211> LENGTH: 363 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 577 gaagtgeage tggtggagte tgggggagge ttggtacage etggeaggte eetgagaete 60 tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120 ccagggaagg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat 180 geggaetetg tgaagggeeg atteaceate teeagagaea aegeeaagea eteeetgtat 240 ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgt aaaagaggtg 300 actacgggat actactacgg tatggacgtc tggggccaag ggaccacggt caccgtctcc 360 t.ca 363 <210> SEQ ID NO 578 <211> LENGTH: 121 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
Ser Gly Ile Asn Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val50 \\ 0 \\ 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
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
<210> SEO ID NO 579
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<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
<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
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<210> SEQ ID NO 583

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<211> LENGTH: 42
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 583
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<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
                5
<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 tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc
                                                                       60
atcacttgct gggccagtca gggcattagc agttatttag cctggtatca gaaaaaacca
                                                                      120
gggaaagccc ctaacctcct gatctatgat gcatccactt tgcaaagtgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca cactcagcag cctgcagcct
gaagattttg caacttatta ctgtcaacag cttaatattt acccattcac tttcggccct
                                                                      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
                                   10
Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Gly Ile Ser Ser Tyr
                                25
Leu Ala Trp Tyr Gln Lys Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
                           40
Tyr Asp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Leu Ser Ser Leu Gln Pro
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ile Tyr Pro Phe
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
           100
                                105
<210> SEQ ID NO 587
<211> LENGTH: 18
<212> TYPE: DNA
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<210> SEQ ID NO 588
<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
<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
<210> SEQ ID NO 591
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 591
caacaqctta atatttaccc 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
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gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc
teetgtgeag cetetggatt cacetttgat gattatgeea tgeactgggt ceggeaaget
ccagggaagg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat
geggaetetg tgaagggeeg atteaceate teeagagaea aegeeaagea eteeetgtat
ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgt aaaagaggtg
                                                                      300
actacqqqat actactacqq tatqqacqtc tqqqqccaaq qqaccacqqt caccqtctcc
                                                                     363
tca
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 594
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
Ser Gly Ile Asn Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
                       55
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys His Ser Leu Tyr
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys
Val Lys Glu Val Thr Thr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly
Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 595
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 595
qacatccaqt tqacccaqtc tccatccttc ctqtctqcat ctqtaqqaqa caqaqtcacc
                                                                      60
atcacttqct qqqccaqtca qqqcattaqc aqttatttaq cctqqtatca qaaaaaacca
                                                                     120
gggaaagccc ctaacctcct gatctatgat gcatccactt tgcaaagtgg ggtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca cactcagcag cctgcagcct
                                                                     240
gaagattttg caacttatta ctgtcaacag cttaatattt acccattcac tttcggccct
                                                                     300
gggaccaaag tggatatcaa a
                                                                     321
<210> SEQ ID NO 596
<213> ORGANISM: Artificial Sequence
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<211> LENGTH: 107

<212> TYPE: PRT

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 596

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Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Gly Ile Ser Ser Tyr Leu Ala Trp Tyr Gln Lys Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Asp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Leu Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ile Tyr Pro Phe 90 Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys 100 <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 tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60 teetgtgeag eetetggatt eacetttgat gattatgeea tgeactgggt eeggeaaget ccagggaagg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat geggaetetg tgaagggeeg atteaceate teeagagaea aegeeaagaa eteeetgtat ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgt aaaagaggtg actacgggat actactacgg tatggacgtc tgggggcaag ggaccacggt caccgtctcc <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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 40 Ser Gly Ile Asn Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys 90 Val Lys Glu Val Thr Thr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly 100 105 Gln Gly Thr Thr Val Thr Val Ser Ser 115

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<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 599
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atcacttgcc gggccagtca gggcattagc agttatttag cctggtatca gcaaaaacca
                                                                     120
qqqaaaqccc ctaaqctcct qatctatqat qcatccactt tqcaaaqtqq qqtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct
                                                                     240
gaagattttg caacttatta ctgtcaacag cttaatattt acccattcac tttcggccct
                                                                     300
                                                                     321
qqqaccaaaq tqqatatcaa a
<210> SEO 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
                                    10
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Tyr
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
Tyr Asp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ile Tyr Pro Phe
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
<210> SEQ ID NO 601
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 601
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                                                                      60
teetgtgeag cetetggatt eaegtttagt agetatgeea tgaactgggt eegecagget
                                                                     120
ccagggaagg ggctggattg ggtctcaggt atcagtggta atggtggtag cacctactac
                                                                     180
gcagactccg tgaagggccg gttcaccatc tccagagaca tttccaagaa cacgctgtat
                                                                     240
gtgcaaatgc acagcctgag agtcgaggac acggccgttt actactgtgc gaaagcccgt
                                                                     300
tattacgatt tttggggggg gaatttcgat ctctggggcc gtggcaccca ggtcactgtc
                                                                     360
tcctca
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<210> SEQ ID NO 602 <211> LENGTH: 122

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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
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
Lys Gly Arg Phe Thr Ile Ser Arg Asp Ile Ser Lys Asn Thr Leu Tyr
Val Gln Met His Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Lys Ala Arg Tyr Tyr Asp Phe Trp Gly Gly Asn Phe Asp Leu Trp
Gly Arg Gly Thr Gln Val Thr Val Ser Ser
       115
<210> SEQ ID NO 603
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 603
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                                                                       24
<210> SEQ ID NO 604
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 604
Gly Phe Thr Phe Ser Ser Tyr Ala
<210> SEQ ID NO 605
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 605
atcagtggta atggtggtag cacc
                                                                       2.4
<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
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1 5

