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(54) THERAPEUTIC USES OF ANTI-PCSK9 ANTIBODIES

(71) Applicant: REGENERON

PHARMACEUTICALS, INC.,

Tarrytown, NY (US)

(72) Inventors: Mark W. Sleeman, Melbourne (AU);

Joel H. Martin, Putnam Valley, NY (US); Tammy T. Huang, Goldens Bridge, NY (US); Douglas MacDonald,

New York, NY (US)

(73) Assignee: Regeneron Pharmaceuticals, Inc.,

Tarrytown, NY (US)

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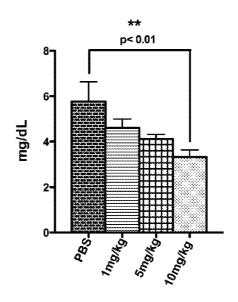
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Primary Examiner — Cherie M Stanfield (74) Attorney, Agent, or Firm — Swanson & Bratschun, L.L.C.

(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.

10 Claims, 14 Drawing Sheets



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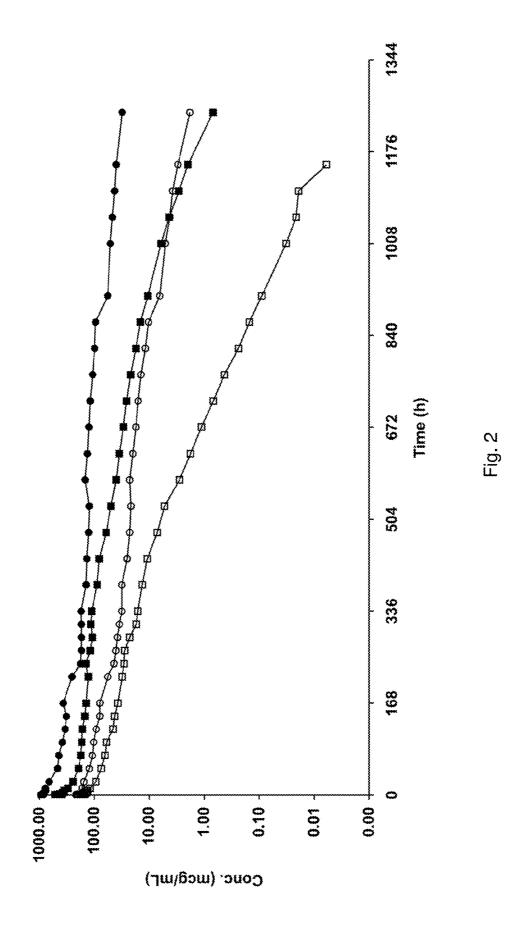
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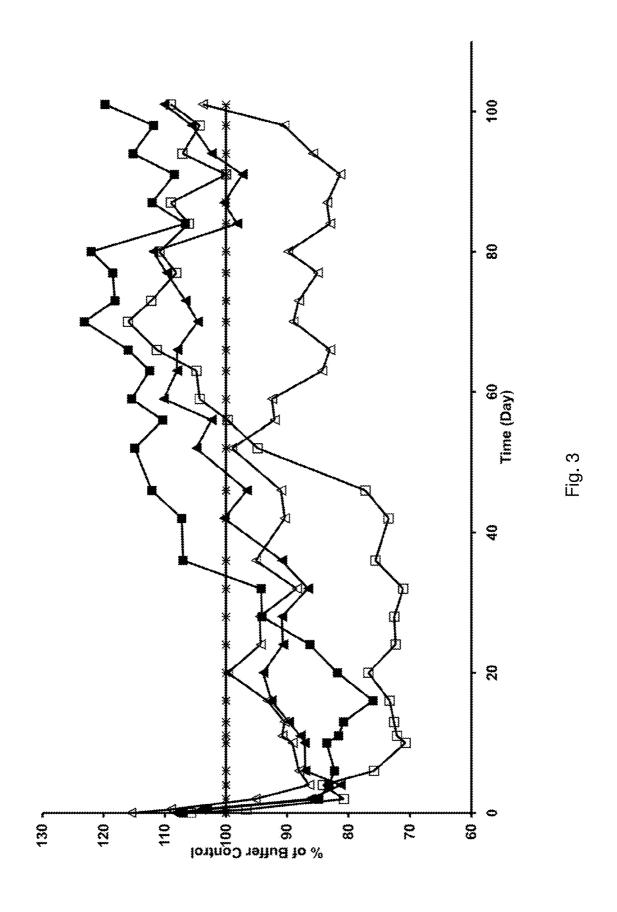
Schäfer et al. (Mar. 14-16, 2011) "Cholesterol lowering effect of SAR236553/REGN727, a fully human PCSK9 blocking monoclonal antibody in male Syrian hamster," Presented as a poster at the Drugs Affecting Lipid Metabolism (DALM)—XVII International Symposium, Mar. 14-16, 2011, Doha, Qatar.

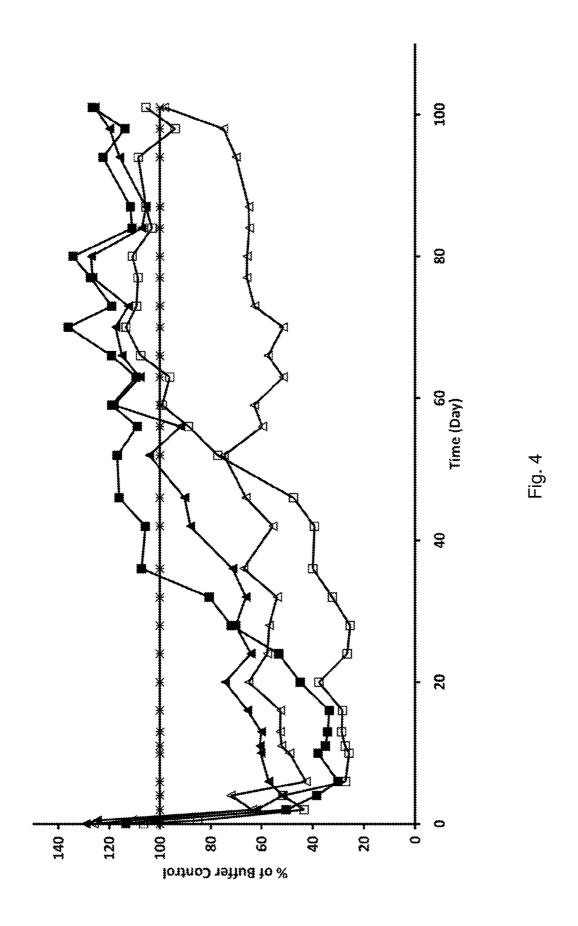
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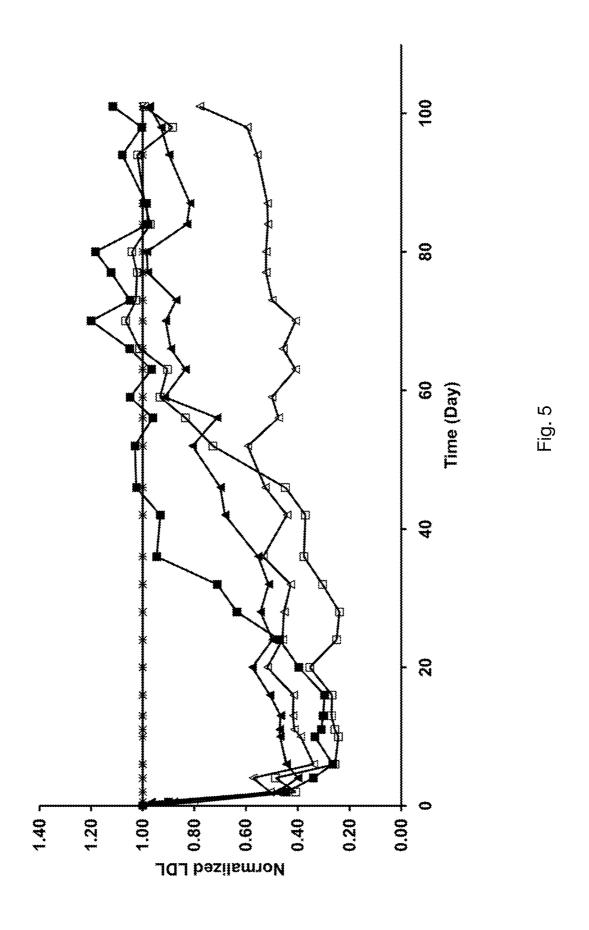
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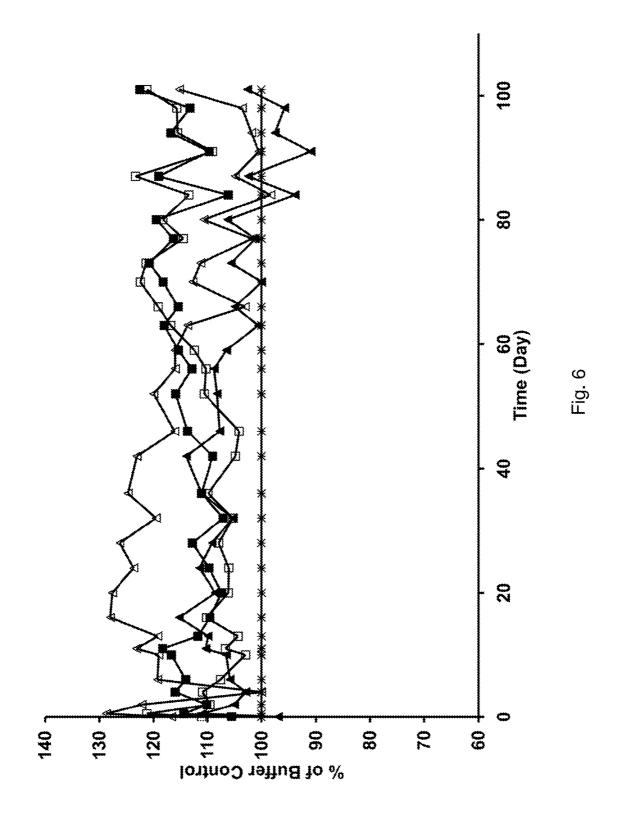
<u>Fig.</u> 1

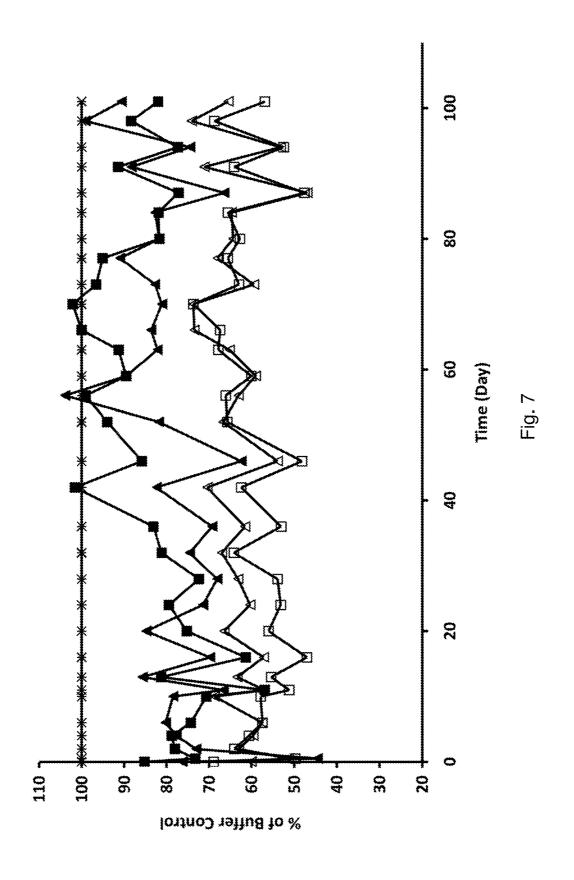


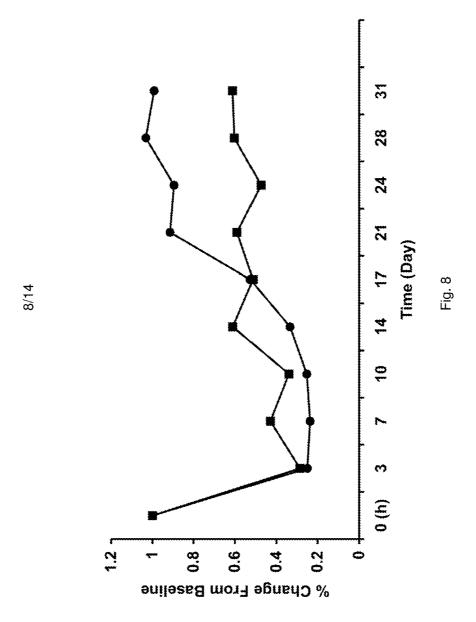


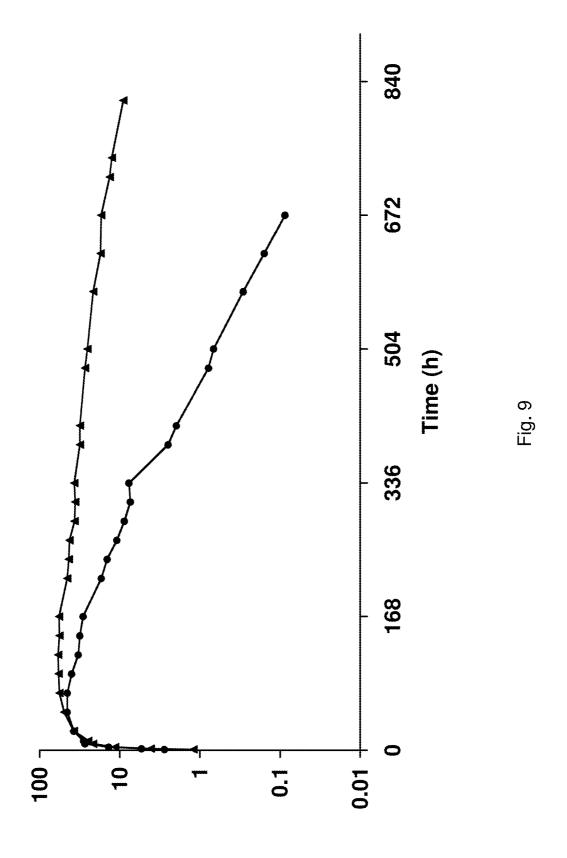


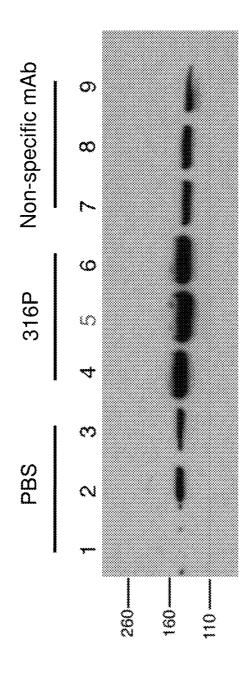




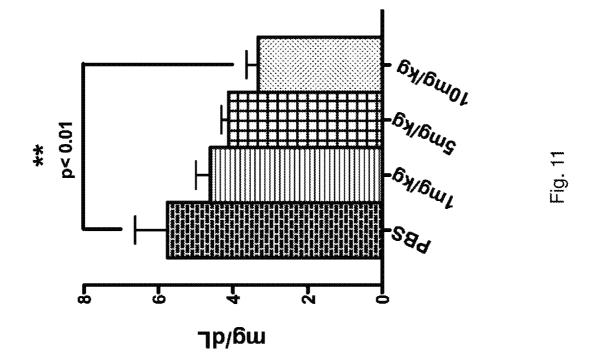


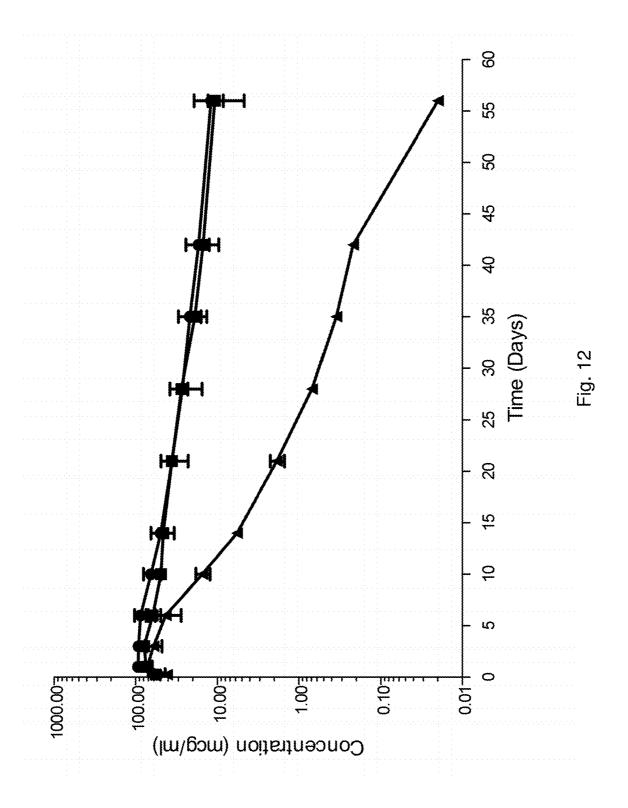


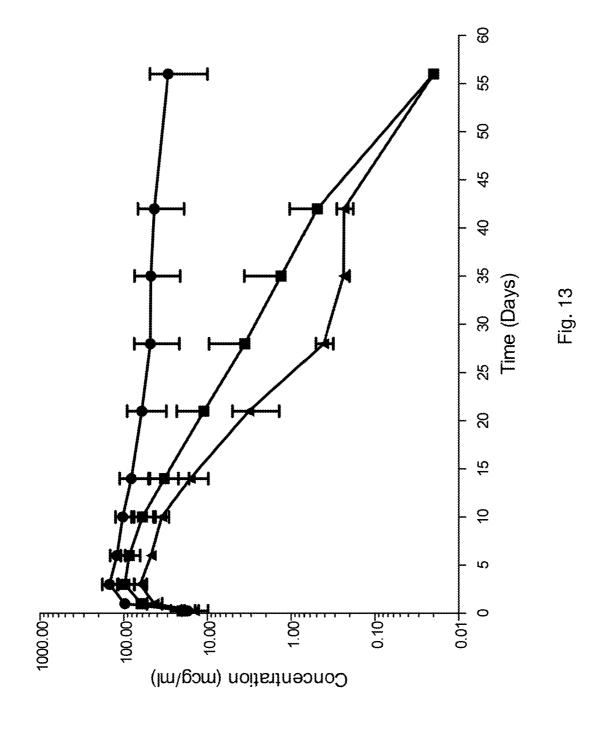


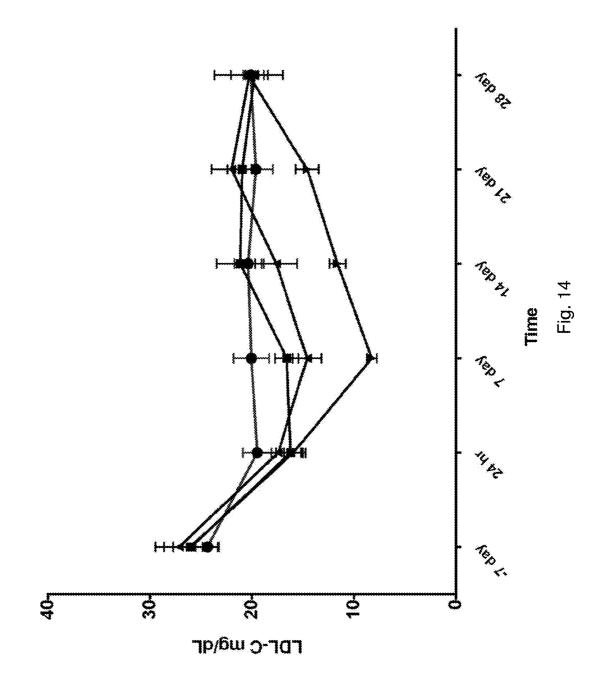


Jan. 24, 2017









1

THERAPEUTIC USES OF ANTI-PCSK9 **ANTIBODIES**

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 13/690,585, filed on 30 Nov. 2012, which is a continuation of U.S. application Ser. No. 12/949,846 filed on 19 Nov. 2010, now U.S. Pat. No. 8,501,184, Issued 6 Aug. 2013, which is a divisional of U.S. application Ser. No. 12/637,942, filed 15 Dec. 2009, now U.S. Pat. No. 8,062, 640, Issued 22 Nov. 2011, which claims the benefit under 35 USC §119(e) of U.S. Provisional 61/261,776 filed 17 Nov. 15 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 specifi- 25 cally bind human proprotein convertase subtilisin/kexin type 9 (PCSK9), and therapeutic methods of using those antibodies.