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<210> SEQ ID NO 607
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 607
gcgaaagccc gttattacga tttttggggg gggaatttcg atctc
<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
                                    1.0
<210> SEQ ID NO 609
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 609
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ctctcctgca gggccagtca gagtgttagc atcaggtact tagcctggta tcagcagaaa
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca
gacaggttca gtgtcagtgt gtctgggaca gacttcactc tcaccatcac tagactggag
cctgaagatt ttgcagtcta ttactgtcag caatatggta gttcaccgct cactttcggc
ggagggacca aggtggagat caaa
<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
                                    10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ile Arg
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
Val Ser Val Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
```

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<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
<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
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<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 614
Gly Ala Ser
<210> SEQ ID NO 615
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 615
                                                                          27
cagcaatatg gtagttcacc gctcact
<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:
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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 617
gaggtgcagt tgttggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt cacgtttagt agctatgcca tgaactgggt ccgccaggct
ccagggaagg ggctggattg ggtctcaggt atcagtggta atggtggtag cacctactac
                                                                     180
gcagactccg tgaagggccg gttcaccatc tccagagaca tttccaagaa cacgctgtat
                                                                     240
qtqcaaatqc acaqcctqaq aqtcqaqqac acqqccqttt actactqtqc qaaaqcccqt
                                                                     300
tattacgatt tttggggggg gaatttcgat ctctggggcc gtggcaccct ggtcactgtc
                                                                     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
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp Val
                            40
Ser Gly Ile Ser Gly Asn Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
Lys Gly Arg Phe Thr Ile Ser Arg Asp Ile Ser Lys Asn Thr Leu Tyr
Val Gln Met His Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
Ala Lys Ala Arg Tyr Tyr Asp Phe Trp Gly Gly Asn Phe Asp Leu Trp
Gly Arg Gly Thr Leu Val Thr Val Ser Ser
<210> SEQ ID NO 619
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 619
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc
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ctctcctgca gggccagtca gagtgttagc atcaggtact tagcctggta tcagcagaaa
                                                                     120
cctggccagg ctcccagget cctcatctat ggtgcatcca gcagggccac tggcatccca
                                                                     180
gacaggttca gtgtcagtgt gtctgggaca gacttcactc tcaccatcac tagactggag
                                                                     240
cctgaagatt ttgcagtcta ttactgtcag caatatggta gttcaccgct cactttcggc
                                                                      300
ggagggacca aggtggagat caaa
                                                                     324
<210> SEQ ID NO 620
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 620 Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ile Arg Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Val Ser Val Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 <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 teetgtgeag cetetggatt caegtttagt agetatgeea tgagetgggt eegeeagget ccagggaagg ggctggagtg ggtctcagct atcagtggta atggtggtag cacctactac gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagcccgt tattacgatt tttggggggg gaatttcgat ctctggggcc gtggcaccct ggtcactgtc tcctca <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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 25 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 40 Ser Ala Ile Ser Gly Asn Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 70 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 90 Ala Lys Ala Arg Tyr Tyr Asp Phe Trp Gly Gly Asn Phe Asp Leu Trp 105

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Gly Arg Gly Thr Leu Val Thr Val Ser Ser
      115
<210> SEQ ID NO 623
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 623
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc
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ctctcctgca gggccagtca gagtgttagc atcaggtact tagcctggta ccagcagaaa
                                                                     120
cctqqccaqq ctcccaqqct cctcatctat qqtqcatcca qcaqqqccac tqqcatccca
                                                                     180
qacaqqttca qtqqcaqtqq qtctqqqaca qacttcactc tcaccatcaq caqactqqaq
                                                                     240
cctgaagatt ttgcagtgta ttactgtcag caatatggta gttcaccgct 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
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ile Arg
                                25
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 625
<211> LENGTH: 381
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 625
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctgggggcctc agtgaaggtc
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tcctgcaagg cttctggtta cacctttacc acctatggta tcagttgggt acgacaggcc
                                                                     120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
                                                                     180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
                                                                     240
atggagetga ggageetgag atetgaegae aeggeeattt attactgtte gagagategt
                                                                     300
ttagtagtac cacctgccct ttattattcc tactacgtta tggacgtctg gggccaaggg
                                                                     360
                                                                      381
accacggtca ccgtctcctc a
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<210> SEQ ID NO 626
<211> LENGTH: 127
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 626
Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Asn Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
                           40
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
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
                               105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<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
<210> SEQ ID NO 629
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 629
atcagcggtt acaatggtaa aaca
                                                                       24
<210> SEQ ID NO 630
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 630

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Ile Ser Gly Tyr Asn Gly Lys Thr
<210> SEQ ID NO 631
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 631
toqaqaqato qtttaqtaqt accacctqcc ctttattatt cctactacqt tatqqacqtc
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<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
Val Met Asp Val
<210> SEQ ID NO 633
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 633
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atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
tacacttttg gccaggggac caagctggag atcaaa
<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
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
                    70
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
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90
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
<210> SEQ ID NO 635
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 635
caaagcctcg tatacagtga tggaaacacc tac
                                                                        33
<210> SEQ ID NO 636
<211> LENGTH: 11
<211> ZYPE: 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
<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
<210> SEQ ID NO 639
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 639
                                                                        27
atgcaaggta cacactggcc gtacact
<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
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<210> SEQ ID NO 641 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 641 caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc 60 teetgeaagg ettetggtta cacetttace acetatggta teagttgggt acgacaggee 120 cctqqacaaq qqcttqaqtq qatqqqatqq atcaqcqqtt acaatqqtaa aacaaacqat 180 gcacagaagt tocaggacag agtogccatg accacagaca catocacgag cacagoctac 240 atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt 300 ttagtagtac cacctgccct ttattattcc tactacgtta tggacgtctg gggccaaggg 360 accacqqtca ccqtctcctc a 381 <210> SEQ ID NO 642 <211> LENGTH: 127 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 642 Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Asn Pro Gly Ala 5 10 15 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr 25 Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Ser Tyr Tyr Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <210> SEQ ID NO 643 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 643 gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60 atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120 tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac 180 tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240 agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg 300 tacacttttg gccaggggac caagctggag atcaaa

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<210> SEQ ID NO 644
<211> LENGTH: 112
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 644
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
                                  90
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
           100
                               105
<210> SEQ ID NO 645
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 645
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teetgeaagg ettetggtta cacetttace acetatggta teagetgggt gegacaggee
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac
atggagetga ggageetgag atetgaegae aeggeegtgt attactgtte gagagategt
ttaqtaqtac cacctqccct ttattattcc tactacqtta tqqacqtctq qqqqcaaqqq
                                                                     381
accacqqtca ccqtctcctc a
<210> SEQ ID NO 646
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 646
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
                                   1.0
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
                           40
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Tyr Ala Gln Lys Leu
                      55
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
                    70
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Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Ser Tyr Tyr Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <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 tetggggtee cagacagatt cageggeagt gggteaggea etgattteae aetgaaaate 240 agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac 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 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 105 100 <210> SEO ID NO 649 <211> LENGTH: 381 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 649 caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc 60 teetgeaagg ettetggtta cacetttace acetatggta teagttgggt acgaeaggee 120 cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat 180 gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac

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atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg gggccaaggg
accacggtca ccgtctcctc a
<210> SEQ ID NO 650
<211> LENGTH: 127
<212> TYPE: PRT
<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
                                   10
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe 50 \\ \, 60
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Tyr Tyr Tyr
            100
                                105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<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
<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
<210> SEQ ID NO 653
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 653
atcagcggtt acaatggtaa aaca
                                                                        24
<210> SEQ ID NO 654
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<211> LENGTH: 8

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 654
Ile Ser Gly Tyr Asn Gly Lys Thr
<210> SEQ ID NO 655
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 655
tcqaqaqatc qtttaqtaqt accacctqcc cttaattatt actactacqt tatqqacqtc
                                                                       60
<210> SEO 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
                                   10
Val Met Asp Val
<210> SEQ ID NO 657
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 657
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atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
                                                                      240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
                                                                      300
tacacttttg gccaggggac 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
                                    1.0
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
                                25
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
                            40
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
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Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
<210> SEQ ID NO 659
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 659
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                                                                        3.3
<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
<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
<210> SEQ ID NO 663
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 663
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atgcaaggta cacactggcc gtacact
<210> SEQ ID NO 664
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 664
Met Gln Gly Thr His Trp Pro Tyr Thr
<210> SEQ ID NO 665
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 665
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                                                                      60
teetgeaagg ettetggtta cacetttaec acetatggta teagttgggt acgacaggee
                                                                     120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
                                                                     180
gcacagaagt tocaggacag agtogcoatg accacagaca catocacgag cacagoctac
                                                                     240
atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt
                                                                     300
ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg gggccaaggg
                                                                     360
accacggtca ccgtctcctc 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
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Tyr Tyr Tyr
                               105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
       115
                           120
<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
atotoctgca ggtotagtca aagootogta tacagtgatg gaaacacota ottgaattgg
                                                                     120
tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
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-continued tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg tacacttttg gccaggggac caagctggag atcaaa <210> SEQ ID NO 668 <211> LENGTH: 112 <212> TYPE: PRT <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 10 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105 <210> SEQ ID NO 669 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 669 caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc tcctgcaagg cttctggtta cacctttacc acctatggta tcagctgggt gcgacaggcc cctqqacaaq qqcttqaqtq qatqqqatqq atcaqcqqtt acaatqqtaa aacaaactat 180 240 qcacaqaaqc tccaqqqcaq aqtcaccatq accacaqaca catccacqaq cacaqcctac 300 atggagetga ggageetgag atetgaegae aeggeegtgt attactgtte gagagategt ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg ggggcaaggg 360 accacqqtca ccqtctcctc a 381 <210> SEQ ID NO 670 <211> LENGTH: 127 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 670 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr 25

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 35 40 45

-continued

```
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Tyr Ala Gln Lys Leu
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Tyr Tyr
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 671
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 671
qatqttqtqa tqactcaqtc tccactctcc ctqcccqtca cccttqqaca qccqqcctcc
                                                                      60
atotoctgca ggtotagtca aagootogta tacagtgatg gaaacacota ottgaattgg
                                                                      120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac
                                                                      180
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
                                                                      240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
                                                                      300
tacacttttg gccaggggac 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
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
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
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
                                  90
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
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caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc

379 380 -continued teetgeaagg ettetggtta eacetttace acetatggta teagttgggt acgaeaggee cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac atggagctga ggagcctgag atctgacgac acggccattt attactgttc gagagatcgt ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg gggccaaggg 360 accaeggtea cegteteete 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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 40 Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr 70 75 Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 675 <211> LENGTH: 24 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 675 qqttacacct ttaccaccta tqqt 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 5 <210> SEQ ID NO 677 <211> LENGTH: 24 <212> TYPE: DNA

<210> SEQ ID NO 677
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 677

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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
<400> SEQUENCE: 678
Ile Ser Gly Tyr Asn Gly Lys Thr
<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> SEO 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
                                     10
Val Met Asp Val
<210> SEQ ID NO 681
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 681
gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc
                                                                        60
atotoctgca ggtotagtca aagootogta tacagtgatg gaaacacota ottgaattgg
                                                                       120
tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
                                                                       180
tetggggtee cagacagatt cageggeagt gggteaggea etgattteae aetgaaaate
                                                                       240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac 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> SEOUENCE: 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
```

```
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
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
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
                                105
<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
<210> SEQ ID NO 685
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 685
aaggtttct
<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
<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
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385 386

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<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
<210> SEQ ID NO 689
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 689
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teetgeaagg ettetggtta eacetttace acetatggta teagttgggt acgaeaggee
                                                                     120
cctggacaag ggcttgagtg 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
accacggtca ccgtctcctc 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
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 691
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 691

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

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Tyr Ala Gln Lys Leu
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr
                               105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                          120
<210> SEQ ID NO 695
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 695
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atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
                                                                     120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
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
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
                       55
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
                   70
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
           100
                               105
<210> SEQ ID NO 697
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 697
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teetgtgeag cetetggatt cacetteagt gaccactaca tgagetggat cegecagget
ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat
                                                                     180
gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat
                                                                     240
ctacatatqa acaqcctcaq aqccqacqac acqqccqtqt attactqtqc qaqaqatcaq
                                                                     300
qqatatattq qctacqactc qtattattac tattcctacq qtatqqacqt ctqqqqccaa
                                                                     384
gggaccacgg tcaccgtcgc ctca
<210> SEQ ID NO 698
<211> LENGTH: 128
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 698
Gln Val His Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
Ser Tyr Ile Ser Asn Asp Gly Gly Thr Lys Tyr Tyr Val Asp Ser Val
Glu Gly Arg Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
Leu His Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Ser
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
<210> SEQ ID NO 699
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 699
ggattcacct tcagtgacca ctac
                                                                       24
<210> SEQ ID NO 700
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 700
Gly Phe Thr Phe Ser Asp His Tyr
                5
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<210> SEQ ID NO 701 <211> LENGTH: 24

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 701
attagtaatg atggtggtac caaa
<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
<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 Ser
Tyr Gly Met Asp Val
<210> SEQ ID NO 705
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 705
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                                                                       60
ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
                                                                      120
tetggecagg eteccagget ceteatetat ggtgeateca geagggecae tggeatecea
                                                                      180
gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag
                                                                      240
cctgaagatt ttgaagtgta 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:
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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 706
Lys Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Pro Leu Phe Pro Gly
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
Phe Leu Ala Trp Tyr Gln Gln Lys Ser Gly Gln Ala Pro Arg Leu Leu
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Glu
Pro Glu Asp Phe Glu Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
<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
<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
<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
<210> SEQ ID NO 711
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 711
caagtatatg gtaactcact cact
<210> SEQ ID NO 712
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 712
Gln Val Tyr Gly Asn Ser Leu Thr
<210> SEO ID NO 713
<211> LENGTH: 384
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 713
caggtgcagc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc
                                                                       60
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct
                                                                      120
ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat
                                                                      180
gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat
ctacatatga acagecteag agecgaegae aeggeegtgt attactgtge gagagateag
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa
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
                                    10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
                               25
Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
                            40
Ser Tyr Ile Ser Asn Asp Gly Gly Thr Lys Tyr Tyr Val Asp Ser Val
Glu Gly Arg Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
Leu His Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
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<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
ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
                                                                      120
totogocago otoccagoot cotcatotat optocatoca goagogocac togocatocca
                                                                      180
qacaqqttca qtqqcaqtqq qtctqqqacc qacttcactc tcaccatcaq cqqactqqaq
                                                                      240
cctgaagatt ttgaagtgta ttattgtcaa gtatatggta actcactcac tttcggcgga
                                                                      300
                                                                      321
gggaccaagg tggagatcaa a
<210> SEO ID NO 716
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 716
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Pro Leu Phe Pro Gly
                                    10
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
Phe Leu Ala Trp Tyr Gln Gln Lys Ser Gly Gln Ala Pro Arg Leu Leu
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Glu
                    70
Pro Glu Asp Phe Glu Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 717
<211> LENGTH: 384
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 717
caggtgcagc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct
                                                                      120
ccaqqqaaqq qqctqqaqtq qqtttcatac attaqtaatq atqqtqqtac caaatactac
                                                                      180
gcagactctg tgaagggccg attcaccatc tccagggaca acgccaagaa ctcactgtat
                                                                      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
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<213> ORGANISM: Artificial Sequence

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<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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 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 Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <210> SEQ ID NO 719 <211> LENGTH: 321 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 719 gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc ctctcctgca gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag cctgaagatt ttgcagtgta ttactgtcaa gtatatggta actcactcac tttcggcgga gggaccaagg tggagatcaa a <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 10 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Val Tyr Gly Asn Ser Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

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100 105 <210> SEQ ID NO 721 <211> LENGTH: 378 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 721 caaattetge tggtgeaate tggaeetgag gtgaaggage etggggeete agtgaaggte 60 teetgeaagg ettetggtta cacetttace aactaegeta teagetgggt gegacaggte 120 cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat 180 gcacatgaag tocagggcag agtcaccatg accacagaca catccacgac cacagcctac 240 atggagetga ggageetgag atetgaegae aeggeeatgt attaetgtge gagagggggt 300 gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg ccaagggacc 360 378 acggtcaccg tctcctca <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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Ala Ile Ser Trp Val Arg Gln Val Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala His Glu Val Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly 105 Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 115 <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

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<400> SEQUENCE: 724
Gly Tyr Thr Phe Thr Asn Tyr Ala
<210> SEQ ID NO 725
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 725
                                                                       24
gtcagcgctt acaatggtca caca
<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
<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 ccccacttct 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
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> SEOUENCE: 729
gatattgtga tgactcagtt tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                       60
ateteetgea ggtetagtea gageeteetg catattaatg aatacaacta tttggattgg
                                                                      120
tacctaaaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaactccg
                                                                      300
tggacgttcg gccaagggac caaggtggaa atcaaa
                                                                      336
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<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
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ile
Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
                               105
<210> SEQ ID NO 731
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 731
cagageetee tgeatattaa tgaatacaae 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
<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
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1

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<210> SEQ ID NO 735
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 735
atgcaagete ttcaaactee gtggacg
                                                                        2.7
<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
<210> SEQ ID NO 737
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 737
caggttcagc tggtgcagtc tggacctgag gtgaaggagc ctgggggcctc agtgaaggtc
                                                                        60
teetgeaagg ettetggtta cacetttace aactaegeta teagetgggt gegacaggte
                                                                       120
cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat
gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac
                                                                       240
atggagctga ggagcctgag atctgacgac acggccatgt attactgtgc gagaggggt
gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg ccaagggacc
acggtcaccg tctcctca
<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
                                    10
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
                                25
Ala Ile Ser Trp Val Arg Gln Val Pro Gly Gln Gly Leu Glu Trp Met
                            40
Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala His Glu Val
                        55
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Ala Tyr
                    70
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys
                                     90
Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
            100
                                105
```

```
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<210> SEQ ID NO 739
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 739
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                       60
atctcctgca ggtctagtca gagcctcctg catattaatg aatacaacta tttggattgg
                                                                      120
tacctaaaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtc tattactgca tgcaagctct tcaaactccg
                                                                      300
tggacgttcg gccaagggac 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
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ile
                                25
Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser
Pro Gln Leu Leu Ile Tyr Leu Gly Phe Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                                105
<210> SEQ ID NO 741
<211> LENGTH: 378
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 741
caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctgggggcctc agtgaaggtc
                                                                       60
tectgeaagg cttetggtta cacetttace aactacgeta teagetgggt gegacaggee
                                                                      120
cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat
                                                                      180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac
                                                                      240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagggggt
                                                                      300
gtagtegtge cagttgetee ceaettetae aaeggtatgg aegtetgggg geaagggaee
                                                                      360
                                                                      378
acggtcaccg tctcctca
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<210> SEQ ID NO 742
<211> LENGTH: 126
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 742
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
                         40
Gly Trp Val Ser Ala Tyr Asn Gly His Thr Asn Tyr Ala Gln Lys Leu
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                                   90
Ala Arg Gly Gly Val Val Val Pro Val Ala Pro His Phe Tyr Asn Gly
           100
                              105
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<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
atotoctgca ggtctagtca gagcctcctg catattaatg aatacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct tcaaactccg
                                                                     300
tggacgttcg gccaagggac caaggtggaa atcaaa
<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
                       10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ile
                               25
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
                       55
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
```