STATEMENT OF RELATED ART

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a proprotein convertase belonging to the proteinase K subfamily of the secretory subtilase family. The encoded protein is synthesized as a soluble zymogen that undergoes auto- 35 catalytic intramolecular processing in the endoplasmic reticulum. Evidence suggest that PCSK9 increases plasma LDL cholesterol by promoting degradation of the LDL receptor, which mediates LDL endocytosis in the liver, the major route of LDL clearance from circulation. The structure of PCSK9 protein shows that it has a signal sequence, followed by a prodomain, a catalytic domain that contains a conserved triad of residues (D186, H226 and S386), and a C-terminal domain. It is synthesized as a soluble 74-kDa 45 precursor that undergoes autocatalytic cleavage in the ER, generating a 14-kDa prodomain and 60-kDa catalytic fragment. The autocatalytic activity has been shown to be required for secretion. After cleavage the prodomain remains tightly associated with the catalytic domain.

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

BRIEF SUMMARY OF THE INVENTION

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

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

(i) capable of reducing serum total cholesterol at least about 25-35% and sustaining the reduction over at least a 24 65 day period relative to a predose level, preferably the reduction in serum total cholesterol is at least about 30-40%;

2

- (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

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 50 binding affinity for PCSK9 at an acidic pH relative to a neutral pH, as measured by surface plasmon resonance. In a specific embodiment, the antibody or fragment thereof exhibits a decreased binding affinity at an acidic pH.

In another embodiment, the antibody or antigen-binding 55 fragment binds human, human GOF mutation D374Y, cynomolgus monkey, rhesus monkey, mouse, rat and hamster

In one embodiment, the antibody or antigen-binding fragment binds human and monkey PCSK9, but does not 60 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'), or scFv fragment), and may be modified to affect functionality, e.g., to eliminate residual effector functions (Reddy et al. (2000) J. Immunol. 164:1925-1933).

In one embodiment, the invention comprises an antibody or antigen-binding fragment of an antibody comprising a

heavy chain variable region (HCVR) selected from the group consisting of SEQ ID NO:2, 18, 22, 26, 42, 46, 50, 66, 70, 74, 90, 94, 98, 114, 118, 122, 138, 142, 146, 162, 166, 170, 186, 190, 194, 210, 214, 218, 234, 238, 242, 258, 262, 266, 282, 286, 290, 306, 310, 314, 330, 334, 338, 354, 358, 362, 378, 382, 386, 402, 406, 410, 426, 430, 434, 450, 454, 458, 474, 478, 482, 498, 502, 506, 522, 526, 530, 546, 550, 554, 570, 574, 578, 594, 598, 602, 618, 622, 626, 642, 646, 650, 666, 670, 674, 690, 694, 698, 714, 718, 722, 738 and 742, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the HCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NO:50, 66, 70, 74, 90, 94, 122, 138, 142, 218, 234, 238, 242, 258, 262, 314, 330 and 334. In a more specific 15 embodiment, the HCVR comprises SEQ ID NO:90 or 218.

3

In one embodiment, the antibody or fragment thereof further comprises a light chain variable region (LCVR) selected from the group consisting of SEQ ID NO:10, 20, 24, 34, 44, 48, 58, 68, 72, 82, 92, 96, 106, 116, 120, 130, 20 140, 144, 154, 164, 168, 178, 188, 192, 202, 212, 216, 226, 236, 240, 250, 260, 264, 274, 284, 288, 298, 308, 312, 322, 332, 336, 346, 356, 360, 370, 380, 384, 394, 404, 408, 418, 428, 432, 442, 452, 456, 466, 476, 480, 490, 500, 504, 514, 524, 528, 538, 548, 552, 562, 572, 576, 586, 596, 600, 610, 25 620, 624, 634, 644, 648, 658, 668, 672, 682, 692, 696, 706, 716, 720, 730, 740 and 744, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the LCVR comprises an amino acid sequence selected from 30 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 35 comprises a HCVR and LCVR (HCVR/LCVR) sequence pair selected from the group consisting of SEQ ID NO: 2/10, 18/20, 22/24, 26/34, 42/44, 46/48, 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 98/106, 114/116, 118/120, 122/130, 138/140, 142/144, 146/154, 162/164, 166/168, 170/178, 40 186/188, 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, 45 426/428, 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/ 55 240, 242/250, 258/260, 262/264, 314/322, 330/332 and 334/336. In a more specific embodiment, the HCVR/LCVR pair comprises SEQ ID NO:90/92 or 218/226.

In a second aspect, the invention features an antibody or antigen-binding fragment of an antibody comprising a heavy 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

4

from the group consisting of SEQ ID NO:16, 40, 64, 88, 112, 136, 160, 184, 208, 232, 256, 280, 304, 328, 352, 376, 400, 424, 448, 472, 496, 520, 544, 568, 592, 616, 640, 664, 688, 712 and 736, or substantially similar sequences thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In one embodiment, the HCDR3/LCDR3 sequence pair is selected from the group consisting of SEQ ID NO:56/64, 80/88, 128/136, 224/232, 248/256 and 320/328. In a more specific embodiment, the HCDR3/LCDR3 sequence pair comprises SEQ ID NO:80/88 or 224/232

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

In a related embodiment, the invention comprises an antibody or antigen-binding fragment of an antibody which specifically binds 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 embodi-

ment, 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 5 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 10 that specifically bind hPCSK9 and neutralize PCSK9 activity, wherein the antibody or fragment thereof exhibits one or more of the following characteristics: (i) capable of reducing serum total cholesterol at least about 25-35% and sustaining the reduction over at least a 24 day period relative to a 15 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 least about 25-40% relative to predose level; (iv) does not reduce serum HDL cholesterol or reduces serum HDL cholesterol no more than 5% relative to predose level; (v) binds an epitope comprising amino acid residue 238 of hPCSK9 (SEQ ID NO:755); (vi) exhibits an enhanced 25 binding affinity (K_D) for hPCSK9 at pH 5.5 relative to the K_D at pH 7.4, as measured by plasmon surface resonance, wherein the enhanced affinity is at least about a 20- to 50-fold increase in affinity; (vii) binds human, human GOF mutation D374Y, cynomolgus monkey, rhesus monkey, 30 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

In one embodiment, the invention provides fully human 35 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: 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 45 to predose level; (iv) binds an epitope comprising amino acid residue 366 of hPCSK9 (SEQ ID NO:755); (v) does not exhibit an enhanced binding affinity for PCSK9 at an acidic pH relative to a neutral pH, as measured by surface plasmon resonance; (vi) binds human and monkey PCSK9, but does 50 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 55 molecules encoding anti-PCSK9 antibodies or fragments thereof. Recombinant expression vectors carrying the nucleic acids of the invention, and host cells into which such vectors have been introduced, are also encompassed by the invention, as are methods of producing the antibodies by 60 culturing the host cells under conditions permitting production of the antibodies, and recovering the antibodies pro-

In one embodiment, the invention provides an antibody or fragment thereof comprising a HCVR encoded by a nucleic 65 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,

6

121, 137, 141, 145, 161, 165, 169, 185, 189, 193, 209, 213, 217, 233, 237, 241, 257, 261, 265, 281, 285, 289, 305, 309, 313, 329, 333, 337, 353, 357, 361, 377, 381, 385, 401, 405, 409, 425, 429, 433, 449, 453, 457, 473, 477, 481, 497, 501, 505, 521, 525, 529, 545, 549, 553, 569, 573, 577, 593, 597, 601, 617, 621, 625, 641, 645, 649, 665, 669, 673, 689, 693, 697, 713, 717, 721, 737 and 741, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. In one embodiment, the HCVR is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 49, 65, 69, 73, 89, 93, 121, 137, 141, 217, 233, 237, 241, 257, 261, 313, 329 and 333. In more 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, predose level; (iii) capable of reducing serum triglyceride at 20 129, 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, (i) capable of reducing serum LDL cholesterol at least about 40 415, 439, 463, 487, 511, 535, 559, 583, 607, 631, 655, 679, 703 and 727, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; and a LCDR3 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 15, 39, 63, 87, 111, 135, 159, 183, 207, 231, 255, 279, 303, 327, 351, 375, 399, 423, 447, 471, 495, 519, 543, 567, 591, 615, 639, 663, 687, 711 and 735, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. In one embodiment, the HCDR3 and LCDR3 comprise a sequence pair encoded by the nucleic acid sequence of SEQ ID NO: 55/63, 79/87, 127/135, 223/231, 247/255 and 319/327, respectively. In more specific embodiments, the HCDR3 and LCDR3 comprise a sequence pair encoded by the nucleic acid sequence of SEQ ID NO: 79/87 and 223/231.

In a further embodiment, the antibody or fragment thereof further comprises, a HCDR1 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 3, 27, 51, 75, 99, 123, 147, 171, 195, 219, 243, 267, 291, 315, 339, 363, 387, 411, 435, 459, 483, 507, 531, 555, 579, 603, 627, 651, 675, 699 and 723, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; a HCDR2 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:5, 29, 53, 77, 101, 125, 149, 173, 197, 221, 245, 269, 293, 317, 341, 365, 389, 413, 437, 461, 485, 509, 533, 557, 581, 605, 629, 653, 677, 701 and 725,

or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; a LCDR1 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 11, 35, 59, 83, 107, 131, 155, 179, 203, 227, 251, 275, 299, 323, 5 347, 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 10 consisting of SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, 205, 229, 253, 277, 301, 325, 349, 373, 397, 421, 445, 469, 493, 517, 541, 565, 589, 613, 637, 661, 685, 709 and 733, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. 15 In one embodiment, the heavy and light chain CDR sequences are encoded by the nucleic acid sequences of SEQ ID NO: 51, 53, 55, 59, 61, 63; 75, 77, 79, 83, 85, 87; 123, 125, 127, 131, 133, 135; 219, 221, 223, 227, 229, 231; 243, 245, 247, 251, 253, 255; and 315, 317, 319, 323, 325, 327, 20 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 further embodiment, the antibody or fragment thereof further comprise a HCDR1 sequence of the formula X¹-X²- $X^3-X^4-X^5-X^6-X^7X^8$ (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 45 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 NO:746), wherein X^1 is Ile, X^2 is Ser or Asn, X^3 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 50 formula $X^1-X^2-X^3-X^4-X^5-X^6-X^7-X^8-X^9-X^{10}-X^{11}-X^{12}$ (SEQ ID NO:748) wherein X¹ is Gln, X² is Ser, X³ is Val or Leu, X⁴ is 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 55 formula X¹-X²-X³ (SEQ ID NO:749) wherein X¹ is Trp or Leu, X² 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 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 8

7-27, J_H gene segment 2, V_K gene segment 4-1 and J_K gene segment 2; or (b) V_H gene segment 3-7, D_H gene segment 2-8, J_H gene segment 6, V_K gene segment 2-28 and J_K gene segment 4.

In a sixth aspect, the invention features an antibody or antigen-binding fragment thereof that binds to a PCSK9 protein of SEQ ID NO:755, wherein the binding of the antibody or fragment thereof to a variant PCSK9 protein is less than 50% of the binding between the antibody or fragment thereof and the PCSK9 protein of SEQ ID NO:755. In specific embodiment, the antibody or fragment thereof binds to the variant PCSK9 protein with a binding affinity (K_D) which is less than about 50%, less than about 60%, less than about 70%, less than about 80%, less than about 90% or less than about 95% compared to the binding to PCSK9 (SEQ ID NO:755).

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

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

The invention encompasses anti-PCSK9 antibodies having a modified glycosylation pattern. In some applications, modification to remove undesirable glycosylation sites may be useful, or 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 puptake and or bile acid re-absorption; capable of increasing lipoprotein catabolism (such as niacin); and/or activators of the LXR transcription factor that plays a role in cholesterol elimination such as 22-hydroxycholesterol.

In an eighth aspect, the invention features methods for inhibiting hPCSK9 activity using the anti-PCSK9 antibody or antigen-binding portion of the antibody of the invention, wherein the therapeutic methods comprise administering a therapeutically effective amount of a pharmaceutical composition comprising an antibody or antigen-binding fragment of an antibody of the invention. The disorder treated is any disease or condition which is improved, ameliorated, inhibited or prevented by removal, inhibition or reduction of PCSK9 activity. Specific populations treatable by the thera-20 peutic 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 25 intolerant or statin uncontrolled; and subjects at risk for developing hypercholesterolemia who may be preventably treated. Other indications include dyslipidemia associated with secondary causes such as Type 2 diabetes mellitus, cholestatic liver diseases (primary biliary cirrhosis), neph- 30 rotic syndrome, hypothyroidism, obesity; and the prevention and treatment of atherosclerosis and cardiovascular diseases.

In specific embodiments of the method of the invention, the anti-hPCSK9 antibody or antibody fragment of the invention is useful to reduce elevated total cholesterol, ³⁵ non-HDL cholesterol, LDL cholesterol, and/or apolipoprotein B (apolipoprotein B100).

The antibody or antigen-binding fragment of the invention may be used alone or in combination with a second agent, for example, an HMG-CoA reductase inhibitor and/or 40 other lipid lowering drugs.

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

BRIEF DESCRIPTION OF THE FIGURES

- FIG. 1. Sequence comparison tables of heavy chain (A) and light chain (B) variable regions and CDRs of antibodies H1H316P and H1M300N.
- FIG. 2. Antibody concentrations in serum over time. 316P 50 5 mg/kg (\square); 300N 5 mg/kg (\bigcirc); 316P 15 mg/kg (\blacksquare); 300N 15 mg/kg (\bullet).
- FIG. 3. Serum total cholesterol level as a percentage of change over buffer control. Buffer control (*); 316P 5 mg/kg (\blacksquare); 300N 5 mg/kg (\triangle); 316P 15 mg/kg (\square); 300N 15 55 mg/kg (Δ).
- FIG. 4. Serum LDL cholesterol level as a percentage of change over buffer control: Buffer Control (*); 316P 5 mg/kg (\blacksquare); 300N 5 mg/kg (\triangle); 316P 15 mg/kg (\square); 300N 15 mg/kg (Δ).
- FIG. 5. Serum LDL cholesterol level normalized to buffer control. Buffer control (*); 316P 5 mg/kg (\blacksquare); 300N 5 mg/kg (\triangle); 316P 15 mg/kg (\square); 300N 15 mg/kg (Δ).
- FIG. 6. Serum HDL cholesterol level as a percentage of change over buffer control. Buffer control (*); 316P 5 mg/kg 65 (■); 300N 5 mg/kg (▲); 316P 15 mg/kg (□); 300N 15 mg/kg (Δ).

10

- FIG. 7. Serum triglyceride level expressed as a percentage of change over buffer control. Buffer control (*); 316P 5 mg/kg (\blacksquare); 300N 5 mg/kg (\triangle); 316P 15 mg/kg (\square); 300N 15 mg/kg (Δ).
- FIG. 8. Serum LDL cholesterol level expressed as a percentage of change over baseline following a single dose subcutaneous administration. 316P 5 mg/kg (■); 300N 5 mg/kg (●).
- FIG. 9. Antibody concentrations in serum over time following a single dose subcutaneous administration. 316P 5 mg/kg (♠); 300N 5 mg/kg (♠).
- 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 (ℍ) 316P 10 mg/kg (ℍ).
- FIG. 12. Anti-hPCSK9 mAb serum pharmacokinetic profile in C57BL/6 mice. Single dose of Control I mAb (●) at 10 mg/kg; 316P (▲) at 10 mg/kg and 300N (■) at 10 mg/kg.
- FIG. 13. Anti-hPCSK9 mAb serum pharmacokinetic profile in hPCSK9 heterozygous mice. Single dose of Control I mAb (●) at 10 mg/kg; 316P (▲) at 10 mg/kg and 300N (■) at 10 mg/kg.
- FIG. 14. Effect of 316P on serum LDL cholesterol levels in Syrian Hamster fed a normal diet. Buffer control (♠); 316P 1 mg/kg (♠); 316P 5 mg/kg (♥).

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 polypep60 tide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region ("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 20 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 25 or a consensus of such sequences. Positions for substitution within CDRs and amino acids to substitute can also be selected empirically. Empirical substitutions can be conservative or non-conservative substitutions.

The term "human antibody", as used herein, is intended to include antibodies having variable and constant regions derived from human germline immunoglobulin sequences. The human mAbs of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (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 include mAbs in which CDR sequences derived from the germline of another mammalian species (e.g., 40 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 45 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, 50 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 55 nonetheless considered antibodies that "specifically bind" hPCSK9, as used herein.

The term "high affinity" antibody refers to those mAbs having a binding affinity to hPCSK9 of at least 10^{-10} M; preferably 10^{-11} M; even more preferably 10^{-12} M, as 60 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 of 1×10^{-3} s⁻¹ or less, preferably 1×10^{-4} s⁻¹ or less, as 65 determined by surface plasmon resonance, e.g., BIA-CORETM.

12

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

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

An "isolated antibody", as used herein, is intended to refer to an antibody that is substantially free of other mAbs having different antigenic specificities (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 5 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. 10 See, e.g., Pearson (1994) Methods Mol. Biol. 24: 307-331, which is herein incorporated by reference. Examples of groups of amino acids that have side chains with similar chemical properties include 1) aliphatic side chains: glycine, alanine, valine, leucine and isoleucine; 2) aliphatic-hydroxyl side chains: serine and threonine; 3) amide-containing side chains: asparagine and glutamine; 4) aromatic side chains: phenylalanine, tyrosine, and tryptophan; 5) basic side chains: lysine, arginine, and histidine; 6) acidic side chains: aspartate and glutamate, and 7) sulfur-containing side 20 chains: cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamate-aspartate, and asparagine-glutamine. Alternatively, a conservative replacement is any change having a 25 positive value in the PAM250 log-likelihood matrix disclosed in Gonnet et al. (1992) Science 256: 1443 45, herein incorporated by reference. A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

Sequence similarity for polypeptides is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitu- 35 tions. For instance, GCG software contains programs such as GAP and BESTFIT which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organ- 40 isms or between a wild type protein and a mutein thereof. See, e.g., GCG Version 6.1. Polypeptide sequences also can be compared using FASTA with default or recommended parameters; a program in GCG Version 6.1. FASTA (e.g., FASTA2 and FASTA3) provides alignments and percent 45 sequence identity of the regions of the best overlap between the query and search sequences (Pearson (2000) supra). Another preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program 50 BLAST, especially BLASTP or TBLASTN, using default parameters. See, e.g., Altschul et al. (1990) J. Mol. Biol. 215: 403 410 and (1997) Nucleic Acids Res. 25:3389 402, each of which is herein incorporated by reference.

In specific embodiments, the antibody or antibody fragment for use in the method of the invention may be monospecific, bispecific, or multispecific. Multispecific antibodies may be specific for different epitopes of one target polypeptide or may contain antigen-binding domains specific for epitopes of more than one target polypeptide. An 60 exemplary bi-specific antibody format that can be used in the context of the present invention involves the use of a first immunoglobulin (Ig) CH3 domain and a second Ig CH3 domain, wherein the first and second Ig CH3 domains differ from one another by at least one amino acid, and wherein at least one amino acid difference reduces binding of the bispecific antibody to Protein A as compared to a bi-specific

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

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

Preparation of Human Antibodies

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

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

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

The frequency of appearance of the second form in various intact IgG isotypes is due to, but not limited to, structural differences associated with the hinge region isotype of the antibody. A single amino acid substitution in the hinge region of the human IgG4 hinge can significantly reduce the appearance of the second form (Angal et al.

(1993) Molecular Immunology 30:105) to levels typically observed using a human IgG1 hinge. The instant invention encompasses antibodies having one or more mutations in the hinge, CH2 or CH3 region which may be desirable, for example, in production, to improve the yield of the desired 5 antibody form.

Generally, a VELOCIMMUNETM 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 10 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 15 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 20 antigen-specific lymphocytes.

Initially, high affinity chimeric antibodies are isolated having a human variable region and a mouse constant region. As described below, the antibodies are characterized and selected for desirable characteristics, including affinity, 25 selectivity, epitope, etc. The mouse constant regions are replaced with a desired human constant region to generate the fully human antibody of the invention, for example wild-type or modified IgG1 or IgG4 (for example, SEQ ID NO:751, 752, 753). While the constant region selected may 30 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 35 (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 40 (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 45 Science 9: 487-496) (herein specifically incorporated by reference in its entirety).

The term "epitope" refers to a site on an antigen to which B and/or T cells respond. B-cell epitopes can be formed both from contiguous amino acids or noncontiguous amino acids 50 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, 55 and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation.

Modification-Assisted Profiling (MAP), also known as Antigen Structure-based Antibody Profiling (ASAP) is a method that categorizes large numbers of monoclonal antibodies (mAbs) directed against the same antigen according to the similarities of the binding profile of each antibody to chemically or enzymatically modified antigen surfaces (US 2004/0101920, herein specifically incorporated by reference in its entirety). Each category may reflect a unique epitope 65 either distinctly different from or partially overlapping with epitope represented by another category. This technology

allows rapid filtering of genetically identical mAbs, such that characterization can be focused on genetically distinct mAbs. When applied to hybridoma screening, MAP may facilitate identification of rare hybridoma clones that produce mAbs having the desired characteristics. MAP may be used to sort the anti-PCSK9 mAbs of the invention into groups of mAbs binding different epitopes.

16

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

In various embodiments, the anti-hPCSK9 antibody or antigen-binding fragment of an antibody binds an epitope within the propeptide domain (residues 31 to 152 of SEQ ID NO:755); more specifically, an epitope from about residue 31 to about residue 90 or from about residue 90 to about residue 152; more specifically, the antibody or antibody fragment of the invention binds an epitope within the fragment from about residue 31 to about residue 60, from about residue 60 to about residue 90, from about residue 85 to about residue 110, from about residue 100 to about residue 130, from about residue 125 to about residue 150, from about residue 135 to about residue 152, and/or from about residue 140 to about residue 152.

In some embodiments, the anti-hPCSK9 antibody or antigen-binding fragment of an antibody binds an epitope within the C-terminal domain, (residues 426 to 692 of SEQ ID NO:755); more specifically, an epitope from about residue 426 to about residue 570 or from about residue 570 to about residue 692; more specifically, the antibody or antibody fragment of the invention binds an epitope within the fragment from about residue 450 to about residue 500, from about residue 500 to about residue 550, from about residue 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 $(\sim 0.7 \times 10^{-9} \text{ M to } \sim 36 \times 10^{-9} \text{ M})$ and a similar shortening in $T_{1/2}$ (from ~120 to ~2 min). In a specific embodiment, the 5 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 15 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 20 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 25 clonal antibody conjugated to a therapeutic moiety ("immuthe 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 30 reference anti-PCSK9 antibody, the above-described binding methodology is performed in two orientations: In a first orientation, the reference antibody is allowed to bind to a PCSK9 molecule under saturating conditions followed by assessment of binding of the test antibody to the PCSK9 35 molecule. In a second orientation, the test antibody is allowed to bind to a PCSK9 molecule under saturating conditions followed by assessment of binding of the reference antibody to the PCSK9 molecule. If, in both orientations, only the first (saturating) antibody is capable of 40 binding to the PCSK9 molecule, then it is concluded that the test antibody and the reference antibody compete for binding to PCSK9. As will be appreciated by a person of ordinary skill in the art, an antibody that competes for binding with a reference antibody may not necessarily bind to the iden- 45 tical epitope as the reference antibody, but may sterically block binding of the reference antibody by binding an overlapping or adjacent epitope.

Two antibodies bind to the same or overlapping epitope if each competitively inhibits (blocks) binding of the other to 50 the antigen. That is, a 1-, 5-, 10-, 20- or 100-fold excess of one antibody inhibits binding of the other by at least 50% but preferably 75%, 90% or even 99% as measured in a competitive binding assay (see, e.g., Junghans et al., Cancer Res. 1990 50:1495-1502). Alternatively, two antibodies have the 55 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 60 eliminate binding of the other.

Additional routine experimentation (e.g., peptide mutation and binding analyses) can then be carried out to confirm whether the observed lack of binding of the test antibody is in fact due to binding to the same epitope as the reference 65 antibody or if steric blocking (or another phenomenon) is responsible for the lack of observed binding. Experiments of

18

this sort can be performed using ELISA, RIA, surface plasmon resonance, flow cytometry or any other quantitative or qualitative antibody-binding assay available in the art.

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

Immunoconjugates

The invention encompasses a human anti-PCSK9 mononoconjugate"), 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 Q15R, N44S, K52N, V57M, R69K, E79Q, and V82I (by IMGT; Q355R, N384S, K392N,

V397M, R409K, E419Q, and V422I by EU) in the case of IgG4 antibodies. Variations on the bi-specific antibody format described above are contemplated within the scope of the present invention.

Bioequivalents

The anti-PCSK9 antibodies and antibody fragments of the present invention encompass proteins having amino acid sequences that vary from those of the described mAbs, but that retain the ability to bind human PCSK9. Such variant mAbs and antibody fragments comprise one or more addi- 10 tions, 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 15 that comprise one or more additions, deletions, or substitutions of nucleotides when compared to the disclosed sequence, but that encode an anti-PCSK9 antibody or antibody fragment that is essentially bioequivalent to an anti-PCSK9 antibody or antibody fragment of the invention. 20 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 25 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 30 their absorption but not in their rate of absorption and yet may be considered bioequivalent because such differences in the rate of absorption are intentional and are reflected in the labeling, are not essential to the attainment of effective body drug concentrations on, e.g., chronic use, and are considered 35 medically insignificant for the particular drug product studied. In one embodiment, two antigen-binding proteins are bioequivalent if there are no clinically meaningful differences in their safety, purity, and potency.

In one embodiment, two antigen-binding proteins are 40 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 45 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 55 function of time; (b) an in vitro test that has been correlated with and is reasonably predictive of human in vivo bioavailability data; (c) an in vivo test in humans or other mammals in which the appropriate acute pharmacological effect of the antibody (or its target) is measured as a function of time; and (d) in a well-controlled clinical trial that establishes safety, efficacy, or bioavailability or bioequivalence of an antibody.

Bioequivalent variants of anti-PCSK9 antibodies of the invention may be constructed by, for example, making various substitutions of residues or sequences or deleting 65 terminal or internal residues or sequences not needed for biological activity. For example, cysteine residues not essen-

tial 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

20

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

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 LIPOFEC-TINTM), DNA conjugates, anhydrous absorption pastes, oilin-water and water-in-oil emulsions, emulsions carbowax (polyethylene glycols of various molecular weights), semisolid 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 local.

The pharmaceutical composition can be also delivered in a vesicle, in particular a liposome (see Langer (1990) Science 249:1527-1533; Treat et al. (1989) in Liposomes in 25 the Therapy of Infectious Disease and Cancer, Lopez Berestein and Fidler (eds.), Liss, New York, pp. 353-365; Lopez-Berestein, ibid., pp. 317-327; see generally ibid.).

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

The injectable preparations may include dosage forms for 40 intravenous, subcutaneous, intracutaneous and intramuscular injections, drip infusions, etc. These injectable preparations may be prepared by methods publicly known. For example, the injectable preparations may be prepared, e.g., by dissolving, suspending or emulsifying the antibody or its 45 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 50 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 oil)], etc. As the oily medium, there are employed, 55 e.g., sesame oil, soybean oil, etc., which may be used in combination with a solubilizing agent such as benzyl benzoate, benzyl alcohol, etc. The injection thus prepared is preferably filled in an appropriate ampoule. A pharmaceutical composition of the present invention can be delivered 60 subcutaneously or intravenously with a standard needle and syringe. In addition, with respect to subcutaneous delivery, a pen delivery device readily has applications in delivering a pharmaceutical composition of the present invention. Such a pen delivery device can be reusable or disposable. A 65 reusable pen delivery device generally utilizes a replaceable cartridge that contains a pharmaceutical composition. Once

all of the pharmaceutical composition within the cartridge has been administered and the cartridge is empty, the empty cartridge can readily be discarded and replaced with a new cartridge that contains the pharmaceutical composition. The pen delivery device can then be reused. In a disposable pen

pen delivery device can then be reused. In a disposable pen delivery device, there is no replaceable cartridge. Rather, the disposable pen delivery device comes prefilled with the pharmaceutical composition held in a reservoir within the device. Once the reservoir is emptied of the pharmaceutical

22

composition, the entire device is discarded.

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

EXAMPLES

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure

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

Example 1

Generation of Human Antibodies to Human PCSK9

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

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

Example 2

Gene Utilization Analysis

To analyze the structure of the mAbs produced, the ⁴⁵ nucleic acids encoding antibody variable regions were cloned and sequenced. The predicted amino acid sequences of the variable regions were confirmed by N-terminal amino acid sequencing. From the nucleic acid sequence and predicted amino acid sequence of the mAbs, gene usage was ⁵⁰ identified for each antibody chain.

TABLE 1

	Heavy C	hain Variable	Region	Light C Variable l	
Antibody	VH	D	ЛН	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

24
TABLE 1-continued

		Heavy C	hain Variable :	Region	Light C Variable F	
5	Antibody	VH	D	JH	VK	JK
	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
0	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
5	H1M496	3-13	6-19	4	3-15	3
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 biosensor surface plasmon resonance assay (BIA-CORETM T100). Each antibody was captured at a flow rate of 4 μ l/min for 90 sec on a goat anti-mouse IgG polyclonal antibody surface created through direct chemical coupling to a BIACORETM chip to form a captured antibody surface. Human PCSK9-myc-myc-his (hPCSK9-mmh) at a concentration of 50 nM or 12.5 nM was injected over the captured antibody surfaces at a flowrate of 50 μ l/min for 300 sec, and antigen-antibody dissociation was monitored for 15 min at either 25° C. or 37° C. (K_D =pM; $T_{1/2}$ =min).

TABLE 2

	25°	C.	37°	. C.
Antibody	\mathbf{K}_D	T _{1/2}	\mathbf{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 (BIACORE™ T100). Each selected antibody was captured at a flowrate of
 2 μl/min for 6 min on a goat anti-human IgG polyclonal antibody surface created through direct chemical coupling to a BIACORE™ chip to form a captured antibody surface.

40

45

50

Human PCSK9-mmh at a concentration of 50 nM or 12.5 nM was injected over the captured antibody surface at a flowrate of 70 μ l/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

	25	25° C. 3		° C.
Antibody	\mathbf{K}_D	T _{1/2}	K_D	T _{1/2}
H1H313P	244	230	780	60
H1H314P	3990	65	3560	43
H1H315P	129	151	413	35
H1H316P	377	42	1080	11
H1H317P	30400	137	18600	70
H1H318P	972	59	1690	28
H1H320P	771	28	1930	8
H1H321P	865	106	3360	23
H1H334P	3750	46	15900	8

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

TABLE 4

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

Example 4

Effect of pH on Antigen Binding Affinity

The effects of pH on antigen binding affinity for CHO cell-produced fully human anti-hPCSK9 mAbs was assessed as described above. The mAbs tested are fully human versions of H1H316P ("316P") (HCVR/LCVR SEO 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/ 226; CDR sequences SEO ID NO:220/222/224 and 228/ 230/232). Human PCSK9-myc-myc-his (hPCSK9-mmh) was captured on an anti-myc mAb surface either at a high density (about 35 to 45 resonance units) (RU) or at a low density (about 5 to 14 RU). Each antibody, at 50 nM in HBST (pH 7.4 or pH 5.5) was injected over the captured hPCSK9 surface at a flow rate of 100 μl/ml for 1.5 min at 25° C. and antigen-antibody dissociation was monitored for 10 65 min. Control I: anti-hPCSK9 mAb SEQ ID NO:79/101 (WO 2008/063382) ($K_D = pM; T_{1/2} = min$).

TABLE 5

		High h Density	PCSK9 Surface		1		PCSK9 Surface	;
	pH	7.4	рН	5.5	pН	7.4	рН	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 15 assay 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), cynomolgus monkey (Macaca fascicularis) PCSK9 (mfPCSK9, SEQ ID NO:761) (mfPCSK9), rat (Rattus norvegicus) PCSK9 (rPCSK9, SEQ ID NO:763), and his-tagged Syrian golden hamster (Mesocricetus auratus) PCSK9 (maPCSK9, SEQ ID NO:762) (maPCSK9), ranging from 11 to 100 nM, were injected over the antibody surface at the flow rate of 100 µl/ml for 1.5 min and antigenantibody dissociation was monitored in real time for 5 min at either 25° C. (Table 6) or 37° C. (Table 7). Control II: 30 anti-hPCSK9 mAbs SEQ ID NO:67/12 (WO 2009/026558) (NB: no binding was observed under the experimental condition) ($K_D = pM$; $T_{1/2} = min$).

TABLE 6

pH Effect at 25° C.				
	pН	[7.4	pН	I 5.5
Antigen	\mathbf{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 2	22 63 166 8 87 349	39 11 13 23 8 5
		300)N	
hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh	1100 NB 1310 2170 NB NB	76 NB 46 31 NB NB	3100 NB 9030 38500 NB NB rol I	5 NB 3 0.4 NB NB
hPCSK9-mmh mPCSK9-mmh hPCSK9(D347Y)-mmh mfPCSK9-mmh maPCSK9-h rPCSK9-mmh	33100 NB 71000 362000 NB NB	14 NB 11 0.2 NB NB Contr	1740 NB 7320 67200 NB NB rol II	31 NB 30 3 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

Binding Specificity of Anti-hPCSK9 mAbs

	pH Effect at 3	7° C.			
	рН	pH 7.4		pH 5.5	
Antigen	\mathbf{K}_D	T _{1/2}	${\bf K}_D$	T _{1/2}	
		3	16P		
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	
		30	00N		
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	
naPCSK9-h	NB	NB	NB	NB	
rPCSK9-mmh	NB	NB	NB	NB	
		Cor	ıtrol 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	
		Con	trol II		
hPCSK9-mmh	284	87	20	44	
mPCSK9-mmh	8680	3	89	3	
hPCSK9(D347Y)-mmh	251	57	483	26	
nfPCSK9(D34/1)-mmn	180	127	483 214	26 65	
maPCSK9-h	8830	0.5	ND	ND	
rPCSK9p-mmh	30200	1	233	1	

Example 5

Anti-hPCSK9 mAbs Binding to hPCSK9 with Point Mutation D374Y

The binding affinity of selected anti-hPCSK9 mAbs to hPCSK9 with a gain of function (GOF) point mutation of D374Y (hPCSK9(D374Y)-mmh) was determined as 45 described above. Each antibody was captured at a flowrate of 40 µl/min for 8-30 sec on a goat anti-human IgG polyclonal antibody surface created through direct chemical coupling to a 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 hPCSK9(D374Y)-mmh and antibody was monitored for 15 min at 25° C. Control III: anti-hPCSK9 mAbs SEQ ID NO:49/23 (WO 2009/026558) ($K_D = pM$; $T_{1/2} = min$).

TABLE 8

Antibody	K_D	T _{1/2}	60
316P	1780	14	
300N	1060	49	
Control I	23600	25	
Control II	66	216	
Control III	1020	126	65

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. human PCSK1 (hPCSK1) (SEQ ID NO:759), human PCSK7 (hPCSK7) (SEQ ID NO:760), or mouse PCSK9 were injected (100 nM) over the captured mAb surface and allowed to bind at 25° C. for 5 min. Changes in RU were recorded. Results: 300N and Control I bound only to hPCSK9, and 316P bound both hPCSK9 and mPCSK9.

The binding specificities of anti-hPCSK9 mAbs were determined by ELISA. Briefly, anti-hPCSK9 antibody was coated on a 96-well plate. Human PCSK9-mmh, 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 antihPCSK9 mAbs exhibited significant binding to hPCSK1 or 25 hPCSK7.

Example 7

Cross-Reactivity of Anti-hPCSK9 mAbs

Cross-reactivity of anti-hPCSK9 mAbs with mmPCSK9, mfPCSK9, mPCSK9, maPCSK9, or rPCSK9 was determined using BIACORETM3000. Briefly, anti-hPCSK9 mAbs were captured on an anti-hFc surface created through direct chemical coupling to a BIACORE™ chip. Purified tagged hPCSK9, hPCSK9(D374Y), mmPCSK9, mfPCSK9, mPCSK9, maPCSK9, or rPCSK9, each at 1.56 nM to 50 nM, was injected over the antibody surface at either 25° C. or 37° C. Binding between 316P, 300N, Control I, Control II, or Control III and the PCSK9 proteins was determined $(K_D = pM; T_{1/2} = min)$ (ND=not determined).

TABLE 9

316P mAb							
	37	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						
	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		

50

55

	300N m.	Ab		
	37	37° C.		
Antigen	${\bf K}_D$	T _{1/2}	K_D	$T_{1/2}$
mPCSK9-mmh maPCSK9-h rPCSK9-mmh	NB NB NB	NB NB NB	NB NB NB	NB NB NB

TABLE 11

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

TABLE 12

	Control II	mAb		
	37	° C.	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

TABLE 13

Control III mAb							
	37°	C.	25° C.				
Antigen	\mathbf{K}_D	$T_{1/2}$	\mathbf{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			

Example 8

Inhibition of Binding Between hPCSK9 and hLDLR Domains

The ability of selected anti-hPCSK9 mAbs to block 60 hPCSK9 binding to human LDLR full length extracellular domain (hLDLR-ecto SEQ ID NO:758), hLDLR EGF-A domain (amino acids 313-355 of SED ID NO:758), or hLDLR EGF-AB domains (amino acids of 314-393 of SEQ ID NO:758) (LDLR Genbank number NM_000527) was 65 evaluated using BIACORETM 3000. Briefly, hLDLR-ecto, EGF-A-hFc, or EGF-AB-hFc protein was amine-coupled on

30

a CM5 chip to create a receptor or receptor fragment surface. Selected anti-hPCSK9 mAbs, at 62.5 nM (2.5 fold excess over antigen), were premixed with 25 nM of hPCSK9-mmh, followed by 40 min incubation at 25° C. to allow antibody-antigen binding to reach equilibrium to form equilibrated solutions. The equilibrated solutions were injected over the receptor or receptor fragment surfaces at 2 µl/min for 40 min at 25° C. Changes in RU due to the binding of the anti-hPCSK9 mAbs to hLDLR-ecto, EGF-A-hFc, or EGF-AB-hFc were determined. Results show that H1H316P and H1M300N blocked the binding of hPCSK9-mmh to hLDLR-ecto, hLDLR EGF-A domain, and hLDLR EGF-AB domains; H1H320P blocked the binding of hPCSK9-mmh to hLDLR-ecto and hLDLR EGF-A domain; and H1H321P blocked the binding of hPCSK9-mmh to hLDLR EGF-A domain.