```
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 745
<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: 745
Xaa Xaa Xaa Xaa Xaa Xaa Xaa
     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
<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
10
Xaa Xaa Xaa Xaa
<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> SEOUENCE: 748
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<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
<400> SEQUENCE: 749
Xaa Xaa Xaa
<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
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
                        10
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
             85
                                 90
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
                          120
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
                     135
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
                  150
                                      155
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                              185
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
                 200
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Lys	Ala 210	Leu	Pro	Ala	Pro	Ile 215	Glu	Lys	Thr	Ile	Ser 220	Lys	Ala	Lys	Gly
Gln 225	Pro	Arg	Glu	Pro	Gln 230	Val	Tyr	Thr	Leu	Pro 235	Pro	Ser	Arg	Asp	Glu 240
Leu	Thr	Lys	Asn	Gln 245	Val	Ser	Leu	Thr	Cys 250	Leu	Val	Lys	Gly	Phe 255	Tyr
Pro	Ser	Asp	Ile 260	Ala	Val	Glu	Trp	Glu 265	Ser	Asn	Gly	Gln	Pro 270	Glu	Asn
Asn	Tyr	Lys 275	Thr	Thr	Pro	Pro	Val 280	Leu	Asp	Ser	Asp	Gly 285	Ser	Phe	Phe
Leu	Tyr 290	Ser	Lys	Leu	Thr	Val 295	Asp	Lys	Ser	Arg	Trp 300	Gln	Gln	Gly	Asn
Val 305	Phe	Ser	Cys	Ser	Val 310	Met	His	Glu	Ala	Leu 315	His	Asn	His	Tyr	Thr 320
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Phe	Pro	Glu 35	Pro	Val	Thr	Val	Ser 40	Trp	Asn	Ser	Gly	Ala 45	Leu	Thr	Ser
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Tyr	Thr	Сув	Asn	Val 85	Asp	His	Lys	Pro	Ser 90	Asn	Thr	Lys	Val	Asp 95	Lys
Arg	Val	Glu	Ser 100	ГÀа	Tyr	Gly	Pro	Pro 105	CÀa	Pro	Ser	CÀa	Pro 110	Ala	Pro
Glu	Phe	Leu 115	Gly	Gly	Pro	Ser	Val 120	Phe	Leu	Phe	Pro	Pro 125	Lys	Pro	Lys
Asp	Thr 130	Leu	Met	Ile	Ser	Arg 135	Thr	Pro	Glu	Val	Thr 140	Cys	Val	Val	Val
Asp 145	Val	Ser	Gln	Glu	Asp 150	Pro	Glu	Val	Gln	Phe 155	Asn	Trp	Tyr	Val	Asp 160
Gly	Val	Glu	Val	His 165	Asn	Ala	ГЛа	Thr	Lys 170	Pro	Arg	Glu	Glu	Gln 175	Phe
Asn	Ser	Thr	Tyr 180	Arg	Val	Val	Ser	Val 185	Leu	Thr	Val	Leu	His 190	Gln	Asp
Trp	Leu	Asn 195	Gly	Lys	Glu		Lys 200	Cya	Lys	Val	Ser	Asn 205	Lys	Gly	Leu
Pro	Ser 210	Ser	Ile	Glu	ГÀа	Thr 215	Ile	Ser	ГЛа	Ala	220	Gly	Gln	Pro	Arg
Glu 225	Pro	Gln	Val	Tyr	Thr 230	Leu	Pro	Pro	Ser	Gln 235	Glu	Glu	Met	Thr	Lys 240

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1860

cago	atgac	ca t	aaco	etaco	aa aa	aaaa	actac	aco	ecta	acta	acto	acaqt	ac o	ecte	cctggg	1920
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His 65	Arg	Cys	Ala	Lys	Asp 70	Pro	Trp	Arg	Leu	Pro 75	Gly	Thr	Tyr	Val	Val 80	
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Pro	Glu 210	Glu	Asp	Gly	Thr	Arg 215	Phe	His	Arg	Gln	Ala 220	Ser	Lys	Cys	Asp	
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Leu	Ala 290	Gly	Gly	Tyr	Ser	Arg 295	Val	Leu	Asn	Ala	Ala 300	Cys	Gln	Arg	Leu	
Ala 305	Arg	Ala	Gly	Val	Val 310	Leu	Val	Thr	Ala	Ala 315	Gly	Asn	Phe	Arg	Asp 320	
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Glu	Asp 50	Gly	Leu	Ala	Asp	Ala 55	Pro	Glu	His	Gly	Ala 60	Thr	Ala	Thr	Phe
His 65	Arg	Cys	Ala	Lys	Asp 70	Pro	Trp	Arg	Leu	Pro 75	Gly	Thr	Tyr	Val	Val 80
Val	Leu	Lys	Glu	Glu 85	Thr	His	Arg	Ser	Gln 90	Ser	Glu	Arg	Thr	Ala 95	Arg
Arg	Leu	Gln	Ala 100	Gln	Ala	Ala	Arg	Arg 105	Gly	Tyr	Leu	Thr	Lys 110	Ile	Leu
His	Val	Phe 115	His	His	Leu	Leu	Pro 120	Gly	Phe	Leu	Val	Lys 125	Met	Ser	Gly
Asp	Leu 130	Leu	Glu	Leu	Ala	Leu 135	Lys	Leu	Pro	His	Val 140	Asp	Tyr	Ile	Glu
Glu 145	Asp	Ser	Ser	Val	Phe 150	Ala	Gln	Ser	Ile	Pro 155	Trp	Asn	Leu	Glu	Arg 160
Ile	Thr	Pro	Ala	Arg 165	Tyr	Arg	Ala	Asp	Glu 170	Tyr	Gln	Pro	Pro	Lys 175	Gly
Gly	Ser	Leu	Val 180	Glu	Val	Tyr	Leu	Leu 185	Asp	Thr	Ser	Ile	Gln 190	Ser	Asp
His	Arg	Glu 195	Ile	Glu	Gly	Arg	Val 200	Met	Val	Thr	Asp	Phe 205	Glu	Ser	Val
Pro	Glu 210	Glu	Asp	Gly	Thr	Arg 215	Phe	His	Arg	Gln	Ala 220	Ser	Lys	Càa	Asp
Ser 225	His	Gly	Thr	His	Leu 230	Ala	Gly	Val	Val	Ser 235	Gly	Arg	Asp	Ala	Gly 240
Val	Ala	Lys	Gly	Ala 245	Gly	Leu	Arg	Ser	Leu 250	Arg	Val	Leu	Asn	Сув 255	Gln
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Thr 385	Ser	Gln	Ala	Ala	Ala 390	His	Val	Ala	Gly	Ile 395	Ala	Ala	Met	Met	Leu 400
Ser	Ala	Glu	Pro	Glu 405	Leu	Thr	Leu	Ala	Glu 410	Leu	Arg	Gln	Arg	Leu 415	Ile
His	Phe	Ser	Ala 420	Lys	Asp	Val	Ile	Asn 425	Glu	Ala	Trp	Phe	Pro 430	Glu	Asp
Gln	Arg	Val 435	Leu	Thr	Pro	Asn	Leu 440	Val	Ala	Ala	Leu	Pro 445	Pro	Ser	Thr

His Arg Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His $_{\rm 450}$

Ser 465	Gly	Pro	Thr	Arg	Met 470	Ala	Thr	Ala	Val	Ala 475	Arg	Cys	Ala	Gln	Asp 480
Glu	Glu	Leu	Leu	Ser 485	CAa	Ser	Ser	Phe	Ser 490	Arg	Ser	Gly	Lys	Arg 495	Arg
Gly	Glu	Arg	Ile 500	Glu	Ala	Gln	Gly	Gly 505	Lys	Arg	Val	Cys	Arg 510	Ala	His
Asn	Ala	Phe 515	Gly	Gly	Glu	Gly	Val 520	Tyr	Ala	Ile	Ala	Arg 525	Сув	Cys	Leu
Leu	Pro 530	Gln	Val	Asn	Cys	Ser 535	Val	His	Thr	Ala	Pro 540	Pro	Ala	Gly	Ala
Ser 545	Met	Gly	Thr	Arg	Val 550	His	Cys	His	Gln	Gln 555	Gly	His	Val	Leu	Thr 560
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Pro	Val	Leu	Arg 580	Pro	Arg	Gly	Gln	Pro 585	Asn	Gln	Cys	Val	Gly 590	His	Arg
Glu	Ala	Ser 595	Ile	His	Ala	Ser	Cys	Cys	His	Ala	Pro	Gly 605	Leu	Glu	Cha
Lys	Val 610	Lys	Glu	His	Gly	Ile 615	Pro	Ala	Pro	Gln	Glu 620	Gln	Val	Ile	Val
Ala 625	Cys	Glu	Asp	Gly	Trp 630	Thr	Leu	Thr	Gly	Сув 635	Ser	Pro	Leu	Pro	Gly 640
Thr	Ser	His	Val	Leu 645	Gly	Ala	Tyr	Ala	Val 650	Asp	Asn	Thr	Cys	Val 655	Val
Arg	Ser	Arg	Asp	Val	Ser	Thr	Thr	Gly 665	Ser	Thr	Ser	Lys	Glu 670	Ala	Val
Ala	Ala	Val 675	Ala	Ile	Cys	Cys	Arg 680	Ser	Arg	His	Leu	Val 685	Gln	Ala	Ser
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Lys 225	Cha	Asp	Ser	His	Gly 230	Thr	His	Leu	Ala	Gly 235	Val	Val	Ser	Gly	Arg 240
Asp	Ala	Gly	Val	Ala 245	Lys	Gly	Thr	Ser	Leu 250	His	Ser	Leu	Arg	Val 255	Leu
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Gln 385	Ser	Gly	Thr	Ser	Gln 390	Ala	Ala	Ala	His	Val 395	Ala	Gly	Ile	Val	Ala 400
Arg	Met	Leu	Ser	Arg 405	Glu	Pro	Thr	Leu	Thr 410	Leu	Ala	Glu	Leu	Arg 415	Gln
Arg	Leu	Ile	His 420	Phe	Ser	Thr	ГÀа	Asp 425	Val	Ile	Asn	Met	Ala 430	Trp	Phe
Pro	Glu	Asp 435	Gln	Gln	Val	Leu	Thr 440	Pro	Asn	Leu	Val	Ala 445	Thr	Leu	Pro
Pro	Ser 450	Thr	His	Glu	Thr	Gly 455	Gly	Gln	Leu	Leu	Cys 460	Arg	Thr	Val	Trp
Ser 465	Ala	His	Ser	Gly	Pro 470	Thr	Arg	Thr	Ala	Thr 475	Ala	Thr	Ala	Arg	Cys 480
Ala	Pro	Glu	Glu	Glu 485	Leu	Leu	Ser	Cys	Ser 490	Ser	Phe	Ser	Arg	Ser 495	Gly
_	Arg		500	_				505					510		_
_	Ala	515				_	520		_		-	525			
Cys	Сув 530	Leu	Val	Pro	Arg	Ala 535	Asn	СЛа	Ser	Ile	His 540	Asn	Thr	Pro	Ala
Ala	Arg	Ala	Gly	Leu	Glu	Thr	His	Val	His	Cys	His	Gln	Lys	Asp	His