The ability of the mAbs to block hPCSK9 binding to hLDLR-ecto, hLDLR EGF-A domain, or hLDLR EGF-AB ²⁰ domains was also evaluated with an ELISA-based immunoassay. Briefly, hLDLR-ecto, hLDLR EGF-A-hFc or hLDLR EGF-AB-hFc, each at 2 μg/ml, was coated on a 96-well plate in PBS buffer overnight at 4° C., and nonspecific binding sites blocked with BSA. This plate was used to measure free hPCSK9-mmh in a PCSK9-mmh solution pre-equilibrated with varying concentrations of antihPCSK9 mAbs. A constant amount of hPCSK9-mmh (500 pM) was pre-mixed with varied amounts of antibody, ranging from 0 to ~50 nM in serial dilutions, followed by 1 hr incubation at room temperature (RT) to allow antibodyantigen binding to reach equilibrium. The equilibrated sample solutions were transferred to receptor or receptor fragment coated plates. After 1 hour of binding, the plates 35 were washed and bound hPCSK9-mmh detected using HRP conjugated anti-myc antibody. IC₅₀ values (in pM) were determined as the amount of antibody required to achieve 50% reduction of hPCSK9-mmh bound to the plate-coated receptor or receptor fragment. The results show that specific mAbs functionally block PCSK9 from binding the three receptors at both neutral pH (7.2) and acidic pH (5.5).

TABLE 14

		pH 7.2			pH 5.5	
			Plate Coatii	ng 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	_	>100,000	>100,000	_	>100,000	>100,000
I						
Control	288	510	274	411	528	508
II						
Control III	303	635	391	742	787	1073

The ability of the mAbs to block hPCSK9 GOF mutant hPCSK9(D374Y)-mmh binding to hLDLR EGF-A domain or hLDLR EGF-AB domain (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

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

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

TABLE 16

,	1 nM mmPCSK9-mmh			1 nM mP	CSK9-mmh
	hLDLR- ecto	EGF-	EGF- AB	EGF-	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 30 at neutral pH (7.2) (Table 17) acidic pH (5.5, Table 18) with the ELISA-based immunoassay described above using a constant amount of 0.5 nM of hPCSK9-mmh, 1 nM of mmPCSK9-mmh, 1 nM of rPCSK9-mmh, 1 nM of maPCSK9-h, 0.3 nM of mfPCSK9-mmh, or 1 nM of 35 mPCSK9-mmh.

TABLE 17

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

TABLE 18

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

The ability of 316P and Control I to block hPCSK9 60 binding to hLDLR was also determined. Briefly, either recombinant hLDLR or hLDLR-EGFA-mFc was immobilized onto BIACORE™ 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 65 hPCSK9 mAbs to hPCSK9-mmh, mPCSK9-mmh, at 250 nM) was incubated at RT for 1 hr, and then injected over the hLDLR or hLDLR-EGFA surface at the flow rate of

10 μl/ml for 15 min at 25° C. Changes in RU due to the binding between the free hPCSK9-mmh in the mixture to either hLDLR or hLDLR-EGFA were recorded. The binding of hPCSK9 to either hLDLR or hLDLR-EGFA was completely blocked by 316P and 300N but not by Control I mAb.

Example 9

Epitope Mapping

In order to determine epitope-binding specificity, three chimeric PCSK9-mmh proteins were generated in which specific human PCSK9 domains were substituted with mouse PCSK9 domains. Chimeric protein #1 consists of a mouse PCSK9 pro-domain (amino acid residues 1-155 of SEQ ID NO:757) followed by a human PCSK9 catalytic domain (residues 153-425 of SEQ ID NO:755) and a mouse PCSK9 C-terminal domain (residues 429-694 SEQ ID NO:757) (mPro-hCat-mC-term-mmh). Chimeric protein #2 consists of a human PCSK9 pro-domain (residues 1-152 of SEQ ID NO:755) followed by a mouse PCSK9 catalytic domain (residues 156-428 of SEQ ID NO:757) and a mouse PCSK9 C-terminal (hPro-mCat-mC-term-mmh). Chimeric 25 protein #3 consists of mouse PCSK9 pro-domain and a mouse PCSK9 catalytic domain followed by a human PCSK9 C-terminal domain (residues 426-692 of SEQ ID NO:755) (mPro-mCat-hC-term-mmh). In addition, hPCSK9 with a point mutation of D374Y (hPCSK9 (D374Y)-mmh) was generated.

Binding specificity of mAbs to test proteins hPCSK9mmh, mouse PCSK9-mmh, chimeric proteins #1, #2, and #3, and hPCSK9 (D374Y)-mmh were tested as follows: the mAbs were coated on a 96-well plate overnight at 4° C., then each test protein (1.2 nM) was added to the plate. After 1 hr binding at RT, the plate was washed and bound test protein detected using HRP-conjugated anti-myc polyclonal antibody (++=OD>1.0; +=OD 0.4-1.0; -=OD<0.4).

TABLE 19

				Chin	neric Pr	otein	_
	Antibody	hPCSK9	mPCSK9	#1	#2	#3	hPCSK9(D374Y)
45	H1M300	++	_	++	+	_	++
15	H1M309	++	_	_	_	++	++
	H1M312	++	-	-	-	++	++
	H1M492	++	_	-	-	_	+
	H1M493	++	-	-	-	++	++
	H1M494	++	-	-	+	++	++
50	H1M495	++	-	-	-	++	++
30	H1M496	++	-	-	-	++	++
	H1M497	++	-	-	++	+	++
	H1M498	++	-	-	-	+	++
	H1M499	++	_	-	-	++	++
	H1M500	++	-	++	-	_	++
	H1M502	++	-	-	-	++	++
55	H1M503	++	_	-	++	-	++
	H1M504	++	_	-	-	_	+
	H1M505	++	_	++	+	-	++
	H1M508	++	_	-	_	++	++
	H1H318P	++	_	++	-	_	++
	H1H334P	++	_	++	-	_	++
60	H1H316P	++	++	++	++	++	++
	H1H320P	++	_	-	++	_	++
	Control I	++	-	-	-	++	++

Binding specificity of 316P, 300N and control antimmPCSK9-mmh, mfPCSK9-mmh, rPCSK9-mmh, chimeric proteins #1, #2, and #3, and hPCSK9 (D374Y)-mmh

15

were tested as described above except that the protein concentration is 1.7 nM (-=OD<0.7; +=OD 0.7-1.5; ++=OD>1.5).

TABLE 20

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

Similar results for selected mAbs were obtained by BIA-CORETM binding assay. Briefly, 316P, 300N, or Control I 20 mAb was captured on an amine-coupled anti-hFc CM5 chip and 100 nM of each protein injected over the mAb-captured surface. Changes in RU due to the binding of each protein to the mAb surface was determined.

TABLE 21

		_	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 cross-reacts with mPCSK9-mmh, a cross-competition ELISA assay was developed to determine binding domain specificity. Briefly, mAbs specific for chimeric protein #1, #2, or #3, were first coated on a 96-well plate overnight at 1 µg/ml. Human PCSK9-mmh (2 µg/ml) was then added to each well followed by 1 hr incubation at RT. 316P (1 µg/ml) was added and incubated for another hour at RT. Platebound 316P was detected using HRP-conjugated anti-hFc polyclonal antibody. Although 316P binding to hPCSK9-mmh was not affected by the presence of mAbs specific for either chimeric protein #2 or chimeric protein #3, 316P binding to hPCSK9-mmh was greatly reduced by the presence of antibody specific for chimeric protein #1.

Example 10

BIACORETM-Based Antigen Binding Profile Assessment

Antibody binding profiles were also established for 316P, 300N, Control I, II, and III mAbs using BIACORETM1000. 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.

34

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

TABLE 23

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

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

TABLE 24

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

Example 12

Neutralization of Biological Effect of hPCSK9 In Vivo

To assess the biological effect of neutralizing PCSK9, hPCSK9 was over-expressed in C57BL/6 mice by hydrodynamic delivery (HDD) of DNA constructs encoding full-length hPCSK9-mmh. 4 mice (C57BL/6) were injected with empty vector/saline (control), and 16 mice were injected with a 50 μg hPCSK9-mmh-DNA/saline mixture in the tail vein equal to 10% of their body weight. At day 7 after HDD, delivery of hPCSK9 resulted in a 1.6-fold elevation of total cholesterol, 3.4-fold elevation in LDL-cholesterol (LDL-C) and a 1.9-fold elevation in non-HDL cholesterol (relative to 15 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, 25 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 35 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) 40 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 45 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 55 12-hour diurnal cycle. The dark cycle could be interrupted for study- or facility-related activities. The animals were individually housed in cages that comply with the Animal Welfare Act and recommendations set forth in The Guide for the Care and Use of Laboratory Animals (National Research 60 Council 1996).

Diet and Feeding.

Animals were fed twice per day according to SNBL USA SOPs. Animals were fasted when required by specific procedures (e.g., prior to blood draws for serum chemistry, 65 urine collection, or when procedures involving sedation are performed). The diet was routinely analyzed for contami-

36

nants and found to be within manufacturer's specifications. No contaminants were expected to be present at levels that would interfere with the outcome of the study.

Experimental Design.

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

Acclimation Period.

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

Blood Collection.

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

PK Study.

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

Serum samples were analyzed using an optimized ELISA (enzyme-linked 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) C_{max} (µg/ml) $T_{1/2}$ (h)	0.428 184 83	0.105 527 184	4.02 226 215	0.428 1223 366	

Serum Chemistry.

Blood samples were collected at pre-dose, 12 hr, 48 hr, and subsequently once every 48 hr, for clinical chemistry analysis, in particular lipid profiles (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 5 (GLOB); Albumin/Globulin Ratio (A/G); Chloride (CI); 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 10 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. 15 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 20 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 25 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 compa- 30 rable doses (50% LDL-C suppression for 28 days following a 5 mg/kg dose and 50% LDL-C suppression for approximately 90 days following a 15 mg/kg dose). There was little or no measurable change in liver function as determined by ALT and AST measurements. All animals receiving an 35 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 $_{\rm 40}$ 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 $\mu g/ml$, 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	84	
C _{max} (μg/ml)	46	63	
T _{1/2} (h)	64	286	

Example 14

Attenuation of LDL Receptor Degradation by Anti-hPCSK9 Antibodies

To assess the biological effect of PCSK9 on hepatic LDL receptor levels and subsequent effects on serum LDL-C

38

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 PCSK9mediated increases in total cholesterol and LDL cholesterol (LDL-C=2.49 mg/dl at baseline and 3.1 mg/dl 6 hours after PCSK9; a 25% increase compared to 135% with vehicle). Prior administration of the non-hPCSK9 specific mAb blocked LDL-C increases by approximately 27% from PBS alone (LDL-C=4.1 mg/dl compared to PBS 5.6 mg/dl). Analysis of LDL receptor levels in a separate cohort of mice (n=3 per treatment group) revealed a significant reduction in LDL receptor levels with PCSK9 administration, which was blocked by 316P but not by the non-hPCSK9 specific mAb (FIG. 10).

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

Example 15

Mouse PK Studies

A PK study was conducted in 6-week-old C57BL/6 mice and 11-15 week old hPCSK9 heterozygous mice. A single injection of Control I, 316P, or 300N, each at 10 mg/kg, was administered SC. Serum bleeds were measured for hlgG 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 μ g/ml, while both 300N and 316P levels were below the quantifiable limit (BQL) of 0.02 μ 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 µl/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).

E366 of hPCSK9 (SEQ ID NO:755). Additionally, the BIACORETM assays show that 300N binding affinity and $T_{1/2}$ were reduced between 2- to >10-fold when a residue at 147 or 380 was mutated. Specifically, K_D was reduced from about 0.69×10^{-9} M to between about 2.9×10^{-9} M when any of S147 or V380 were mutated; while $T_{1/2}$ was shortened from about 120 min to between about 24-66 min. Compared to 316P, 300N binding to hPCSK9 was not reduced by a mutation at residue 238.

In contrast, Control I antibody did not exhibit an altered binding affinity or $T_{1/2}$ in response to any of the positional mutations tested; Control II antibody exhibited a 40-fold decreased affinity when residue 215 was mutated (R215E) (from ~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 antihPCSK9 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 mmhtagged variant hPCSK9 in CHO-k1 transient transfection

TABLE 27

	316P		316P300NC		Cont	trol I Cor		Control II		Control III	
	K_D	T _{1/2}	\mathbf{K}_D	T _{1/2}	\mathbf{K}_D	$T_{1/2}$	\mathbf{K}_D	T _{1/2}	\mathbf{K}_D	T _{1/2}	
WT	1.00	37	0.69	120	30.6	16	0.10	333	0.60	481	
P70A	1.42	32	1.68	80	19.0	16	0.24	168	0.90	325	
S127R	2.40	36	1.87	110	25.0	18	0.26	288	0.55	550	
D129G	1.27	36	1.40	88	22.9	18	0.19	257	0.75	445	
S147F	1.29	32	9.07	24	21.1	15	0.22	178	0.23	1468	
S153R	5.64	4	0.56	141	36.6	17	0.09	322	3.33	60	
E159R	6.96	5	0.82	94	31.7	16	0.08	350	2.97	68	
T162R	0.98	43	0.58	140	29.0	17	0.09	322	0.48	362	
D192R	1.35	28	0.75	119	30.2	15	0.09	326	nb	nb	
R194E	0.38	71	0.65	129	31.4	16	0.07	389	nb	nb	
E197R	1.42	27	0.67	115	30.2	17	0.09	339	nb	nb	
R215H	0.86	41	1.03	98	37.8	17	0.65	49	0.74	272	
R215E	0.90	43	1.81	77	44.0	16	4.48	12	0.78	276	
F216L	1.83	32	0.99	121	21.2	15	1.35	39	0.33	880	
R237E	2.48	15	1.03	109	29.6	15	0.07	481	5.89	43	
D238R	410	1	0.78	123	25.9	19	0.24	144	0.14	1273	
A341R	1.54	21	0.34	190	28.7	18	0.08	340	0.88	200	
D343R	7.88	6	1.18	89	27.0	16	0.08	402	4.13	66	
R357H	6.26	30	6.53	66	26.4	13	0.63	165	1.91	896	
E366K	2.92	13	36.0	2	28.8	18	0.46	69	0.38	808	
D374Y	2.04	15	0.66	83	25.0	17	0.08	285	1.02	161	
V380M	0.48	63	2.82	28	25.9	17	0.15	177	0.35	711	
P70A, S147F	1.18	34	7.87	24	23.5	18	0.23	164	0.79	348	
E366K, V380M	3.33	12	78.3	1	25.5	18	0.59	60	0.52	551	

The results show that when residue D238 was mutated, the binding affinity of 316P for hPCSK9 was reduced >400-fold, from a $\rm K_D$ of 1×10^{-9} M to 410×10^{-9} M; and $\rm T_{1/2}$ shortened about 30-fold, from 37 to 1 min, indicating that 316P binds an epitope on hPCSK9 comprising D238 of hPCSK9 (SEQ ID NO:755). Additionally, BIACORETM assays show that 316P binding affinity and $\rm T_{1/2}$ 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 1×10^{-9} M to between about $5\text{-}8\times10^{-9}$ M when any one of S153, E159 or D343 were 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 K_D of from about 0.7×10^{-9} M to about 36×10^{-9} 65 M and a shorter $T_{1/2}$ from about 120 to 2 min. These results indicate that 300N binds an epitope on hPCSK9 comprising

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

TABLE 28

)	hPCSK9 or Variant	316P	300N	Control I	Control II	Control III
	hPCSK9(WT)	++	++	++	++	++
	hPCSK9(S127R)	++	++	++	++	++
	hPCSK9(D129G)	++	++	++	++	++
	hPCSK9(S153R)	++	++	++	++	++
5	hPCSK9(R215H)	++	++	++	++	++
	hPCSK9(F216L)	++	++	++	++	++

TABLE 28-continued

41 42 Example 17

hPCSK9 or Variant	316P	300N	Control I	Control II	Control III
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)					

Effect of 316P on Normolipemic and Hyperlipemic Hamster

The ability of anti-PCSK9 mAb 316P to reduce serum LDL-C was tested in normolipemic or hyperlipemic Gold Syrian hamsters (Mesocricetus auratus). Male Syrian Hamsters, age 6-8 weeks, weighing between 80-100 grams, were allowed to acclimate for a period of 7 days before entry into the study. All animals were placed on either a standard chow diet or a hyperlipemic diet of chow supplemented with 0.1% cholesterol and 10% coconut oil. The 316P mAb was delivered to hamsters by a single subcutaneous injection at doses of 1, 3, or 10 mg/kg for normolipemic hamsters and ¹⁵ at doses of 3, 10, or 30 mg/kg for hyperlipemic hamsters. Serum samples were taken from all groups at 24 hr and 7, 14, and 22 days post injection, at which time serum lipid levels were assessed and compared to baseline levels taken 7 days prior to the administration of the mAbs. Circulating 20 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.