545					550					555					560
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Arg	Arg	Gln	Pro 580	Ala	Leu	Arg	Ser	Arg 585	Arg	Gln	Pro	Gly	Gln 590	Cys	Val
Gly	His	Gln 595	Ala	Ala	Ser	Val	Tyr 600	Ala	Ser	Сув	Cys	His 605	Ala	Pro	Gly
Leu	Glu 610	Сла	ГЛа	Ile	ГЛа	Glu 615	His	Gly	Ile	Ser	Gly 620	Pro	Ser	Glu	Gln
Val 625	Thr	Val	Ala	Cys	Glu 630	Ala	Gly	Trp	Thr	Leu 635	Thr	Gly	Cys	Asn	Val 640
Leu	Pro	Gly	Ala	Ser 645	Leu	Thr	Leu	Gly	Ala 650	Tyr	Ser	Val	Asp	Asn 655	Leu
Сув	Val	Ala	Arg 660	Val	His	Asp	Thr	Ala 665	Arg	Ala	Asp	Arg	Thr 670	Ser	Gly
Glu	Ala	Thr 675	Val	Ala	Ala	Ala	Ile 680	Сув	Cys	Arg	Ser	Arg 685	Pro	Ser	Ala
Lys	Ala 690	Ser	Trp	Val	Gln										
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	2 > T? 3 > OF			Homo	sa]	piens	3								
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Val	Leu	Thr 35	Cya	Gly	Pro	Ala	Ser 40	Phe	Gln	Cya	Asn	Ser 45	Ser	Thr	Cys
Ile	Pro 50	Gln	Leu	Trp	Ala	Сув 55	Asp	Asn	Asp	Pro	Asp 60	Cys	Glu	Asp	Gly
Ser 65	Asp	Glu	Trp	Pro	Gln 70	Arg	Сув	Arg	Gly	Leu 75	Tyr	Val	Phe	Gln	Gly 80
Asp	Ser	Ser	Pro	Сув 85	Ser	Ala	Phe	Glu	Phe 90	His	CAa	Leu	Ser	Gly 95	Glu
Сув	Ile	His	Ser 100	Ser	Trp	Arg	Cys	Asp 105	Gly	Gly	Pro	Asp	Cys 110	Lys	Asp
Lys	Ser	Asp 115	Glu	Glu	Asn	Cys	Ala 120	Val	Ala	Thr	Сув	Arg 125	Pro	Asp	Glu
Phe	Gln 130	Cha	Ser	Asp	Gly	Asn 135	Cha	Ile	His	Gly	Ser 140	Arg	Gln	Cha	Asp
Arg 145	Glu	Tyr	Asp	CÀa	Lys 150	Asp	Met	Ser	Asp	Glu 155	Val	Gly	Cys	Val	Asn 160
Val	Thr	Leu	Cys	Glu 165	Gly	Pro	Asn	Lys	Phe 170	Lys	CÀa	His	Ser	Gly 175	Glu
Cys	Ile	Thr	Leu 180	Asp	Lys	Val	Cys	Asn 185	Met	Ala	Arg	Asp	Сув 190	Arg	Asp
Trp	Ser	Asp 195	Glu	Pro	Ile	Lys	Glu 200	Сла	Gly	Thr	Asn	Glu 205	CÀa	Leu	Asp
Asn	Asn 210	Gly	Gly	Cys	Ser	His 215	Val	Сув	Asn	Asp	Leu 220	Lys	Ile	Gly	Tyr
Glu	Cys	Leu	Cys	Pro	Asp	Gly	Phe	Gln	Leu	Val	Ala	Gln	Arg	Arg	Cys

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Val	Asn	Leu	Glu 260	Gly	Gly	Tyr	ГÀа	Сув 265	Gln	Сув	Glu	Glu	Gly 270	Phe	Gln
Leu	Asp	Pro 275	His	Thr	Lys	Ala	Cys 280	Lys	Ala	Val	Gly	Ser 285	Ile	Ala	Tyr
Leu	Phe 290	Phe	Thr	Asn	Arg	His 295	Glu	Val	Arg	Lys	Met 300	Thr	Leu	Asp	Arg
Ser 305	Glu	Tyr	Thr	Ser	Leu 310	Ile	Pro	Asn	Leu	Arg 315	Asn	Val	Val	Ala	Leu 320
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Arg	Met	Ile	Cys 340	Ser	Thr	Gln	Leu	Asp 345	Arg	Ala	His	Gly	Val 350	Ser	Ser
Tyr	Asp	Thr 355	Val	Ile	Ser	Arg	Asp 360	Ile	Gln	Ala	Pro	Asp	Gly	Leu	Ala
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Thr 385	Val	Ser	Val	Ala	390	Thr	ГЛа	Gly	Val	395	Arg	ГÀа	Thr	Leu	Phe 400
Arg	Glu	Asn	Gly	Ser 405	Lys	Pro	Arg	Ala	Ile 410	Val	Val	Asp	Pro	Val 415	His
Gly	Phe	Met	Tyr 420	Trp	Thr	Asp	Trp	Gly 425	Thr	Pro	Ala	Lys	Ile 430	Lys	Lys
Gly	Gly	Leu 435	Asn	Gly	Val	Asp	Ile 440	Tyr	Ser	Leu	Val	Thr 445	Glu	Asn	Ile
Gln	Trp 450	Pro	Asn	Gly	Ile	Thr 455	Leu	Asp	Leu	Leu	Ser 460	Gly	Arg	Leu	Tyr
Trp 465	Val	Asp	Ser	ГÀа	Leu 470	His	Ser	Ile	Ser	Ser 475	Ile	Asp	Val	Asn	Gly 480
Gly	Asn	Arg	Lys	Thr 485	Ile	Leu	Glu	Asp	Glu 490	Lys	Arg	Leu	Ala	His 495	Pro
Phe	Ser	Leu	Ala 500	Val	Phe	Glu	Asp	Lys 505	Val	Phe	Trp	Thr	Asp 510	Ile	Ile
Asn	Glu	Ala 515	Ile	Phe	Ser	Ala	Asn 520	Arg	Leu	Thr	Gly	Ser 525	Asp	Val	Asn
Leu	Leu 530	Ala	Glu	Asn	Leu	Leu 535	Ser	Pro	Glu	Asp	Met 540	Val	Leu	Phe	His
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Ser	Asn	Gly	Gly	Сув 565	Gln	Tyr	Leu	CÀa	Leu 570	Pro	Ala	Pro	Gln	Ile 575	Asn
Pro	His	Ser	Pro 580	ГÀа	Phe	Thr	CAa	Ala 585	CÀa	Pro	Asp	Gly	Met 590	Leu	Leu
Ala	Arg	Asp 595	Met	Arg	Ser	CAa	Leu 600	Thr	Glu	Ala	Glu	Ala 605	Ala	Val	Ala
Thr	Gln 610	Glu	Thr	Ser	Thr	Val 615	Arg	Leu	Lys	Val	Ser 620	Ser	Thr	Ala	Val
Arg 625	Thr	Gln	His	Thr	Thr 630	Thr	Arg	Pro	Val	Pro 635	Asp	Thr	Ser	Arg	Leu 640
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Asn	Glu	Trp 35	Ala	Ala	Glu	Ile	Pro 40	Gly	Gly	Pro	Glu	Ala 45	Ala	Ser	Ala
Ile	Ala 50	Glu	Glu	Leu	Gly	Tyr 55	Asp	Leu	Leu	Gly	Gln 60	Ile	Gly	Ser	Leu
Glu 65	Asn	His	Tyr	Leu	Phe 70	Lys	His	Lys	Asn	His 75	Pro	Arg	Arg	Ser	Arg 80
Arg	Ser	Ala	Phe	His 85	Ile	Thr	Lys	Arg	Leu 90	Ser	Asp	Asp	Asp	Arg 95	Val
Ile	Trp	Ala	Glu 100	Gln	Gln	Tyr	Glu	Lys 105	Glu	Arg	Ser	Lys	Arg 110	Ser	Ala
Leu	Arg	Asp 115	Ser	Ala	Leu	Asn	Leu 120	Phe	Asn	Asp	Pro	Met 125	Trp	Asn	Gln
Gln	Trp 130	Tyr	Leu	Gln	Asp	Thr 135	Arg	Met	Thr	Ala	Ala 140	Leu	Pro	Lys	Leu
Asp 145	Leu	His	Val	Ile	Pro 150	Val	Trp	Gln	Lys	Gly 155	Ile	Thr	Gly	Lys	Gly 160
Val	Val	Ile	Thr	Val 165	Leu	Asp	Asp	Gly	Leu 170	Glu	Trp	Asn	His	Thr 175	Asp
Ile	Tyr	Ala	Asn 180	Tyr	Asp	Pro	Glu	Ala 185	Ser	Tyr	Asp	Phe	Asn 190	Asp	Asn
Aap	His	Asp 195	Pro	Phe	Pro	Arg	Tyr 200	Asp	Pro	Thr	Asn	Glu 205	Asn	Lys	His
Gly	Thr 210	Arg	Сув	Ala	Gly	Glu 215	Ile	Ala	Met	Gln	Ala 220	Asn	Asn	His	Lys
Cys 225	Gly	Val	Gly	Val	Ala 230	Tyr	Asn	Ser	Lys	Val 235	Gly	Gly	Ile	Arg	Met 240
Leu	Asp	Gly	Ile	Val 245	Thr	Asp	Ala	Ile	Glu 250	Ala	Ser	Ser	Ile	Gly 255	Phe
Asn	Pro	Gly	His 260	Val	Asp	Ile	Tyr	Ser 265	Ala	Ser	Trp	Gly	Pro 270	Asn	Asp
Aap	Gly	Lys 275	Thr	Val	Glu	Gly	Pro 280	Gly	Arg	Leu	Ala	Gln 285	Lys	Ala	Phe
Glu	Tyr 290	Gly	Val	Lys	Gln	Gly 295	Arg	Gln	Gly	Lys	Gly 300	Ser	Ile	Phe	Val
Trp 305	Ala	Ser	Gly	Asn	Gly 310	Gly	Arg	Gln	Gly	Asp 315	Asn	CAa	Asp	Cys	Asp 320
Gly	Tyr	Thr	Asp	Ser 325	Ile	Tyr	Thr	Ile	Ser 330	Ile	Ser	Ser	Ala	Ser 335	Gln
Gln	Gly	Leu	Ser 340	Pro	Trp	Tyr	Ala	Glu 345	Lys	Cys	Ser	Ser	Thr 350	Leu	Ala
Thr	Ser	Tyr 355	Ser	Ser	Gly	Asp	Tyr 360	Thr	Asp	Gln	Arg	Ile 365	Thr	Ser	Ala
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Ala Pro Leu Ala Ala Gly Ile Phe Ala Leu Ala Leu Glu Ala Asn Pro 390 Asn Leu Thr Trp Arg Asp Met Gln His Leu Val Val Trp Thr Ser Glu Tyr Asp Pro Leu Ala Asn Asn Pro Gly Trp Lys Lys Asn Gly Ala Gly Leu Met Val Asn Ser Arg Phe Gly Phe Gly Leu Leu Asn Ala Lys Ala Leu Val Asp Leu Ala Asp Pro Arg Thr Trp Arg Ser Val Pro Glu Lys 455 Lys Glu Cys Val Val Lys Asp Asn Asp Phe Glu Pro Arg Ala Leu Lys Ala Asn Gly Glu Val Ile Ile Glu Ile Pro Thr Arg Ala Cys Glu Gly 490 Gln Glu Asn Ala Ile Lys Ser Leu Glu His Val Gln Phe Glu Ala Thr 505 Ile Glu Tyr Ser Arg Arg Gly Asp Leu His Val Thr Leu Thr Ser Ala 520 Ala Gly Thr Ser Thr Val Leu Leu Ala Glu Arg Glu Arg Asp Thr Ser Pro Asn Gly Phe Lys Asn Trp Asp Phe Met Ser Val His Thr Trp Gly 550 555 Glu Asn Pro Ile Gly Thr Trp Thr Leu Arg Ile Thr Asp Met Ser Gly Arg Ile Gln Asn Glu Gly Arg Ile Val Asn Trp Lys Leu Ile Leu His 585 Gly Thr Ser Ser Gln Pro Glu His Met Lys Gln Pro Arg Val Tyr Thr Ser Tyr Asn Thr Val Gln Asn Asp Arg Arg Gly Val Glu Lys Met Val 615 Asp Pro Gly Glu Glu Gln Pro Thr Gln Glu Asn Pro Lys Glu Asn Thr Leu Val Ser Lys Ser Pro Ser Ser Ser Ser Val Gly Gly Arg Arg Asp Glu Leu Glu Glu Gly Ala Pro Ser Gln Ala Met Leu Arg Leu Leu Gln Ser Ala Phe Ser Lys Asn Ser Pro Pro Lys Gln Ser Pro Lys Lys Ser 680 Pro Ser Ala Lys Leu Asn Ile Pro Tyr Glu Asn Phe Tyr Glu Ala Leu 695 Glu Lys Leu Asn Lys Pro Ser Gln Leu Lys Asp Ser Glu Asp Ser Leu 710 Tyr Asn Asp Tyr Val Asp Val Phe Tyr Asn Thr Lys Pro Tyr Lys His 730 Arg Asp Asp Arg Leu Leu Gln Ala Leu Val Asp Ile Leu Asn Glu Glu 745 Asn <210> SEQ ID NO 760 <211> LENGTH: 785 <212> TYPE: PRT <213> ORGANISM: Homo sapiens <400> SEQUENCE: 760

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Pro	Trp	Val 35	Met	Gly	Leu	Ala	Gly 40	Thr	Gly	Gly	Pro	Asp 45	Gly	Gln	Gly
Thr	Gly 50	Gly	Pro	Ser	Trp	Ala 55	Val	His	Leu	Glu	Ser 60	Leu	Glu	Gly	Asp
Gly 65	Glu	Glu	Glu	Thr	Leu 70	Glu	Gln	Gln	Ala	Asp 75	Ala	Leu	Ala	Gln	Ala 80
Ala	Gly	Leu	Val	Asn 85	Ala	Gly	Arg	Ile	Gly 90	Glu	Leu	Gln	Gly	His 95	Tyr
Leu	Phe	Val	Gln 100	Pro	Ala	Gly	His	Arg 105	Pro	Ala	Leu	Glu	Val 110	Glu	Ala
Ile	Arg	Gln 115	Gln	Val	Glu	Ala	Val 120	Leu	Ala	Gly	His	Glu 125	Ala	Val	Arg
Trp	His 130	Ser	Glu	Gln	Arg	Leu 135	Leu	Arg	Arg	Ala	Lys 140	Arg	Ser	Val	His
Phe 145	Asn	Asp	Pro	Lys	Tyr 150	Pro	Gln	Gln	Trp	His 155	Leu	Asn	Asn	Arg	Arg 160
Ser	Pro	Gly	Arg	Asp 165	Ile	Asn	Val	Thr	Gly 170	Val	Trp	Glu	Arg	Asn 175	Val
Thr	Gly	Arg	Gly 180	Val	Thr	Val	Val	Val 185	Val	Asp	Asp	Gly	Val 190	Glu	His
Thr	Ile	Gln 195	Asp	Ile	Ala	Pro	Asn 200	Tyr	Ser	Pro	Glu	Gly 205	Ser	Tyr	Asp
Leu	Asn 210	Ser	Asn	Asp	Pro	Asp 215	Pro	Met	Pro	His	Pro 220	Asp	Val	Glu	Asn
Gly 225	Asn	His	His	Gly	Thr 230	Arg	Cys	Ala	Gly	Glu 235	Ile	Ala	Ala	Val	Pro 240
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Gly	Ile	Arg	Val 260	Leu	Asp	Gly	Pro	Leu 265	Thr	Asp	Ser	Met	Glu 270	Ala	Val
Ala	Phe	Asn 275	Lys	His	Tyr	Gln	Ile 280	Asn	Asp	Ile	Tyr	Ser 285	Сув	Ser	Trp
Gly	Pro 290	Asp	Asp	Asp	Gly	Lys 295	Thr	Val	Asp	Gly	Pro 300	His	Gln	Leu	Gly
305 Lys	Ala	Ala	Leu	Gln	His 310	Gly	Val	Ile	Ala	Gly 315	Arg	Gln	Gly	Phe	Gly 320
Ser	Ile	Phe	Val	Val 325	Ala	Ser	Gly	Asn	Gly 330	Gly	Gln	His	Asn	Asp 335	Asn
CAa	Asn	Tyr	Asp 340	Gly	Tyr	Ala	Asn	Ser 345	Ile	Tyr	Thr	Val	Thr 350	Ile	Gly
Ala	Val	Asp 355	Glu	Glu	Gly	Arg	Met 360	Pro	Phe	Tyr	Ala	Glu 365	Glu	Cys	Ala
Ser	Met 370	Leu	Ala	Val	Thr	Phe 375	Ser	Gly	Gly	Asp	380 Lys	Met	Leu	Arg	Ser
Ile 385	Val	Thr	Thr	Asp	Trp 390	Asp	Leu	Gln	Lys	Gly 395	Thr	Gly	Cys	Thr	Glu 400
Gly	His	Thr	Gly	Thr 405	Ser	Ala	Ala	Ala	Pro 410	Leu	Ala	Ala	Gly	Met 415	Ile
Ala	Leu	Met	Leu 420	Gln	Val	Arg	Pro	Сув 425	Leu	Thr	Trp	Arg	Asp 430	Val	Gln