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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 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
cagagtgtta gcagcaac
                                                                       18
<210> SEQ ID NO 12
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<211> LENGTH: 6 <212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<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
<210> SEQ ID NO 14
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<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
cagcagtata ataactggcc tccattcact
                                                                        30
<210> SEQ 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
                                                                       120
tectgtgcag cetetggatt tactetaagt agttacgaca tgcaetgggt cegecaatet
acaggaaaag gtctggagtg ggtctcagct attggttcta ccggtgacac atactatcca
                                                                       180
ggctccgtga agggccgatt caccatcacc agagaaaaag ccaagaactc cgtgtatctt
                                                                       240
caaatgaaca geetgagage eggggaeaeg getgtgtatt aetgtgtaag agaggggtgg
                                                                       300
gaggtaccct ttgactactg gggccaggga accctggtca ccgtctcctc a
                                                                       351
```

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<210> SEQ ID NO 18
<211> LENGTH: 117
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 18
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 Leu Ser Ser Tyr
Asp Met His Trp Val Arg Gln Ser 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 Thr Arg Glu Lys Ala Lys Asn Ser Val Tyr Leu
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val
               85
                                   90
Arg Glu Gly Trp Glu Val Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
                                105
           100
Val Thr Val Ser Ser
       115
<210> SEQ ID NO 19
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 19
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccgcc
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca ccagaaacct
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
aggttcagtg gcattgggtc tgggacagag ttcactctca ttatcagcag cctgcagtct
gaagattttg cattttattt ctgtcagcag tataataact ggcctccatt cactttcggc
cctgggacca aagtggatat caaa
<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
                                    10
Glu Arg Ala Ala Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
                               25
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
    50
                        55
Ile Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Ser
```

```
65
Glu Asp Phe Ala Phe Tyr Phe Cys Gln Gln Tyr Asn Asn Trp Pro Pro
               85
                                    90
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
           100
<210> SEQ ID NO 21
<211> LENGTH: 351
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 21
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
teetgtgeag cetetggatt tactetaagt agttacgaca tgeactgggt cegecaaget
acaggaaaag gtctggagtg ggtctcagct attggttcta ccggtgacac atactatcca
qqctccqtqa aqqqccqatt caccatctcc aqaqaaaatq ccaaqaactc cttqtatctt
                                                                      240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgtaag agaggggtgg
                                                                     300
                                                                     351
gaggtaccct ttgactactg gggccaggga accctggtca ccgtctcctc a
<210> SEO 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
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 Val
Arg Glu Gly Trp Glu Val Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu
Val Thr Val Ser Ser
       115
<210> SEQ ID NO 23
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 23
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc
                                                                      60
ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct
                                                                      120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
                                                                      180
```

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aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240 gaagattttg cagtttatta ctgtcagcag tataataact ggcctccatt cactttcggc 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 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 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 <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 ctgggaggtc cctgagactc 60 tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatacattat ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat ctggaaatga acagcctgag agccgaggac acggcaatgt actattgtgc gagagagaag 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 5 10 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 20 25 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
    50
                        55
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
Ser Ser
<210> SEQ ID NO 27
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 27
ggattcacct tcagtagcta tggc
                                                                       24
<210> SEQ ID NO 28
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 28
Gly Phe Thr Phe Ser Ser Tyr Gly
                5
<210> SEQ ID NO 29
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 29
ataggatttg atggaagtaa tata
                                                                       24
<210> SEQ ID NO 30
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 30
Ile Gly Phe Asp Gly Ser Asn Ile
<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
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<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
gecatecaga tgacccagte teettecace etgtetgeat etgtaggaga cagagteace
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tataatagtt attacacttt tggccagggg
                                                                     300
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
                         10
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 Asn Ser Tyr Tyr Thr
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
<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
```

<210> SEQ ID NO 36

<211> LENGTH: 6

<212> TYPE: PRT

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<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
<210> SEQ ID NO 38
<211> LENGTH: 3
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 38
Lys Ala Ser
 1
<210> SEQ ID NO 39
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 39
caacagtata atagttatta cact
                                                                        24
<210> SEQ ID NO 40
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 40
Gln Gln Tyr Asn Ser Tyr Tyr Thr
<210> SEQ ID NO 41
<211> LENGTH: 342
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 41
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
                                                                        60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct
                                                                       120
ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatacattat
                                                                       180
ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat
                                                                       240
ctggaaatga acagcctgag agccgaggac acggcaatgt actattgtgc gagagagaag
```

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ggtttagact ggggccaggg aaccctggtc accgtctcct ca
                                                                     342
<210> SEQ ID NO 42
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 42
Gln Val Gln Leu Val Glu Ser Gly Gly 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 65 70 75 80
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
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
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                      60
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 agatcaaa
<210> SEQ ID NO 44
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 44
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 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
                       55
```

```
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                   70
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> SEQUENCE: 45
                                                                      60
caqqtqcaqc tqqtqqaqtc tqqqqqaqqc qtqqtccaqc ctqqqaqqtc cctqaqactc
teetgtgeag cetetggatt cacetteagt agetatggea tgeactgggt cegecagget
ccaggcaagg ggctggagtg ggtggcagtt ataggatttg atggaagtaa tatatactat
                                                                      180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat
                                                                      240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagagaag
                                                                      300
ggtttagact ggggccaggg aaccctggtc accgtctcct ca
                                                                      342
<210> SEQ ID NO 46
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 46
Gln Val Gln Leu Val Glu Ser Gly Gly 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 47
<211> LENGTH: 319
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 47
gacatecaga tgacecagte teetteeace etgtetgeat etgtaggaga cagagteace
                                                                      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
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
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
                   70
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 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
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct
ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatatattat
ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat
ctggaaatga acagcctgag agccgaggac acggcagtgt attattgtgc gagagagaag
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
                5
                                  10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
           20
                              25
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
    50
                        55
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
Ser Ser
<210> SEQ ID NO 51
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 51
ggattcacct tcagtagcta tggc
                                                                       24
<210> SEQ ID NO 52
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 52
Gly Phe Thr Phe Ser Ser Tyr Gly
                5
<210> SEQ ID NO 53
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 53
ataggatttg atggaagtaa tata
                                                                       24
<210> SEQ ID NO 54
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 54
Ile Gly Phe Asp Gly Ser Asn Ile
<210> SEQ ID NO 55
<211> LENGTH: 21
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 55
                                                                       21
gcgagagaga agggtttaga c
<210> SEQ ID NO 56
<211> LENGTH: 7
```

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<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> SEQUENCE: 57
gccatccaga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc
atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagtt
tggtatcagc agaaaccagg acagceteet aagttgetee tttactggge etetaceegg
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc
atcagcagcc tgcaggctga agatgtggca aattattact gtcaccaata ttacagtatt
ccgtggacgt tcggccaagg gaccaaggtg gagatcaaac ga
                                                                      342
<210> SEQ ID NO 58
<211> LENGTH: 114
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 58
Ala Ile Gln Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
                                  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 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
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36

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<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
                5
<210> SEQ ID NO 61
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 61
tgggcctct
<210> SEQ ID NO 62
<211> LENGTH: 3
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 62
Trp Ala Ser
<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
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct
                                                                       120
ccaggcaagg ggctggagtg ggtggcgttt ataggatttg atggaagtaa tatatattat
                                                                       180
ggagactccg tgaggggccg aatcatcata tccagagaca attccgagaa cacgttgtat
```

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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 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 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 Ser Ser <210> SEQ ID NO 67 <211> LENGTH: 339 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 67 gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagtt tggtatcagc agaaaccagg acagceteet aagttgetee tttactggge etetaceegg gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc atcagcagcc tgcaggctga agatgtggca aattattact gtcaccaata ttacagtatt ccgtggacgt tcggccaagg gaccaaggtg gaaatcaaa <210> SEQ ID NO 68 <211> LENGTH: 113 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 68 Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly 1.0 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

75 76

-continued

55 Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 70 75 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 <210> SEQ ID NO 69 <211> LENGTH: 342 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 69 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 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 <210> SEQ ID NO 70 <211> LENGTH: 114 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 70 Gln Val Gln Leu Val Glu Ser Gly Gly 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 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 71 <211> LENGTH: 339 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 71

gacategtga tgacceagte tecagactee etggetgtgt etetgggega gagggeeace

60

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atcaactgca agtccagcca gagtgttttt cacacctcca acaataagaa ctacttagct
                                                                      120
tggtaccagc agaaaccagg acagceteet aagetgetea tttactggge etetaceegg
                                                                      180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc
                                                                      240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcaccaata ttacagtatt
ccgtggacgt tcggccaagg gaccaaggtg gaaatcaaa
                                                                      339
<210> SEQ ID NO 72
<211> LENGTH: 113
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 72
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Phe His Thr
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 Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys His Gln
Tyr Tyr Ser Ile Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
           100
                                105
Lys
<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
tcctgtgcag cctctggatt cacctttaac aactatgcca tgaactgggt ccgccaggct
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
```

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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
<210> SEQ ID NO 75
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 75
ggattcacct ttaacaacta tgcc
                                                                        24
<210> SEQ ID NO 76
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 76
Gly Phe Thr Phe Asn Asn Tyr Ala
<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
<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
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<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
atcaactqca aqtccaqcca qaqtqtttta tacaqqtcca acaataqqaa cttcttaqqt
                                                                      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
<210> SEQ ID NO 82
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 82
Asp Ile Gln Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
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
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 65 70 75 75 80
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
                                    90
Tyr Tyr Thr Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
                              105
Lys Arg
<210> SEQ ID NO 83
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 83
cagagtgttt tatacaggtc caacaatagg aacttc
                                                                             36
<210> SEQ ID NO 84
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 84
Gln Ser Val Leu Tyr Arg Ser Asn Asn Arg Asn Phe
<210> SEQ ID NO 85
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 85
                                                                              9
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
<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
                                                                             27
<210> SEQ ID NO 88
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 88
\mbox{\rm Gln} \mbox{\rm Gln} \mbox{\rm Tyr} \mbox{\rm Tyr} \mbox{\rm Thr} \mbox{\rm Thr} \mbox{\rm Pro} \mbox{\rm Tyr} \mbox{\rm Thr}
1
                  5
<210> SEQ ID NO 89
<211> LENGTH: 354
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 89
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tcctgtgcag cctctggatt cacctttaac aactatgcca tgaactgggt ccgccaggct
                                                                      120
ccaggaaagg gactggactg ggtctcaact attagtggta gcggtggtac tacaaactac
gcagactccg tgaagggccg tttcattatt tcccgagaca gttccaaaca cacgctgtat
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattct
aactggggaa atttcgatct ctggggccgt ggcaccctgg tcactgtctc ctca
                                                                      354
<210> SEQ ID NO 90
<211> LENGTH: 118
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 90
Glu Val Gl<br/>n Leu Val Glu Ser Gly Gly Gly Leu Val Gl<br/>n Pro Gly Gly 1 10 15
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
                    70
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 91
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 91
gacategtga tgacccagte tecagactee etggetgtgt etetgggega gagggecace
atcaactqca aqtccaqcca qaqtqtttta tacaqqtcca acaataqqaa cttcttaqqt
tggtaccagc agaaaccagg gcagcctcct aatctactca tttactgggc atctacccgg
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> SEOUENCE: 92
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Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

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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 Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 70 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> SEQUENCE: 93 gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc 60 tectqtqcaq cetetqqatt cacetttaac aactatqcca tqaqetqqqt ceqecaqqet 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 <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 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 70 75 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 105 Leu Val Thr Val Ser Ser 115

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<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 95
gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc
atcaactgca agtccagcca gagtgtttta tacaggtcca acaataggaa cttcttagct
tggtaccagc agaaaccagg acagceteet aagetgetea tttactggge atetaccegg
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc
atcagcagcc tgcaggctga agatgtggca gtttattact gtcaacaata ttatactact
ccgtacactt ttggccaggg gaccaagctg gagatcaaa
<210> SEQ ID NO 96
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 96
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
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
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 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
teetgtgeag tetetggatt cacceteagt agetaegata tgeaetgggt cegecaacet
                                                                     120
acaggaaaag gtctggagtg ggtctcagct attggttcta ctggtgacac atactatcca
qqctccqtqa aqqqccqatt caccatctcc aqaqaaaatq ccaaqaactc cttqtatctt
                                                                     240
caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggatgg
gacgtaccct ttgacttctg gggccaggga accctggtca ccgtctcctc a
<210> SEQ ID NO 98
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<211> LENGTH: 117

<212> TYPE: PRT

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<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 85 90 95
Arg Glu Gly Trp Asp Val Pro Phe Asp Phe Trp Gly Gln Gly Thr Leu 100 \phantom{000} 105 \phantom{000} 110 \phantom{000}
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
<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
                                                                          2.1
attggttcta ctggtgacac a
<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
```

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<210> SEQ ID NO 103
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 103
                                                                         33
gcaagagag gatgggacgt accetttgac ttc
<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
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa
                                                                        300
gggaccaagg tggagatcaa acga
                                                                        324
<210> SEQ ID NO 106
<211> LENGTH: 108
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 106
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 20 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}
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
                    70
                                         75
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Tyr Asn Tyr Pro Trp
                                   90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
```

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<210> SEQ ID NO 107
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 107
caggacatta gaaatgat
                                                                        18
<210> SEQ ID NO 108
<211> LENGTH: 6
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 108
Gln Asp Ile Arg Asn Asp
1
<210> SEQ ID NO 109
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 109
gctgcatcc
                                                                         9
<210> SEQ ID NO 110
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 110
Ala Ala Ser
1
<210> SEQ ID NO 111
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 111
                                                                        27
ctacaagatt acaattaccc gtggacg
<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
<210> SEQ ID NO 113
<211> LENGTH: 351
<212> TYPE: DNA
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 113
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
teetgtgeag tetetggatt cacceteagt agetaegata tgeactgggt cegecaacet
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
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
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
                                                                     120
atcacttqcc qqqcaaqtca qqacattaqa aatqatttaq qctqqtatca qcaqaaacca
gggaaagccc ctaagctcct gatctatgct gcatccagtt tacaaagtgg ggtcccatca
                                                                     180
cggttcagcg gcagtggatc tggcacagat ttcactctca ccatcagcag cctgcagcct
                                                                      240
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa
                                                                      300
                                                                      321
gggaccaagg tggaaatcaa a
<210> SEQ ID NO 116
<211> LENGTH: 107
<212> TYPE: PRT
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<213 > ORGANISM: Artificial Sequence

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<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 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 6.0 tcctgtgcag cctctggatt caccctcagt agctacgata tgcactgggt ccgccaagct 120 acaggaaaag gtctggagtg ggtctcagct attggttcta ctggtgacac atactatcca 180 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggatgg gacgtaccct ttgacttctg gggccaggga accctggtca ccgtctcctc a 351 <210> SEQ ID NO 118 <211> LENGTH: 117 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 118 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 1 $$ 10 $$ 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 40 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 70 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

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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
                                                                      240
gaagattttg caacttatta ctgtctacaa gattacaatt acccgtggac gttcggccaa
                                                                      300
                                                                      321
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
                                    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
                    70
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 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
                                                                       60
acctgcactg tctctgggga ctccatcaat acttactact ggagctggtt ccggcagccc
                                                                      120
ccagggaagg gactggagtg gattgggtat atctattata gtggaaccac caactacaac
                                                                      180
ccctccctca agagtcgagt caccatatca atagacacgc ccaggaacca gttctccctg
aagctgatct ctgtgaccgc agcggacacg gccgtgtatt actgtgcgag agagaggatt
                                                                      300
actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa
                                                                      360
gggaccacgg tcaccgtctc ctca
                                                                      384
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<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
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 Ser
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 123
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 123
ggggactcca tcaatactta ctac
                                                                       2.4
<210> SEQ ID NO 124
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 124
Gly Asp Ser Ile Asn Thr Tyr Tyr
<210> SEQ ID NO 125
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 125
                                                                       2.1
atctattata gtggaaccac c
<210> SEQ ID NO 126
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

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<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
<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
           2.0
<210> SEQ ID NO 129
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 129
gacatccaga tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgct gggccagtca ggacattagc agttatttag cctggtatca gcaaaaacca
gggatagece ctaageteet gatetatget geateeactt tgeaaagtgg ggteeeatea
aggttcggcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct
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
                5
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
    50
                     55
                                            60
```

```
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 Arg
<210> SEQ ID NO 131
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 131
                                                                       18
caggacatta gcagttat
<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
<400> SEQUENCE: 134
Ala Ala Ser
1
<210> SEQ ID NO 135
<211> LENGTH: 27
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 135
caacagetta atagttacce teggacg
                                                                       27
<210> SEQ ID NO 136
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<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
                                                                         240
controlled agagingage caccatation atagacange chapquanca gittetecety
aagetgatet etgtgacege ageggacaeg geegtgtatt aetgtgegag agagaggatt
                                                                         300
actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa
                                                                         360
                                                                         384
gggaccacgg tcaccgtctc ctca
<210> SEO ID NO 138
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 138
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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 100 \hspace{1.5cm} 100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}
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
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aggttcggcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct gaagattttg caacttatta ctgtcaacag cttaatagtt accctcggac gttcggccaa 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 55 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> SEQ ID NO 141 <211> LENGTH: 384 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 141 caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60 acctgcactg tetetgggga etecateaat acttactact ggagetggat eeggeageee ccagggaagg gactggagtg gattgggtat atctattata gtggaaccac caactacaac ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcgag agagaggatt actatgattc ggggagttac cctctactat tactcctacg gtatggacgt ctggggccaa 360 gggaccacgg tcaccgtctc ctca 384 <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 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Asn Thr Tyr 20 25 Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile

			-concinued				
35	40)	45				
Gly Tyr Ile Tyr 5	Tyr Ser Gly Th 55	nr Thr Asn Tyr	Asn Pro Ser Leu 60	Lys			
Ser Arg Val Thr 3	Ile Ser Val As 70	sp Thr Ser Lys 75	Asn Gln Phe Ser	Leu 80			
Lys Leu Ser Ser	Val Thr Ala Al 85	la Asp Thr Ala 90	Val Tyr Tyr Cys 95	Ala			
Arg Glu Arg Ile 1	Thr Met Ile Ar	rg Gly Val Thr 105	Leu Tyr Tyr Tyr 110	Ser			
Tyr Gly Met Asp V	Val Trp Gly Gl 12		Val Thr Val Ser 125	Ser			
<210> SEQ ID NO 143 <211> LENGTH: 321 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 143							
gacatccaga tgacco	caqte tecateet	cc ctqtctqcat	ctqtaqqaqa caqac	tcacc 60			
atcacttgcc gggcaa	-						
gggaaageee etaage							
aggttcagcg gcagt	ggatc tgggacag	gaa ttcactctca	caatcagcag cctgc	agcct 240			
gaagattttg caacti	tatta ctgtcaac	cag cttaatagtt	acceteggae gtteg	gccaa 300			
gggaccaagg tggaaa	atcaa a			321			
<210> SEQ ID NO 144 <211> LENGTH: 107 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 144							
Asp Ile Gln Met	Thr Gln Ser Pr	ro Ser Ser Leu	Ser Ala Ser Val	Gly			
1 Asp Arg Val Thr	5 Ile Thr Cys Ar	10 rq Ala Ser Gln	15 Asp Ile Ser Ser	Tyr			
20	-	25	30	•			
Leu Gly Trp Tyr (35	Gln Gln Lys Pr 40		Pro Lys Arg Leu 45	Ile			
Tyr Ala Ala Ser S 50	Ser Leu Gln Se 55	er Gly Val Pro	Ser Arg Phe Ser 60	Gly			
Ser Gly Ser Gly 5	Thr Glu Phe Th 70	nr Leu Thr Ile 75	Ser Ser Leu Gln	Pro 80			
Glu Asp Phe Ala 5	Thr Tyr Tyr Cy 85	ys Gln Gln Leu 90	Asn Ser Tyr Pro 95	Arg			
Thr Phe Gly Gln (Gly Thr Lys Va	al Glu Ile Lys 105					
<210> SEQ ID NO 145 <211> LENGTH: 378 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 145							

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caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctgggggcctc agtgaaggtc
                                                                       60
teetgeaagg ettetggtta eacetttace aactatggta teagetgggt gegacaggee
cctggacaag gacttgagtt aatgggatgg attagtggtt acaatggtaa cacaaactat
gcacaagaac tccaggccag agtcaccatg accacagaca catccacgag cacagcctac
atggagctga ggaacctgag atctgacgac acggccgtat attactgtgc gagagataga
gtegttgtag cagetgetaa ttactaettt tattetatgg aegtetgggg ccaagggace
                                                                      378
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
                            40
Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Glu Leu
                        55
Gln Ala Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
                    70
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
                               105
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 147
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 147
ggttacacct ttaccaacta tggt
<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
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<213 > ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 149
attagtggtt acaatggtaa caca
                                                                        24
<210> SEQ ID NO 150
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 150
Ile Ser Gly Tyr Asn Gly Asn Thr
<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
                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
                                                                        60
atotoctgca ggtotagtca aagootogta tacagtgatg gagacacota ottgaattgg
                                                                       120
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac
                                                                       180
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgctttcac actgaaaatc
                                                                       240
ageggggtgg aggeegagga tgttggggtt tactaetgea tgcaagetae acaetggeet
                                                                       300
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
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Ala Ile Gln Met Thr Gln Ser Pro Leu Ser Leu Ser Val Thr Leu Gly
                5
                                    10
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
Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
Arq
<210> SEQ ID NO 155
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 155
                                                                       33
caaagcctcg tatacagtga tggagacacc tac
<210> SEQ ID NO 156
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 156
Gln Ser Leu Val Tyr Ser Asp Gly Asp Thr Tyr
<210> SEQ ID NO 157
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 157
aaggtttct
<210> SEQ ID NO 158
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 158
Lys Val Ser
<210> SEQ ID NO 159
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 159
atgcaagcta cacactggcc tcggacg
                                                                       27
<210> SEQ ID NO 160
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 160
Met Gln Ala Thr His Trp Pro Arg Thr
<210> SEQ ID NO 161
<211> LENGTH: 378
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 161
caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctgggggcctc agtgaaggtc
                                                                      60
teetgeaagg ettetggtta eacetttace aactatggta teagetgggt gegacaggee
                                                                     120
cctggacaag gacttgagtt aatgggatgg attagtggtt acaatggtaa cacaaactat
                                                                      180
gcacaagaac tocaggocag agtcaccatg accacagaca catccacgag cacagoctac
                                                                      240
atggagetga ggaacetgag atetgaegae aeggeegtat attaetgtge gagagataga
                                                                      300
gtcgttgtag cagctgctaa ttactacttt tattctatgg acgtctgggg ccaagggacc
                                                                      360
acggtcaccg tctcctca
                                                                      378
<210> SEQ ID NO 162
<211> LENGTH: 126
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 162
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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
                   70
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
                               105
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
       115
                           120
                                                125
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<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
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgctttcac actgaaaatc
ageggggtgg aggeegagga tgttggggtt tactactgea tgeaagetae acaetggeet
cggacgttcg gccaagggac caaggtggaa atcaaa
<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
                                    10
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
Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 165
<211> LENGTH: 378
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 165
caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc
                                                                      60
tcctgcaagg cttctggtta cacctttacc aactatggta tcagctgggt gcgacaggcc
                                                                      120
cctggacaag ggcttgagtg gatgggatgg attagtggtt acaatggtaa cacaaactat
                                                                      180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac
                                                                      240
atggagetga ggageetgag atetgaegae acggeegtgt attactgtge gagagataga
                                                                      300
gtcgttgtag cagctgctaa ttactacttt tattctatgg acgtctgggg ccaagggacc
                                                                      360
acggtcaccg tctcctca
<210> SEQ ID NO 166
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<211> LENGTH: 126

<212> TYPE: PRT

<pre><213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic</pre>							
<400> SEQUENCE: 166							
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15							
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr 20 25 30							
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 35 40 45							
Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu 50 60							
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr 70 75 80							
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys 85 90 95							
Ala Arg Asp Arg Val Val Val Ala Ala Ala Asn Tyr Tyr Phe Tyr Ser 100 105 110							
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 115 120 125							
<210> SEQ ID NO 167 <211> LENGTH: 336 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic							
<400> SEQUENCE: 167 qatqttqtqa tqactcaqtc tccactctcc ctqcccqtca cccttqqaca qccqqcctcc 60							
gatgttgtga tgactcagtc tecactetec etgecegtca ecettggaca geeggeetee 60 ateteetgea ggtetagtca aageetegta tacagtgatg gagacaceta ettgaattgg 120							
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180							
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240							
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaagctac acactggcct 300							
cggacgttcg gccaagggac caaggtggaa atcaaa 336							
<210> SEQ ID NO 168 <211> LENGTH: 112 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic							
<400> SEQUENCE: 168							
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly 1 5 10 15							
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser 20 25 30							
Asp Gly Asp Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser 35 40 45							
Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro 50 55 60							
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 70 75 80							
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala 85 90 95							

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Thr His Trp Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100
                                105
<210> SEQ ID NO 169
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 169
caggtccact tgaaggagtc tggtcctacg ctggtgaaac ccacacagac cctcacgctg
acctgcacct tctctggatt ctcactcatc actagtggag tgggtgtggg ctggattcgt
cagoccoccg gaaaggcoct ggagtggott gcactcattt attggaatgg tgataagcgc
tacageceat etetgaagag caggeteace atcaccaagg acacetecaa aaaccaggtg
                                                                      240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacagg
                                                                      300
ataactgaaa ctagttacta cttctactac ggtatggacg tctggggcca agggaccacg
                                                                      360
gtcaccgtct cctca
                                                                      375
<210> SEQ ID NO 170
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 170
Gln Val His Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
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
<210> SEQ ID NO 171
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 171
ggatteteae teateactag tggagtgggt
                                                                       30
<210> SEQ ID NO 172
<211> LENGTH: 10
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<212> TYPE: PRT <213 > ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 172
Gly Phe Ser Leu Ile Thr Ser Gly Val Gly
    5
<210> SEQ ID NO 173
<211> LENGTH: 21
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 173
atttattgga atggtgataa g
                                                                       21
<210> SEQ ID NO 174
<211> LENGTH: 7
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 174
Ile Tyr Trp Asn Gly Asp Lys
<210> SEQ ID NO 175
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 175
gcacacagga taactgaaac tagttactac ttctactacg gtatggacgt c
                                                                       51
<210> SEQ ID NO 176
<211> LENGTH: 17
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 176
Ala His Arg Ile Thr Glu Thr Ser Tyr Tyr Phe Tyr Tyr Gly Met Asp
Val
<210> SEQ ID NO 177
<211> LENGTH: 339
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 177
gacatecaga tgacecagte tecaetetee etgecegtea eccetggaga geeggeetee
                                                                       60
atctcctgca ggtctagtca gagcctcctg catagtcatg gatacgacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactccg
                                                                      300
```