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Trp Val Thr Asn Glu Ala Gly Phe Ser His Ser His Gln His Gly Phe
Gly Leu Leu Asn Ala Trp Arg Leu Val Asn Ala Ala Lys Ile Trp Thr
Ser Val Pro Tyr Leu Ala Ser Tyr Val Ser Pro Val Leu Lys Glu Asn
Lys Ala Ile Pro Gln Ser Pro Arg Ser Leu Glu Val Leu Trp Asn Val
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Ser Arg Met Asp Leu Glu Met Ser Gly Leu Lys Thr Leu Glu His Val
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Ala Val Thr Val Ser Ile Thr His Pro Arg Arg Gly Ser Leu Glu Leu
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Lys Leu Phe Cys Pro Ser Gly Met Met Ser Leu Ile Gly Ala Pro Arg
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Ser Met Asp Ser Asp Pro Asn Gly Phe Asn Asp Trp Thr Phe Ser Thr
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Val Arg Cys Trp Gly Glu Arg Ala Arg Gly Thr Tyr Arg Leu Val Ile
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Arg Gln Arg Leu Leu Glu Ser Ala Met Ser Gly Lys Tyr Leu His Asp
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Asp Phe Ala Leu Pro Cys Pro Pro Gly Leu Lys Ile Pro Glu Glu Asp
Gly Tyr Thr Ile Thr Pro Asn Thr Leu Lys Thr Leu Val Leu Val Gly
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Cys Phe Thr Val Phe Trp Thr Val Tyr Tyr Met Leu Glu Val Tyr Leu
Ser Gln Arg Asn Val Ala Ser Asn Gln Val Cys Arg Ser Gly Pro Cys
His Trp Pro His Arg Ser Arg Lys Ala Lys Glu Glu Gly Thr Glu Leu
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Glu Ser Arg Gly Pro Pro Thr Thr Ser Asp Leu Leu Ala Pro Asp Leu
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Glu	Asp 50	Gly	Leu	Ala	Asp	Ala 55	Pro	Glu	His	Gly	Ala 60	Thr	Ala	Thr	Phe
His 65	Arg	Сув	Ala	Lys	Asp 70	Pro	Trp	Arg	Leu	Pro 75	Gly	Thr	Tyr	Val	Val 80
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His	Val	Phe 115	His	His	Leu	Leu	Pro 120	Gly	Phe	Leu	Val	Lys 125	Met	Ser	Gly
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His	Arg	Glu 195	Ile	Glu	Gly	Arg	Val 200	Met	Val	Thr	Asp	Phe 205	Glu	Ser	Val
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Gln	Arg	Val 435	Leu	Thr	Pro	Asn	Leu 440	Val	Ala	Ala	Leu	Pro 445	Pro	Ser	Thr

His Arg Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His

Ser Gly Pro Thr Arg Met Ala Thr Ala Val Ala Arg Cys Ala Gln Asp Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg Gly Glu Arg Ile Glu Ala Gln Gly Gly Lys Arg Val Cys Arg Ala His $500 \hspace{1.5cm} 505 \hspace{1.5cm} 510 \hspace{1.5cm}$ Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu 520 Leu Pro Gln Val Asn Cys Ser Val His Thr Ala Pro Pro Ala Gly Ala 535 Ser Met Gly Thr Arg Val His Cys His Gln Gln Gly His Val Leu Thr Gly Cys Ser Ser His Trp Glu Val Glu Asp Leu Gly Thr His Lys Pro Pro Val Leu Arg Pro Arg Gly Gln Pro Asn Gln Cys Val Gly His Arg 585 Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys 600 Lys Val Lys Glu His Gly Ile Pro Ala Pro Gln Glu Gln Val Ile Val Ala Cys Glu Asp Gly Trp Thr Leu Thr Gly Cys Ser Ala Leu Pro Gly 635 Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Glu Glu Ala Val Ala Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Val Gln Ala Ser Gln Glu Leu Gln <210> SEQ ID NO 762 <211> LENGTH: 698 <212> TYPE: PRT <213 > ORGANISM: Mesocricetus auratus <400> SEOUENCE: 762 Met Gly Thr Ser Cys Ser Ala Arg Pro Arg Trp Leu Leu Ser Pro Leu Leu Leu Leu Leu Leu Leu Arg Tyr Met Gly Ala Ser Ala Gln Asp Glu Asp Ala Glu Tyr Glu Glu Leu Met Leu Thr Leu Gln Ser Gln Asp Asp Gly Leu Ala Asp Glu Thr Asp Glu Ala Pro Gln Gly Ala Thr Ala Ala Phe His Arg Cys Pro Glu Glu Ala Trp Arg Val Pro Gly Thr Tyr Ile Val Met Leu Ala Glu Glu Ala Gln Trp Val His Ile Glu Gln Thr Met His Arg Leu Gln Thr Gln Ala Ala Arg Arg Gly Tyr Val Ile Lys 105 Ile Gln His Ile Phe Tyr Asp Phe Leu Pro Ala Phe Val Val Lys Met 120

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Ile 145	Glu	Glu	Asp	Ser	Leu 150	Val	Phe	Ala	Gln	Ser 155	Ile	Pro	Trp	Asn	Leu 160
Asp	Arg	Ile	Ile	Pro 165	Ala	Gly	Arg	Gln	Ala 170	Gln	Glu	Tyr	Ser	Ser 175	Ser
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Thr	Ser	Ile 195	Gln	Ser	Asp	His	Arg 200	Glu	Ile	Glu	Gly	Arg 205	Val	Thr	Val
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Gln 225	Ala	Ser	Lys	Cys	Asp 230	Ser	His	Gly	Thr	His 235	Leu	Ala	Gly	Val	Val 240
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Thr 305	Ala	Cys	Gln	His	Leu 310	Ala	Arg	Thr	Gly	Val 315	Val	Leu	Val	Ala	Ala 320
Ala	Gly	Asn	Phe	Arg 325	Asp	Asp	Ala	Càa	Leu 330	Tyr	Ser	Pro	Ala	Ser 335	Ala
Pro	Glu	Val	Ile 340	Thr	Val	Gly	Ala	Thr 345	Asp	Val	Gln	Asp	Gln 350	Pro	Val
Thr	Leu	Gly 355	Thr	Leu	Gly	Thr	Asn 360	Phe	Gly	Arg	GÀa	Val 365	Asp	Leu	Phe
Ala	Pro 370	Gly	Lys	Asp	Ile	Ile 375	Gly	Ala	Ser	Ser	Asp 380	Cys	Ser	Ala	Cya
Phe 385	Met	Ser	Gln	Ser	Gly 390	Thr	Ser	Gln	Ala	Ala 395	Ala	His	Val	Ala	Gly 400
Ile	Val	Ala	Met	Met 405	Leu	Thr	Leu	Glu	Pro 410	Glu	Leu	Thr	Leu	Thr 415	Glu
Leu	Arg		Arg 420		Ile	His		Ser 425			Asp		Ile 430	Asn	Met
Ala	Trp	Phe 435	Pro	Glu	Asp	Gln	Arg 440	Val	Leu	Thr	Pro	Asn 445	Leu	Val	Ala
Thr	Leu 450	Pro	Pro	Ser	Thr	His 455	Gly	Thr	Gly	Gly	Gln 460	Leu	Leu	Cys	Arg
Thr 465	Val	Trp	Ser	Ala	His 470	Ser	Gly	Pro	Thr	Arg 475	Ala	Ala	Thr	Ala	Thr 480
Ala	Arg	Cys	Ala	Pro 485	Gly	Glu	Glu	Leu	Leu 490	Ser	CÀa	Ser	Ser	Phe 495	Ser
Arg	Ser	Gly	Arg 500	Arg	Arg	Gly	Asp	Arg 505	Ile	Glu	Ala	Ala	Gly 510	Thr	Gln
Gln	Val	Cys 515	Lys	Ala	Leu	Asn	Ala 520	Phe	Gly	Gly	Glu	Gly 525	Val	Tyr	Ala
Val	Ala 530	Arg	Сув	Cys	Leu	Leu 535	Pro	Arg	Ala	Asn	Сув 540	Ser	Ile	His	Thr
Thr	Pro	Ala	Ala	Arg	Thr	Ser	Leu	Glu	Thr	His	Ala	His	Cys	His	Gln

	-continue
555	

545					550					555					560
Lys	Asp	His	Val	Leu 565	Thr	Gly	CAa	Ser	Leu 570	His	Trp	Glu	Val	Glu 575	Gly
Ile	Gly	Val	Gln 580	Pro	Leu	Ala	Val	Leu 585	Arg	Ser	Arg	His	Gln 590	Pro	Gly
Gln	Cys	Thr 595	Gly	His	Arg	Glu	Ala 600	Ser	Val	His	Ala	Ser 605	CÀa	Cha	His
Ala	Pro 610	Gly	Leu	Glu	CÀa	Lys 615	Ile	Lys	Glu	His	Gly 620	Ile	Ser	Gly	Pro
Ala 625	Glu	Gln	Val	Thr	Val 630	Ala	Сув	Glu	Ala	Gly 635	Trp	Thr	Leu	Thr	Gly 640
CAa	Asn	Val	Leu	Pro 645	Gly	Ala	Phe	Ile	Thr 650	Leu	Gly	Ala	Tyr	Ala 655	Val
Asp	Asn	Thr	Cys	Val	Ala	Arg	Ser	Arg 665	Val	Thr	Asp	Thr	Ala 670	Gly	Arg
Thr	Gly	Glu 675	Glu	Ala	Thr	Val	Ala 680	Ala	Ala	Ile	CAa	Cys 685	Arg	Asn	Arg
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Glu	Asp	Gly 35	Asp	Tyr	Glu	Glu	Leu 40	Met	Leu	Ala	Leu	Pro 45	Ser	Gln	Glu
Asp	Ser 50	Leu	Val	Asp	Glu	Ala 55	Ser	His	Val	Ala	Thr 60	Ala	Thr	Phe	Arg
Arg 65	Сла	Ser	Lys	Glu	Ala 70	Trp	Arg	Leu	Pro	Gly 75	Thr	Tyr	Val	Val	Val 80
Leu	Met	Glu	Glu	Thr 85	Gln	Arg	Leu	Gln	Val 90	Glu	Gln	Thr	Ala	His 95	Arg
Leu	Gln	Thr	Trp 100	Ala	Ala	Arg		Gly 105		Val	Ile		Val 110		His
Val	Phe	Tyr 115	Asp	Leu	Phe	Pro	Gly 120	Phe	Leu	Val	ГЛа	Met 125	Ser	Ser	Asp
Leu	Leu 130	Gly	Leu	Ala	Leu	Lys 135	Leu	Pro	His	Val	Glu 140	Tyr	Ile	Glu	Glu
Asp 145	Ser	Leu	Val	Phe	Ala 150	Gln	Ser	Ile	Pro	Trp 155	Asn	Leu	Glu	Arg	Ile 160
Ile	Pro	Ala	Trp	Gln 165	Gln	Thr	Glu	Glu	Asp 170	Ser	Ser	Pro	Asp	Gly 175	Ser
Ser	Gln	Val	Glu 180	Val	Tyr	Leu	Leu	Asp 185	Thr	Ser	Ile	Gln	Ser 190	Gly	His
Arg	Glu	Ile 195	Glu	Gly	Arg	Val	Thr 200	Ile	Thr	Asp	Phe	Asn 205	Ser	Val	Pro
Glu	Glu 210	Asp	Gly	Thr	Arg	Phe 215	His	Arg	Gln	Ala	Ser 220	ГÀа	Cha	Asp	Ser
His	Gly	Thr	His	Leu	Ala	Gly	Val	Val	Ser	Gly	Arg	Asp	Ala	Gly	Val

												COIL	СТП	aca	
225					230					235					240
Ala	Lys	Gly	Thr	Ser 245	Leu	His	Ser	Leu	Arg 250	Val	Leu	Asn	Сув	Gln 255	Gly
rys	Gly	Thr	Val 260	Ser	Gly	Thr	Leu	Ile 265	Gly	Leu	Glu	Phe	Ile 270	Arg	Lys
Ser	Gln	Leu 275	Ile	Gln	Pro	Ser	Gly 280	Pro	Leu	Val	Val	Leu 285	Leu	Pro	Leu
Ala	Gly 290	Gly	Tyr	Ser	Arg	Ile 295	Leu	Asn	Thr	Ala	300 200	Gln	Arg	Leu	Ala
Arg 305	Thr	Gly	Val	Val	Leu 310	Val	Ala	Ala	Ala	Gly 315	Asn	Phe	Arg	Asp	Asp 320
Ala	СЛа	Leu	Tyr	Ser 325	Pro	Ala	Ser	Ala	Pro 330	Glu	Val	Ile	Thr	Val 335	Gly
Ala	Thr	Asn	Ala 340	Gln	Asp	Gln	Pro	Val 345	Thr	Leu	Gly	Thr	Leu 350	Gly	Thr
Asn	Phe	Gly 355	Arg	Cys	Val	Asp	Leu 360	Phe	Ala	Pro	Gly	165 365	Asp	Ile	Ile
Gly	Ala 370	Ser	Ser	Asp	CÀa	Ser 375	Thr	Cys	Tyr	Met	Ser 380	Gln	Ser	Gly	Thr
Ser 385	Gln	Ala	Ala	Ala	His 390	Val	Ala	Gly	Ile	Val 395	Ala	Met	Met	Leu	Asn 400
Arg	Asp	Pro	Ala	Leu 405	Thr	Leu	Ala	Glu	Leu 410	Arg	Gln	Arg	Leu	Ile 415	Leu
Phe	Ser	Thr	Lys 420	Asp	Val	Ile	Asn	Met 425	Ala	Trp	Phe	Pro	Glu 430	Asp	Gln
Arg	Val	Leu 435	Thr	Pro	Asn	Arg	Val 440	Ala	Thr	Leu	Pro	Pro 445	Ser	Thr	Gln
Glu	Thr 450	Gly	Gly	Gln	Leu	Leu 455	Cys	Arg	Thr	Val	Trp 460	Ser	Ala	His	Ser
Gly 465	Pro	Thr	Arg	Thr	Ala 470	Thr	Ala	Thr	Ala	Arg 475	CAa	Ala	Pro	Glu	Glu 480
Glu	Leu	Leu	Ser	Сув 485	Ser	Ser	Phe	Ser	Arg 490	Ser	Gly	Arg	Arg	Arg 495	Gly
Asp	Arg	Ile	Glu 500	Ala	Ile	Gly	Gly	Gln 505	Gln	Val	CÀa	ГÀа	Ala 510	Leu	Asn
Ala	Phe	Gly 515	Gly	Glu	Gly	Val	Tyr 520	Ala	Val	Ala	Arg	Сув 525	Cya	Leu	Leu
Pro	Arg 530	Val	Asn	CÀa	Ser	Ile 535	His	Asn	Thr	Pro	Ala 540	Ala	Arg	Ala	Gly
Pro 545	Gln	Thr	Pro	Val	His 550	CAa	His	Gln	ГÀа	Asp 555	His	Val	Leu	Thr	Gly 560
CAa	Ser	Phe	His	Trp 565	Glu	Val	Glu	Asn	Leu 570	Arg	Ala	Gln	Gln	Gln 575	Pro
Leu	Leu	Arg	Ser 580	Arg	His	Gln	Pro	Gly 585	Gln	CÀa	Val	Gly	His 590	Gln	Glu
Ala	Ser	Val 595	His	Ala	Ser	CAa	600 GÀa	His	Ala	Pro	Gly	Leu 605	Glu	CAa	Lys
Ile	Lys 610	Glu	His	Gly	Ile	Ala 615	Gly	Pro	Ala	Glu	Gln 620	Val	Thr	Val	Ala
625					Thr 630					635					640
Ser	Leu	Pro	Leu	Gly 645	Ala	Tyr	Ser	Val	Asp 650	Asn	Val	CAa	Val	Ala 655	Arg

The Arg Asp Ala Gly Arg Ala Asp Arg Thr Ser Glu Glu Ala Thr Val
660

Ala Ala Ala Ile Cys Cys Arg Ser Arg Pro Ser Ala Lys Ala Ser Trp
675

Val His Gln
690

We claim:

- 1. 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 15 of a HCVR/LCVR amino acid sequence pair having SEQ ID NOs:218/226.
- 2. The antibody or antigen-binding fragment of claim 1 comprising heavy and light chain CDR amino

acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232.

3. The antibody or antigen-binding fragment of claim **2** comprising 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.

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