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```
ctcactttcg gcggagggac caaggtggaa atcaaacga
                                                                   339
<210> SEQ ID NO 178
<211> LENGTH: 113
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 178
Asp Ile Gln 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 20 25 30
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
                              105
Arg
<210> SEQ ID NO 179
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 179
cagageetee tgeatagtea tggatacgae tat
                                                                    33
<210> SEQ ID NO 180
<211> LENGTH: 11
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 180
Gln Ser Leu Leu His Ser His Gly Tyr Asp Tyr
<210> SEQ ID NO 181
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 181
ttgggttct
                                                                     9
<210> SEQ ID NO 182
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 182
Leu Gly Ser
<210> SEQ ID NO 183
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 183
atgcaagctc tacaaactcc gctcact
                                                                        27
<210> SEQ ID NO 184
<211> LENGTH: 9
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 184
Met Gln Ala Leu Gln Thr Pro Leu Thr
                5
<210> SEQ ID NO 185
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 185
cagatcacct tgaaggagtc tggtcctacg ctggtgaaac ccacacagac cctcacgctg
acctgcacct tetetggatt etcactcate actagtggag tgggtgtggg etggattegt
                                                                       120
cagececeg gaaaggeet ggagtggett geacteattt attggaatgg tgataagege
tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacagg
ataactgaaa ctagttacta cttctactac ggtatggacg tctggggcca agggaccacg
                                                                       375
gtcaccgtct cctca
<210> SEQ ID NO 186
<211> LENGTH: 125
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 186
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ile Thr Ser
                                25
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
                        55
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
```

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65 Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr 85 90 Cys Ala His Arg Ile Thr Glu Thr Ser Tyr Tyr Phe Tyr Tyr Gly Met 105 Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 115 120 <210> SEQ ID NO 187 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 187 gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60 atctcctgca 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 300 ctcactttcg gcggagggac caaggtggag atcaaa 336 <210> SEQ ID NO 188 <211> LENGTH: 112 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 188 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly 10 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 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 <210> SEQ ID NO 189 <211> LENGTH: 375 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 189 cagatcacct tgaaggagtc tggtcctacg ctggtgaaac ccacacagac cctcacgctg 60 acctgcacct tctctggatt ctcactcatc actagtggag tgggtgtggg ctggatccgt 120 cagececcag gaaaggeest ggagtggett geacteattt attggaatgg tgataagege 180

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tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacagg
ataactgaaa ctagttacta cttctactac ggtatggacg tctggggcca agggaccacg
gtcaccgtct cctca
                                                                     375
<210> SEQ ID NO 190
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 190
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
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
                   70
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
                                  90
Cys Ala His Arg Ile Thr Glu Thr 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 191
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 191
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
atotoctgca ggtctagtca gagcotoctg catagtcatg gatacgacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactccg
                                                                     300
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                     336
<210> SEQ ID NO 192
<211> LENGTH: 112
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 192
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
               5
```

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser

				concinaca			
	20	2	25	30			
His Gly Tyr 3	Asp Tyr Leu	Asp Trp 1	Tyr Leu Gln	Lys Pro Gly Gln Ser 45			
Pro Gln Leu :	Leu Ile Tyr	Leu Gly S	Ser Asn Arg	Ala Ser Gly Val Pro			
Asp Arg Phe	Ser Gly Ser 70	Gly Ser (Gly Thr Asp 75	Phe Thr Leu Lys Ile			
Ser Arg Val	Glu Ala Glu 85	Asp Val (Gly Val Tyr 90	Tyr Cys Met Gln Ala 95			
	Pro Leu Thr 100		Gly Gly Thr 105	Lys Val Glu Ile Lys 110			
<210> SEQ ID NO 193 <211> LENGTH: 375 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic							
<400> SEQUEN		rataatoat	ataataaaaa	aataaaaaa aataaaaat	a 60		
-				tqqqtqtqqq ctqqatccqt			
	-	•		attggaattc tgataagcg			
				acacctccaa aaaccaggta			
_				catattactg tgcacacaga			
_				totggggcca agggatcacg			
gtcaccgtct c		cecaceae	ggcacggacg	ceegggeea agggaeeaeş	375		
<210> SEQ ID NO 194 <211> LENGTH: 125 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic							
<400> SEQUEN							
Gin He Thr	Leu Lys Glu 5	Ser Gly F	Pro Thr Leu 10	Val Lys Pro Ser Gln 15			
	Leu Thr Cys 20		Ser Gly Phe 25	Ser Leu Ser Thr Ser 30			
Gly Val Gly 35	Val Gly Trp	Ile Arg (Gln Pro Pro	Gly Lys Ala Leu Glu 45			
Trp Leu Ala : 50	Leu Ile Tyr	Trp Asn S	Ser Asp Lys	Arg Tyr Ser Pro Ser 60			
Leu Lys Ser 2 65	Arg Leu Thr 70	Ile Thr I	Lys Asp Thr 75	Ser Lys Asn Gln Val 80			
Val Leu Thr	Met Thr Asn 85	Met Asp I	Pro Val Asp 90	Thr Ala Thr Tyr Tyr 95			
	Arg His Asp 100		Ser Tyr Tyr 105	Phe Tyr Tyr Gly Met			
Asp Val Trp (Gly Gln Gly	Ile Thr V	Val Thr Val	Ser Ser 125			
<210> SEQ ID NO 195 <211> LENGTH: 30							

<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 195
gggttctcac tcagcactag tggagtgggt
                                                                       30
<210> SEQ ID NO 196
<211> LENGTH: 10
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 196
Gly Phe Ser Leu Ser Thr Ser Gly Val Gly
     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
                                                                       21
atttattgga attctgataa g
<210> SEQ ID NO 198
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 198
Ile Tyr Trp Asn Ser Asp Lys
<210> SEQ ID NO 199
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 199
gcacacagac 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
1
                                   10
Val
<210> SEQ ID NO 201
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 201
gacatecaga tgacecagte teegetetee etgecegtea eccetggaga geeggeetee
atotoctgca ggtotagtca gagootocto catagtoatg gatacaacta tttggattgg
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcggt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttgggatt tattactgca tgcaagctct acagactcct
ctcactttcg gcggagggac caaggtggag atcaaacga
<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
                                  10
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 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
Arg
<210> SEQ ID NO 203
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 203
cagageetee tecatagtea tggatacaae tat
<210> SEQ ID NO 204
<211> LENGTH: 11
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 204
Gln Ser Leu Leu His Ser His Gly Tyr Asn Tyr
                5
<210> SEQ ID NO 205
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 205
ttgggttct
                                                                         9
<210> SEQ ID NO 206
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 206
Leu Gly Ser
<210> SEQ ID NO 207
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 207
                                                                        27
atgcaagete tacagactee teteact
<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
                 5
<210> SEQ ID NO 209
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 209
cagateacet tgaaggagte tggteetaet etggtgaaac eetcacagae eetcacgetg
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
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 210
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```
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Ser 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
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
                                                                      180
tccggggtcc ctgacaggtt cagtggcggt ggatcaggca cagattttac actgaaaatc
                                                                      300
agcagagtgg aggctgagga tgttgggatt tattactgca tgcaagctct acagactcct
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                      336
<210> SEQ ID NO 212
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 212
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
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 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 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
           100
                                105
                                                    110
```

-continued

<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 acctgcacct tctctgggtt ctcactcagc actagtggag tgggtgtggg ctggatccgt cagececcag gaaaggeest ggagtggett geacteattt attggaatte tgataagege tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga catgacaget egtectaeta ettetaetae ggtatggaeg tetggggeea agggaeeaeg qtcaccqtct cctca <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 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 Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <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 atctcctqca qqtctaqtca qaqcctcctc cataqtcatq qatacaacta tttqqattqq tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180 tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc agcagagtgg aggetgagga tgttggggtt tattactgca tgcaagctct acagactcct 300

ctcactttcg gcggagggac caaggtggag atcaaa

336

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<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
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
           100
<210> SEO ID NO 217
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 217
gagatgcaac tggtggagtc tgggggaggc ttggtccagc ctggggggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt cacctttagt agtcactgga tgaagtgggt ccgccaggct
ccagggaagg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgttt
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt
gtactaatgg totatgatat ggactactac tactacggta tggacgtctg gggccaaggg
                                                                     381
accacggtca ccgtctcctc a
<210> SEQ ID NO 218
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 218
Glu Met Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                                   1.0
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
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
```

```
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
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                            120
<210> SEQ ID NO 219
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 219
ggattcacct ttagtagtca ctgg
<210> SEQ ID NO 220
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 220
Gly Phe Thr Phe Ser Ser His Trp
1
                 5
<210> SEQ ID NO 221
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 221
ataaaccaag atggaagtga gaaa
                                                                         24
<210> SEQ ID NO 222
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 222
Ile Asn Gln Asp Gly Ser Glu Lys
<210> SEQ ID NO 223
<211> LENGTH: 60
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 223
                                                                        60
gcgagagata ttgtactaat ggtctatgat atggactact actactacgg tatggacgtc
<210> SEQ ID NO 224
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 224
Ala Arg Asp Ile Val Leu Met Val Tyr Asp Met Asp Tyr Tyr Tyr
1
                5
                                    1.0
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
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
atotoctgca ggtctagtca gagcotoctg catagtaatg gaaacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
teeggggtee etgacaggtt eagtggeagt ggateaggea eagattttae aetgaaaate
                                                                     240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaaactct acaaactccg
                                                                     300
                                                                     336
ctcactttcg gcggagggac caaggtggag atcaaa
<210> SEO 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
                                25
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
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
<210> SEQ ID NO 227
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 227
cagageetee tgeatagtaa tggaaacaae tat
                                                                      33
<210> SEQ ID NO 228
<213> ORGANISM: Artificial Sequence
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<211> LENGTH: 11 <212> TYPE: PRT <220> FEATURE:

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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 228
Gln Ser Leu Leu His Ser Asn Gly Asn Asn Tyr
<210> SEQ ID NO 229
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 229
ttgggttct
<210> SEQ ID NO 230
<211> LENGTH: 3
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 230
Leu Gly Ser
<210> SEQ ID NO 231
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 231
atgcaaactc tacaaactcc gctcact
                                                                        27
<210> SEQ ID NO 232
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 232
Met Gln Thr Leu Gln Thr Pro Leu Thr
<210> SEQ ID NO 233
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 233
gaggtgcagc tggtggagtc tgggggaggc ttggtccagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt cacctttagt agtcactgga tgaagtgggt ccgccaggct
                                                                       120
ccagggaagg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat
                                                                       180
gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgttt
                                                                       240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt
                                                                       300
gtactaatgg totatgatat ggactactac tactacggta tggacgtotg gggccaaggg
```

```
accacggtca ccgtctcctc 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
Ala Asn Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val 50 \,
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe 65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                         120
<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
atotootgoa ggtotagtoa gagootootg catagtaatg gaaacaacta tttggattgg
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 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
    50
                       55
                                          60
```

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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 teetgtgeag cetetggatt cacetttagt agteactgga tgagetgggt cegecagget ccagggaagg ggctggagtg ggtggccaac ataaaccaag atggaagtga gaaatactat gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatatt gtactaatgg totatgatat ggactactac tactacggta tggacgtotg ggggcaaggg accacggtca ccgtctcctc a <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 25 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 50 $\,$ 60 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 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 120 <210> SEQ ID NO 239 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 239

180

240 300

360

381

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atctcctgca ggtctagtca gagcctcctg catagtaatg gaaacaacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaaactct acaaactccg
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                      336
<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
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
           100
                                105
<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 eegeeagget
ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat
gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat
                                                                     240
ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt
                                                                      300
gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg gggccaaggg
                                                                      360
accacqqtca ccqtctcctc a
                                                                      381
<210> SEQ ID NO 242
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 242
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
```

```
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
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
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 243
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 243
ggattcacct tcagtagcta tggc
                                                                        24
<210> SEQ ID NO 244
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 244
Gly Phe Thr Phe Ser Ser Tyr Gly
<210> SEQ ID NO 245
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 245
atatcatatg atggaagtaa taaa
<210> SEQ ID NO 246
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 246
Ile Ser Tyr Asp Gly Ser Asn Lys
<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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<400> SEOUENCE: 247
gcgaaaaata ttgtactagt gatgtatgat atagactatc actactatgg gatggacgtc
                                                                       60
<210> SEQ ID NO 248
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 248
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr
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
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                       60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttt taatcgggcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
                                                                      300
ctcactttcg gcggagggac caaggtggag atcaga
                                                                      336
<210> SEQ ID NO 250
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 250
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
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 $35$
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
                                105
<210> SEQ ID NO 251
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 251
cagageetee tgeatagtaa tggatacaae tat
                                                                       33
<210> SEQ ID NO 252
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 252
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
ttgggtttt
                                                                        9
<210> SEQ ID NO 254
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 254
Leu Gly Phe
<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
                                                                       27
<210> SEQ ID NO 256
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 256
Met Gln Ala Leu Gln Thr Pro Leu Thr
<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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caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
teetgtgeag tetetggatt eacetteagt agetatggea tgeactgggt eegeeagget
                                                                      120
ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat
gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat
ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt
gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg gggccaaggg
accacggtca ccgtctcctc a
                                                                      381
<210> SEQ ID NO 258
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 258
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
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
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
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<210> SEQ ID NO 259
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 259
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                       60
atotoctgca ggtctagtca gagcotoctg catagtaatg gatacaacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttt taatcgggcc
                                                                      180
teeggggtee etgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
                                                                      300
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                      336
<210> SEQ ID NO 260
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 260

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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 \$35\$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 261 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 261 caggtgcage tggtggagte tgggggagge gtggtecage etgggaggte cetgagaete 60 teetgtgeag cetetggatt cacetteagt agetatggea tgeactgggt cegecagget 120 ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180 gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240 ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaaatatt 300 gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg ggggcaaggg 360 accacggtca ccgtctcctc a 381 <210> SEQ ID NO 262 <211> LENGTH: 127 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 262 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 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 Ser Tyr Asp Gly Ser Asn Lys 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 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 120

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<210> SEQ ID NO 263
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 263
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                      60
atotoctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
                                                                      336
ctcactttcq qcqqaqqqac caaqqtqqaq atcaaa
<210> SEQ ID NO 264
<211> LENGTH: 112
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 264
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
                                   1.0
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
                            40
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
                                105
<210> SEQ ID NO 265
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 265
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc
                                                                      60
teetgtgeag tetetggatt eacetteagt agetatggea tgeactgggt eegeeagget
                                                                      120
ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat
                                                                      180
gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat
                                                                      240
ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt
gtactagtga tgtatgatat agactatcac tactatggga tggacgtctg gggccaaggg
                                                                      360
accaeggtea eegteteete a
                                                                      381
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<210> SEQ ID NO 266
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 266
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
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 65 70 75 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Asn Cys 85 \hspace{0.5cm} 90 \hspace{0.5cm} 95 \hspace{0.5cm}
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His Tyr Tyr 100 \hspace{1cm} 100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 267
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 267
ggattcacct tcagtagcta tggc
                                                                                24
<210> SEQ ID NO 268
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 268
Gly Phe Thr Phe Ser Ser Tyr Gly
<210> SEQ ID NO 269
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 269
atatcatatg atggaagtaa taaa
<210> SEQ ID NO 270
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 270

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Ile Ser Tyr Asp Gly Ser Asn Lys
<210> SEQ ID NO 271
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 271
gcgaaaaata ttgtactagt gatgtatgat atagactatc actactatgg gatggacgtc
<210> SEQ ID NO 272
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 272
Ala Lys Asn Ile Val Leu Val Met Tyr Asp Ile Asp Tyr His \bar{\text{Tyr}} Tyr
                                    10
Gly Met Asp Val
<210> SEQ ID NO 273
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 273
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
                                                                       60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg
                                                                      120
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttt taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
                                                                      336
ctcactttcg gcggagggac caaggtggag atcaga
<210> SEQ ID NO 274
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 274
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1
                 5
                                    1.0
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
                           40
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
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Arg
                                105
<210> SEQ ID NO 275
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 275
cagageetee tgeatagtaa tggatacaae tat
                                                                       33
<210> SEQ ID NO 276
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 276
Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
                5
<210> SEQ ID NO 277
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 277
ttgggtttt
                                                                        9
<210> SEQ ID NO 278
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 278
Leu Gly Phe
<210> SEQ ID NO 279
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 279
atgcaagete tacaaactee teteact
                                                                       27
<210> SEQ ID NO 280
<211> LENGTH: 9
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 280
Met Gln Ala Leu Gln Thr Pro Leu Thr
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1 <210> SEQ ID NO 281 <211> LENGTH: 381 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 281 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc tcctgtgcag tctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct ccaggcaagg ggctggagtg ggtggcagct atatcatatg atggaagtaa taaatactat gtagactccg tgaagggccg attcaccatc tccagagaca attccaagaa aacgctgtat ctgcaaatga acagcctgag agctgaggac acggctgtgt ataattgtgc gaaaaatatt qtactaqtqa tqtatqatat aqactatcac tactatqqqa tqqacqtctq qqqccaaqqq 381 accacggtca ccgtctcctc a <210> SEQ ID NO 282 <211> LENGTH: 127 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 282 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Val 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 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 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 283 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 283 qatattqtqa tqactcaqtc tccactctcc ctqcccqtca cccctqqaqa qccqqcctcc 60 atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttt 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 284
<211> LENGTH: 112
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 284
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
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 35 40 45
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
                85
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
           100
                                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
tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct
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
<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
                                  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
                            40
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
                        55
```

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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
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                           120
<210> SEQ ID NO 287
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 287
qatattqtqa tqactcaqtc tccactctcc ctqcccqtca cccctqqaqa qccqqcctcc
                                                                      60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg
                                                                      120
tacctqcaqa aqccaqqqca qtctccacaq ctcctqatct atttqqqttt taatcqqqcc
                                                                      180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
                                                                      240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactcct
                                                                     300
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                      336
<210> SEQ ID NO 288
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 288
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
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 289
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 289
cagatcacct tgaaggagtc tggtcctacg ctggtaaaac ccacacagac cctcacgctg
                                                                      60
                                                                      120
```

acctgcacct tetetgggtt etcactcage getagtggag tgggtgtggg etggtteegt

```
cagececcag gaaaggeest ggagtggett geacteattt attggaatga tgataagegt
tacageceat etetaaagaa eageeteace ateaceaagg acaceteeaa aaaceaggtg
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga
atacatctat ggtcctactt ctactacggt atggacgtct ggggccaagg gaccacggtc
accgtctcct ca
                                                                      372
<210> SEQ ID NO 290
<211> LENGTH: 124
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 290
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
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
                   7.0
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
                                                     110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<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
<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
             5
<210> SEQ ID NO 293
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 293
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atttattgga atgatgataa g
                                                                      21
<210> SEQ ID NO 294
<211> LENGTH: 7
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 294
Ile Tyr Trp Asn Asp Asp Lys
<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
                5
<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
atotoctgca ggtctagtca gactotoctg catagtaatg gatacaacta tttcgattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacagatt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggaatt tattactgca tgcaagctct acaaactcct
ctcactttcg gcggagggac caaggtggag atcaga
                                                                     336
<210> SEQ ID NO 298
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 298
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
                         10
            5
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr Leu Leu His Ser
```

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```
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 Arg
<210> SEQ ID NO 299
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 299
cagactetee tgcatagtaa tggatacaae 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
                                   1.0
<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
<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
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<210> SEQ ID NO 304

195 196

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<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
<400> SEQUENCE: 305
cagatcacct tgaaggagte tggteetacg etggtaaaac ecacacagac ecteacgetg
acctgcacct tctctgggtt ctcactcagc gctagtggag tgggtgtggg ctggttccgt
                                                                     120
cagcccccag gaaaggccct ggagtggctt gcactcattt attggaatga tgataagcgt
                                                                      180
tacaqcccat ctctaaaqaa caqcctcacc atcaccaaqq acacctccaa aaaccaqqtq
                                                                      240
qtccttacaa tqaccaacat qqaccctqtq qacacaqcca catattactq tqcacacaqa
                                                                      300
atacatetat ggteetaett etaetaeggt atggaegtet ggggeeaagg gaecaeggte
                                                                     360
accetctcct ca
                                                                     372
<210> SEQ ID NO 306
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 306
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
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
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
       115
                           120
<210> SEQ ID NO 307
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 307

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gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc
atotoctgca ggtotagtca gactotoctg catagtaatg gatacaacta tttcgattgg
                                                                     120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacagatt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggaatt tattactgca tgcaagctct acaaactcct
ctcactttcg gcggagggac caaggtggag atcaaa
                                                                     336
<210> SEQ ID NO 308
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 308
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
                                   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
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 Ile Tyr Tyr Cys Met Gln Ala
Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
           100
                               105
<210> SEQ ID NO 309
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 309
cagatcacct tgaaggagte tggtectacg etggtgaaac ccacacagac cetcacgetg
acctgcacct tctctgggtt ctcactcagc gctagtggag tgggtgtggg ctggatccgt
cagececcag gaaaggeet ggagtggett geacteattt attggaatga tgataagege
tacageceat etetgaagag eaggeteace ateaceaagg acaceteeaa aaaceaggtg
                                                                     240
gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacacaga
                                                                     300
atacatctat ggtcctactt ctactacggt atggacgtct gggggcaagg gaccacggtc
                                                                     360
accgtctcct ca
                                                                     372
<210> SEQ ID NO 310
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 310
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Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln 1 5 10 15

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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 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 311 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 311 gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60 atctcctgca ggtctagtca gactctcctg catagtaatg gatacaacta tttggattgg tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 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> SEQUENCE: 312 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 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 90 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

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 313
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc
                                                                       60
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 taattattcc tactacgtta tggacgtctg gggccaaggg
accacggtca ccgtctcctc a
<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 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
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
                          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
                                                                       24
qqttacacct ttaccaccta tqqt
<210> SEQ ID NO 316
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 316
Gly Tyr Thr Phe Thr Thr Tyr Gly
```

1 5

```
<210> SEQ ID NO 317
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 317
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
<400> SEQUENCE: 318
Ile Ser Gly Tyr Asn Gly Lys Thr
<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 gittagtagt accacotgoo ottaattati ootactaogi tatggaogio
                                                                       60
<210> SEQ ID NO 320
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 320
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Ser Tyr Tyr
                 5
                                    10
Val Met Asp Val
<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
                                                                       60
atotootgoa ggtotagtoa aagootogta tacagtgatg gaaacacota ottgaattgg
                                                                      120
tctcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
                                                                      240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
                                                                      300
tacacttttg gccaggggac caagctggag atcaaa
<210> SEQ ID NO 322
<211> LENGTH: 112
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<212> TYPE: PRT

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<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
                                   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 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
                                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
aaqqtttct
                                                                        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
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<210> SEQ ID NO 327

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<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 327
atgcaaggta cacactggcc gtacact
                                                                      27
<210> SEQ ID NO 328
<211> LENGTH: 9
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 328
Met Gln Gly Thr His Trp Pro Tyr Thr
<210> SEQ ID NO 329
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 329
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc
                                                                      60
teetgeaagg ettetggtta cacetttaec acetatggta teagttgggt acgacaggee
                                                                     120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
                                                                     180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
                                                                     240
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
                                                                     300
ttagtagtac cacctgccct taattattcc tactacgtta tggacgtctg gggccaaggg
accaeggica eegieteete 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
                               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
                       55
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
                   7.0
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
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115 120 125 <210> SEQ ID NO 331 <211> LENGTH: 336 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 331 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 tacacttttg gccaggggac caagctggag atcaaa 336 <210> SEQ ID NO 332 <211> LENGTH: 112 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 332 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 25 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 <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 60 teetgeaagg ettetggtta eacetttace acetatggta teagetgggt gegacaggee 120 cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat 180 gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240 300 atggagetga ggageetgag atetgaegae aeggeegtgt attactgtte gagagategt ttagtagtac cacctgccct taattattcc tactacgtta tggacgtctg ggggcaaggg 360 accacggtca ccgtctcctc a 381

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<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
                                    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 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 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 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
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
tacacttttg gccaggggac caagctggag atcaaa
<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
                                    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 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

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```
65
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
                85
                                    90
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
teetgtgeag cetetggatt cacetteagt agetatagea tggactgggt cegecagget
ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac
gcagactctg tgaagggccg attcaccatc tccagagaca ccgccaagaa ctcactgtat
                                                                      240
ctgcaaatga acagcctgag agacgaggac acggctgttt attactgtgc gagagagggc
                                                                      300
agtagcagac tttttgacta ctggggccag ggaaccctgg tcaccgtctc ctca
                                                                      354
<210> SEO ID NO 338
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 338
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
                                25
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
Leu Gln Met As<br/>n 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
                                                                       24
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<210> SEQ ID NO 340 <211> LENGTH: 8

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<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
<210> SEQ ID NO 342
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 342
Ile Ser Ser Ser Ser 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
gcgagagagg gcagtagcag actttttgac tac
                                                                       33
<210> SEQ ID NO 344
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 344
Ala Arg Glu Gly Ser Ser Arg Leu Phe Asp Tyr
<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
                                                                       60
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagagacca
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
<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
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Trp Tyr
                85
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100
<210> SEQ ID NO 347
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 347
cagagtatta gtagctgg
                                                                         18
<210> SEQ ID NO 348
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 348
Gln Ser Ile Ser Ser Trp
<210> SEQ ID NO 349
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 349
                                                                          9
aaggcgtct
<210> SEQ ID NO 350
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<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
<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
tcctgtgcag cctctggatt caccttcagt agctatagca tggactgggt ccgccaggct
ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac
gcagactctg tgaagggccg attcaccatc tccagagaca ccgccaagaa ctcactgtat
ctgcaaatga acagcctgag agacgaggac acggctgttt attactgtgc gagagagggc
agtagcagac tttttgacta ctggggccag ggaaccctgg tcaccgtctc ctca
<210> SEQ ID NO 354
<211> LENGTH: 118
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 354
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
           2.0
                                25
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
                    70
Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
               85
                                    90
```

```
Ala Arg Glu Gly Ser Ser Arg Leu Phe Asp Tyr Trp Gly Gln Gly Thr
                               105
Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 355
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 355
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagagacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaggtgg agtcccatca
                                                                     180
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
                                                                     240
gaggattttg caacttatta ctgccaacag tataatagtt attggtacac ttttggccag
                                                                     300
qqqaccaaqc tqqaqatcaa a
                                                                      321
<210> SEQ ID NO 356
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 356
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
                                25
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
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
<210> SEQ ID NO 357
<211> LENGTH: 354
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 357
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctggggggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct
ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac
                                                                      180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat
                                                                      240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagagggc
                                                                      300
```

```
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
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
           100
                               105
Leu Val Thr Val Ser Ser
       115
<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
atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca
gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tataatagtt attggtacac ttttggccag
gggaccaagc tggagatcaa a
<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
                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
                   70
                                       75
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
           100
<210> SEQ ID NO 361
<211> LENGTH: 384
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 361
caggtgcacc 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
                                                                     240
ctacatatqa acaqcctcaq aqccqacqac acqqccqtqt attactqtqc qaqaqatcaq
                                                                     300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa
                                                                     360
                                                                     384
gggaccacgg tcaccgtcgc ctca
<210> SEQ ID NO 362
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 362
Gln Val His 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 Ser
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
       115
                           120
                                                125
<210> SEQ ID NO 363
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 363
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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
<210> SEQ ID NO 365
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 365
attagtaatg atggtggtac caaa
                                                                       24
<210> SEQ ID NO 366
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 366
Ile Ser Asn Asp Gly Gly Thr Lys
1
<210> SEQ ID NO 367
<211> LENGTH: 63
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 367
gcgagagatc agggatatat tggctacgac tcgtattatt actattccta cggtatggac
gtc
                                                                       63
<210> SEQ ID NO 368
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 368
Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser
1
                                    1.0
Tyr Gly Met Asp Val
           20
<210> SEQ ID NO 369
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 369
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aaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc
                                                                       60
ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
                                                                      120
tetggecagg etcecagget ceteatetat ggtgeateca geagggecae tggeatecea
gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag
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
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
                                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
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
            100
<210> SEQ ID NO 371
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 371
                                                                       21
cagagtgtta acaacaaatt c
<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
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ggtgcatcc
<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
caagtatatg gtaactcact cact
                                                                       24
<210> SEQ ID NO 376
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 376
Gln Val Tyr Gly Asn Ser Leu Thr
                5
<210> SEQ ID NO 377
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 377
caggtgcagc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc
tcctgtgcag cctctggatt caccttcagt gaccactaca tgagctggat ccgccaggct
ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat
gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat
ctacatatga acagceteag ageegaegae aeggeegtgt attactgtge gagagateag
                                                                      300
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa
                                                                      360
gggaccacgg tcaccgtctc ctca
                                                                      384
<210> SEQ ID NO 378
<211> LENGTH: 128
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 378
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
                                    1.0
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
                                25
            20
                                                    30
```

-continued

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 Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 379 <211> LENGTH: 321 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 379 gaaattgtgt tgacgcagtc tccaggcacc ctgcctttgt ttccagggga aagagccacc 60 ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa 120 tetggecagg etcecagget ceteatetat ggtgeateca geagggecae tggeatecea 180 gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag 240 cctgaagatt ttgaagtgta ttattgtcaa gtatatggta actcactcac tctcggcgga 300 gggaccaagg tggagatcaa a 321 <210> SEQ ID NO 380 <211> LENGTH: 107 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 380 Glu 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 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

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<400> SEQUENCE: 381
caggtgcagc tggtggagtc tgggggaggc ttggtcaagc ctggagggtc cctgagactc
                                                                      60
teetgtgeag cetetggatt cacetteagt gaccactaca tgagetggat eegecagget
ccagggaagg ggctggagtg ggtttcatac attagtaatg atggtggtac caaatactac
gcagactctg tgaagggccg attcaccatc tccagggaca acgccaagaa ctcactgtat
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatcag
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctgggggcaa
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
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
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
ctctcctgca gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
                                                                     120
cctggccagg ctcccagget cctcatctat ggtgcatcca gcagggccac tggcatccca
                                                                     180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag
                                                                     240
cctqaaqatt ttgcaqtqta ttactqtcaa qtatatqqta actcactcac tttcqqcqqa
                                                                     300
gggaccaagg tggagatcaa a
                                                                     321
<210> SEQ ID NO 384
<211> LENGTH: 107
<212> TYPE: PRT
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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<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 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 <210> SEQ ID NO 385 <211> LENGTH: 360 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 385 gaggtgcaga aggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc 60 teetgtacag cetetggatt cacetteagt acttataaca tgaattgggt cegecagget 120 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 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 105 Gly Thr Leu Val Thr Val Ser Ser

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115
                            120
<210> SEQ ID NO 387
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 387
ggattcacct tcagtactta taac
                                                                       24
<210> SEQ ID NO 388
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 388
Gly Phe Thr Phe Ser Thr Tyr Asn
<210> SEQ ID NO 389
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 389
                                                                       2.4
attaggagta gtagtaatta cata
<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
gcgagagatg gcagcagttg gtacgactac tctgactac
                                                                       39
<210> SEQ ID NO 392
<211> LENGTH: 13
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 392
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
1
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<210> SEQ ID NO 393

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<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
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
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
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
                        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
<210> SEQ ID NO 395
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 395
                                                                       18
cagagtatta gtagctgg
<210> SEQ ID NO 396
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 396
Gln Ser Ile Ser Ser Trp
1
<210> SEQ ID NO 397
<211> LENGTH: 9
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 397
aaggcgtct
                                                                          9
<210> SEQ ID NO 398
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<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
<400> SEQUENCE: 400
Gln Gln Tyr Ile Ser Tyr Ser Arg Thr
                 5
<210> SEQ ID NO 401
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 401
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
                                                                         60
teetgtacag cetetggatt cacetteagt aettataaca tgaattgggt eegeeagget
                                                                        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
<210> SEQ ID NO 402
<211> LENGTH: 120
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 402
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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
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
                              105
Gly Thr Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 403
<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 403
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                      60
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
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
                           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
                               105
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<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
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 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
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
                       55
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
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> SEQUENCE: 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
gggaccaagg tggaaatcaa a
                                                                     321
```

<210> SEQ ID NO 408 <211> LENGTH: 107

<21	2 > T 3 > OF 0 > FF	RGANI	ISM:	Art:	ific:	ial S	Seque	ence								
	3 > 01			ORMA'	rion	: Syı	nthet	ic								
< 40	O> SI	EQUE	ICE:	408												
Asp 1	Ile	Gln	Met	Thr 5	Gln	Ser	Pro	Ser	Thr 10	Leu	Ser	Ala	Ser	Val 15	Gly	
Asp	Arg	Val	Thr 20	Ile	Thr	Cys	Arg	Ala 25	Ser	Gln	Ser	Ile	Ser 30	Ser	Trp	
Leu	Ala	Trp 35	Tyr	Gln	Gln	Lys	Pro 40	Gly	Lys	Ala	Pro	Lуs 45	Leu	Leu	Ile	
Tyr	Lys 50	Ala	Ser	Ser	Leu	Glu 55	Ser	Gly	Val	Pro	Ser 60	Arg	Phe	Ser	Gly	
Ser 65	Gly	Ser	Gly	Thr	Glu 70	Phe	Thr	Leu	Thr	Ile 75	Ser	Ser	Leu	Gln	Pro 80	
Asp	Asp	Phe	Ala	Thr 85	Tyr	Tyr	Cys	Gln	Gln 90	Tyr	Ile	Ser	Tyr	Ser 95	Arg	
Thr	Phe	Gly	Gln 100	Gly	Thr	ГЛа	Val	Glu 105	Ile	ГЛа						
<213 <213 <213 <220 <223	D> SH L> LH 2> TY 3> OH D> FH 3> OY	ENGTH (PE: RGAN) EATUR THER	H: 36 DNA ISM: RE: INFO	Art: DRMA			_									
qaq	atqca	aqc t	aqto	qaqt	c to	aaaa	aqqq	cto	qtca	aaqc	caad	aggg	atc (cctqa	agactc	60
															cagget	120
	_						_				_			_	actac	180
										_					ctgtat	240
	-	_			_						_				gatggc	300
_		_	_	_			_			_		_			cctca	360
age	age eş	190 0	acga	caci		jacci	iceg	9 99	cage	, yaa	CCC	-990	Jac (gee	cecca	300
<210> SEQ ID NO 410 <211> LENGTH: 120 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic																
< 40	O> SI	EQUE	ICE :	410												
Glu 1	Val	Gln	Leu	Val 5	Glu	Ser	Gly	Gly	Gly 10	Leu	Val	Lys	Pro	Gly 15	Gly	
Ser	Leu	Arg	Leu 20	Ser	Cys	Thr	Ala	Ser 25	Gly	Phe	Thr	Phe	Ser 30	Thr	Tyr	
Asn	Met	Asn 35	Trp	Val	Arg	Gln	Ala 40	Pro	Gly	Lys	Gly	Leu 45	Glu	Trp	Val	
Ser	Ser 50	Ile	Arg	Ser	Ser	Ser 55	Asn	Tyr	Ile	Tyr	Tyr 60	Ala	Asp	Ser	Val	
Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ala 75	ГЛа	Asn	Ser	Leu	Tyr 80	
Leu	Gln	Met	Asn	Ser 85	Leu	Arg	Ala	Asp	Asp	Thr	Ala	Val	Tyr	Tyr 95	Cya	
Ala	Arg	Asp	Gly	Ser	Ser	Trp	Tyr	Asp	Tyr	Ser	Asp	Tyr	Trp	Gly	Gln	

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100
                                 105
                                                     110
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
                                                                        24
<210> SEQ ID NO 412
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 412
Gly Phe Thr Phe Ser Thr Tyr Asn
<210> SEQ ID NO 413
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 413
attaggagta gtagtaatta cata
                                                                        24
<210> SEQ ID NO 414
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 414
Ile Arg Ser Ser Ser Asn Tyr Ile
1
<210> SEQ ID NO 415
<211> LENGTH: 39
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 415
gcgagagatg gcagcagttg gtacgactac tctgactac
                                                                        39
<210> SEQ ID NO 416
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 416
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
                5
                                    10
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<210> SEQ ID NO 417
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 417
gacatecaga tgacecagte teettecace etgtetgeat etgtaggaga cagagteace
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
                                                                      321
<210> SEQ ID NO 418
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 418
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
                                   1.0
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
                       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
<210> SEQ ID NO 419
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 419
                                                                       18
cagagtatta gtagctgg
<210> SEQ ID NO 420
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 420
Gln Ser Ile Ser Ser Trp
```

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<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
1
                 5
<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
teetgtacag cetetggatt cacetteagt aettataaca 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
<210> SEQ ID NO 426
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 426
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
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
                             105
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
aggttcagcg gcagtggatc tgggacagaa ttcactctca tcatcagcag cctgcagcct
                                                                     240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa
gggaccaagg tggaaatcaa a
                                                                     321
<210> SEQ ID NO 428
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 428
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
                           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
                    70
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
                              105
```

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<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 cacetteagt acttataaca tgaactgggt cegecagget
ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat
                                                                      300
ctqcaaatqa acaqcctqaq aqccqaqqac acqqctqtqt attactqtqc qaqaqatqqc
ageagttggt acgactactc tgactactgg ggccaaggaa ccctggtcac cgtctcctca
                                                                      360
<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
                                   1.0
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
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
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> SEOUENCE: 431
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                      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
```

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<210> SEQ ID NO 432
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 432
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
                                   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 Ile Ser Tyr Ser Arg
               85
                                  90
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
           100
<210> SEO ID NO 433
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 433
gaggtgcagc tggtggagtc tggggggggc ctggtcaagc cgggggggtc cctgagactc
                                                                      60
teetgtacag cetetggatt cacetteagt aettataaca tgaattgggt eegeeagget
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagag ttcactgtat
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
ageagttggt 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 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 Ser Ser Leu Tyr
                   70
                                        75
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
            100
                                105
                                                     110
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
<210> SEQ ID NO 437
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 437
attaggagta gtagtaatta cata
                                                                        24
<210> SEQ ID NO 438
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 438
Ile Arg Ser Ser Ser Asn Tyr Ile
<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
```

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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 teettecace 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
                                                                      321
<210> SEQ ID NO 442
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 442
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
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
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
<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
<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
caacagtata ttagttattc tcggacg
                                                                       2.7
<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
<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 tggggggggc ctggtcaagc cgggggggtc cctgagactc
                                                                       60
tcctgtacag cctctggatt caccttcagt acttataaca tgaattgggt ccgccaggct
                                                                      120
ccagggaagg gactggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagag ttcactgtat
                                                                      240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
                                                                      300
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
<210> SEQ ID NO 450
<211> LENGTH: 120
<212> TYPE: PRT
```

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 450
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
                                     10
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
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 100 \phantom{000} 105 \phantom{000} 110 \phantom{000}
Gly Thr Leu Val Thr Val Ser Ser
        115
<210> SEO ID NO 451
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 451
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                        60
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 452
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 452
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
                                  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
                                         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 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
teetgtgeag cetetggatt cacetteagt aettataaca tgaactgggt eegecagget
ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
                                                                     360
<210> SEQ ID NO 454
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 454
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
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
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
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
gacatecaga tgacecagte teettecace etgtetgeat etgtaggaga cagagteace
                                                                      60
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
```

```
gggaccaagg tggaaatcaa a
                                                                      321
<210> SEQ ID NO 456
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 456
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
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
                   70
                                        75
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg
                85
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> SEQUENCE: 457
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc cgggggggtc cctgagactc
teetgtacag cetetggatt cacetteagt aettataaca tgaattgggt cegeeagget
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 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
                                    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
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
```

```
65
                                         75
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85
                                     90
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> SEOUENCE: 460
Gly Phe Thr Phe Ser Thr Tyr Asn
                5
<210> SEQ ID NO 461
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 461
attaggagta gtagtaatta cata
                                                                         24
<210> SEQ ID NO 462
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 462
Ile Arg Ser Ser Ser Asn Tyr Ile
<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:
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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 464
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr
<210> SEQ ID NO 465
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 465
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
atcacttqcc qqqccaqtca qaqtattaqt aqctqqttqq cctqqtatca acaqatacca
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 466
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 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
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
<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

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<400> SEQUENCE: 468
Gln Ser Ile Ser Ser Trp
<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
<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> SEQUENCE: 472
Gln Gln Tyr Ile Ser Tyr Ser Arg Thr
<210> SEQ ID NO 473
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 473
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
ctgcaaatga acagcctgag agccgatgac acggctgtgt attactgtgc gagagatggc
                                                                      300
agcagttggt acgactactc tgactactgg ggccagggaa ccctggtcac cgtctcctca
                                                                      360
```

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<210> SEQ ID NO 474
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<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
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 85 \\ 90 95
Ala Arg Asp Gly Ser Ser Trp Tyr Asp Tyr Ser Asp Tyr Trp Gly Gln $100$
Gly Thr Leu Val Thr Val Ser Ser
       115
<210> SEO TD NO 475
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 475
gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc
                                                                       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
gggaccaagg tggaaatcaa a
<210> SEQ ID NO 476
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 476
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
                5
                                    1.0
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
                                            60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
                  70
                                        75
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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 teetgtgeag cetetggatt cacetteagt aettataaca tgaactgggt eegecagget ccagggaagg ggctggagtg ggtctcatcc attaggagta gtagtaatta catatactac gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240 300 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatggc agcagttggt acgactactc tgactactgg ggccaaggaa ccctggtcac cgtctcctca 360 <210> SEQ ID NO 478 <211> LENGTH: 120 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 478 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly 1 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 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 479 <211> LENGTH: 321 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 479 gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc atcacttgcc gggccagtca gagtattagt agctggttgg cctggtatca gcagaaacca 120 gggaaagccc ctaagctcct gatctataag gcgtctagtt tagaaagtgg ggtcccatca

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aggttcagcg gcagtggatc tgggacagaa ttcactctca ccatcagcag cctgcagcct	240
gatgattttg caacttatta ctgccaacag tatattagtt attctcggac gttcggccaa	300
gggaccaagg tggaaatcaa a	321
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Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly 1 5 10 15	
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp 20 25 30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 35 40 45	
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60	
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80	
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ile Ser Tyr Ser Arg 85 90 95	
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 105	
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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
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Ser Leu Arg Leu Ser Cys Val Val Ser Gly Phe Thr Phe Gly Asp Tyr 20 25 30	
Asp Met His Trp Val Arg Gln Ala Thr Gly Arg Gly Leu Glu Trp Val 35 40 45	
Ser Gly Ile Ala Pro Ala Gly Asp Thr Ser Tyr Thr Gly Ser Val Lys	

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Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu His Leu
                    70
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
                                105
Leu Val Thr Val Ser Ser
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<223 > OTHER INFORMATION: Synthetic
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<223> OTHER INFORMATION: Synthetic
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Gly Phe Thr Phe Gly Asp Tyr Asp
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic
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<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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Ile Ala Pro Ala Gly Asp Thr
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<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
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<211> LENGTH: 12

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<220> FEATURE:
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Ala Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr
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<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 489
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ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct
ggccaggctc ccagactcct catctatggt gcatccacga gggccactgg cttcccagcc
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct
qaaqattttq caqtttatta ctqtcaqcaq tataataaqt qqcctccqtt cactttcqqc
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
                       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
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
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Phe Lys
           100
<210> SEQ ID NO 491
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 491
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<210> SEQ ID NO 492
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<210> SEQ ID NO 49: <211> LENGTH: 6 <212> TYPE: PRT

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<223 > OTHER INFORMATION: Synthetic
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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
<210> SEQ ID NO 494
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 494
Gly Ala Ser
1
<210> SEQ ID NO 495
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 495
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                                                                        30
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<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
<400> SEQUENCE: 497
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tcctgtgtag tctctggatt caccttcggt gactacgaca tgcactgggt ccgtcaagct
                                                                       120
acaggaagag gtctggagtg ggtctcaggt attgctcctg ctggtgacac atcctataca
                                                                       180
ggetcegtga agggeegatt caccatetee agagagaatg ceaagaacte ettgeatett
                                                                       240
caaatgaaca gcctgacaac cggggacacg gctatatatt attgtgctag agaggatata
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gcagtgcctg gttttgatta ctggggccag ggaaccctgg tcaccgtctc ctca
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 498
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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
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu His Leu 65 70 75 80
Gln Met Asn Ser Leu Thr Thr Gly Asp Thr Ala Ile Tyr Tyr Cys Ala
Arg Glu Asp Ile Ala Val Pro Gly Phe Asp Tyr Trp Gly Gln Gly Thr
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           100
Leu Val Thr Val Ser Ser
       115
<210> SEQ ID NO 499
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 499
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ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct
ggccaggctc ccagactcct catctatggt gcatccacga gggccactgg cttcccagcc
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct
gaagattttg cagtttatta ctgtcagcag tataataagt ggcctccgtt cactttcggc
cctgggacca aagtggatat caaa
<210> SEQ ID NO 500
<211> LENGTH: 108
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 500
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
                                    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
    50
                       55
                                            60
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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 Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys <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 cacetteggt gactacgaca tgcactgggt cegecaaget acaggaaaag gtctggagtg ggtctcagct attgctcctg ctggtgacac atactatcca 180 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240 caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgctag agaggatata 300 gcagtgcctg gttttgatta ctggggccaa ggaaccctgg tcaccgtctc ctca 354 <210> SEQ ID NO 502 <211> LENGTH: 118 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 502 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 10 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asp Tyr Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val Ser Ala Ile Ala Pro Ala 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 Asp Ile Ala Val Pro Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 115 <210> SEQ ID NO 503 <211> LENGTH: 324 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 503 gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60 120

ctctcctgca gggccagtca gagtgttagc agcaacttag cctggtacca gcagaaacct

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ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct
gaagattttg cagtttatta ctgtcagcag tataataagt ggcctccgtt cactttcggc
cctgggacca aagtggatat caaa
                                                                      324
<210> SEQ ID NO 504
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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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
                           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
65
                    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 Ile Lys
           100
                               105
<210> SEQ ID NO 505
<211> LENGTH: 378
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 505
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tcctgcaagg cttctggtta cacctttacc aactacgcta tcagctgggt gcgacaggtc
cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat
gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac
atggagctga ggagcctgag atctgacgac acggccatgt attactgtgc gagaggggt
                                                                      300
gtagtegtge cagttgetee ceaettetae aaeggtatgg aegtetgggg ceaagggace
                                                                      360
acqqtcaccq tctcctca
                                                                      378
<210> SEQ ID NO 506
<211> LENGTH: 126
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<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
                                    1.0
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr \$20\$ \$25\$ 30

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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
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
<210> SEQ ID NO 507
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 507
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                                                                       24
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<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
<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
<210> SEQ ID NO 511
<211> LENGTH: 57
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 511
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<400> SEQUENCE: 515

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<211> LENGTH: 11
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 516
Gln Ser Leu Leu His Ile Asn Glu Tyr Asn Tyr
1 5
<210> SEQ ID NO 517
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 517
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<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
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                                                                       27
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<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
<210> SEQ ID NO 521
<211> LENGTH: 378
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 521
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tcctgcaagg cttctggtta cacctttacc aactacgcta tcagctgggt gcgacaggtc
                                                                      120
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cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat
gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac
atggagetga ggageetgag atetgaegae aeggeeatgt attactgtge gagagggggt
gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg ccaagggacc
acggtcaccg tctcctca
                                                                     378
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 522
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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
                   70
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
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 523
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atctcctqca qqtctaqtca qaqcctcctq catattaatq aatacaacta tttqqattqq
tacctaaaga agccagggca gtctccacag ctcctgatct atttgggttt taatcgggcc
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:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 524
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Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

	Pro	Ala	Ser 20	Ile	Ser	CAa	Arg	Ser 25	Ser	Gln	Ser	Leu	Leu 30	His	Ile	
Asn	Glu	Tyr 35	Asn	Tyr	Leu	Asp	Trp 40	Tyr	Leu	Lys	Lys	Pro 45	Gly	Gln	Ser	
Pro	Gln 50	Leu	Leu	Ile	Tyr	Leu 55	Gly	Phe	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	Сув	Met	Gln 95	Ala	
Leu	Gln	Thr	Pro 100	Trp	Thr	Leu	Gly	Gln 105	Gly	Thr	Lys	Val	Glu 110	Ile	Lys	
<211 <212 <213 <220	L> LE 2> TY 3> OF 0> FE	EQ II ENGTH YPE: RGANI EATUR	H: 37 DNA [SM: RE:	78 Arti			_									
		EQUE														60
		_		_					-	_	-				aaggtc	60 120
															actat	180
															gcctac	240
atg	gagct	ga g	ggago	ectga	ag at	ctga	acgad	c acc	geeg	jtgt	atta	actgt	gc (gagag	gggggt	300
gtag	gtcgt	ege o	agtt	gcto	ec ec	cactt	ctac	c aac	ggta	tgg	acgt	ctg	999 9	gcaaç	gggacc	360
		ecg t		_	ec co	cactt	ctad	c aac	ggta	itgg	acgt	ctg	999 <u>9</u>	gcaag	gggacc	360 378
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<210 <211 <212 <213 <220 <223	gtcac)> SE L> LE 2> TY 3> OF 0> FE 3> OT)> SE	ecg t EQ II ENGTH PE: RGANI EATUR THER	NO NO H: 12 PRT ISM: RE: INFO	526 26 Arti DRMAT	lfici	ial S	Seque nthet	ence cic								
<210 <211 <212 <213 <220 <223	gtcac)> SE L> LE 2> TY 3> OF 0> FE 3> OT)> SE	ecg t EQ II ENGTH PE: RGANI EATUH THER	NO NO H: 12 PRT ISM: RE: INFO	526 26 Arti DRMAT	lfici	ial S	Seque nthet	ence cic								
<210 <211 <212 <213 <220 <223 <400 Gln	Jycac Jy SE Ly LE 2> TY 3> OF FE 3> OT Val	ecg t EQ II ENGTH PE: RGANI EATUR THER	NO H: 12 PRT ISM: E: INFO	526 Arti DRMAT 526 Val	lfici TION: Gln	lal S Syr Ser	Seque nthet Gly	ence cic Ala	Glu 10	Val	Lys	Lys	Pro	Gly 15	Ala	
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<pre></pre>	0)> SE 1> LE 2> TV 33 > OF 33 > OT 0)> SE Val	ccg t EQ III ENGTH (PE: RGANI) FHER GQUEN GIN Lys	NO N	526 Arti 526 Arti 526 Val 5 Ser	fici Gln Cys	al Syr Ser Lys Gln	Gly Ala Ala 40	Ala Ser 25 Pro	Glu 10 Gly	Val Tyr Gln	Lys Thr	Lys Phe Leu 45	Pro Thr 30 Glu	Gly 15 Asn Trp	Ala Tyr Met	
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acgg <210 <211 <212 <213 <222 <400 Gln 1 Ser Ala Gly Gln 65	O> SE() LE() LE() LE() LE() LE() LE() LE() L	EQ III ENGTH YPE: RGANI FHER GQUEN Gln Lys Ser 35	O NO H: 12 PRT ISM: RE: INFO UCE: Leu Val 20 Trp Ser Val	526 Arti DRMAT 526 Val 5 Ser Val Ala	Gln Cys Arg Tyr Met	Ser Lys Gln Asn 55	Gly Ala Ala 40 Gly Thr	Ala Ser 25 Pro His	Glu 10 Gly Gly Thr	Val Tyr Gln Asn Ser 75	Lys Thr Gly Tyr 60	Lys Phe Leu 45 Ala Ser	Pro Thr 30 Glu Gln Thr	Gly 15 Asn Trp Lys	Ala Tyr Met Leu Tyr 80	
<pre></pre>	O> SEL> LE L> LE L> LE L> LE L> LE L> TYPE L>	CCCG t GQ II GQ II FRENGTI FRENGTI FRENGTI FRENGTI FRENGTI GLYS Ser 35 Val Arg	O NO H: 12 PRT ISM: RE: INFC Val 20 Trp Ser Val Arg	526 Arti 526 Val 5 Ser Val Thr	Gln Cys Arg Tyr Met 70 Leu	Lal Syr Ser Lys Gln Asn 55 Thr	Gly Ala Ala 40 Gly Thr	Ala Ser 25 Pro His Asp	Glu 10 Gly Thr Thr	Val Tyr Gln Asn Ser 75	Lys Thr Gly Tyr 60 Thr	Lys Phe Leu 45 Ala Ser Val	Pro Thr 30 Glu Gln Thr	Gly 15 Asn Trp Lys Ala Tyr 95	Ala Tyr Met Leu Tyr 80 Cys	

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<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
atotootgca ggtotagtoa gagootootg catattaatg aatacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct tcaaactccg
tggacgttcg gccaagggac caaggtggaa atcaaa
<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
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
                        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
                               105
<210> SEQ ID NO 529
<211> LENGTH: 351
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 529
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca
                                                                      120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca
                                                                      180
ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaactc cttctatctt
                                                                      240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata
                                                                     300
agaacaccct atgattattg gggccaggga gcccgggtca ccgtctcctc a
                                                                     351
<210> SEQ ID NO 530
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 530
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 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 85 90 95
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
                                                                        2.4
<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
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<210> SEQ ID NO 534
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 534
Ile Gly Ser Thr Gly Asp Thr
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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
gcaagagag gaataagaac accctatgat tat
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<210> SEQ ID NO 536
<211> LENGTH: 11
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 536
Ala Arg Glu Gly Ile Arg Thr Pro Tyr Asp Tyr
<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
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ctctcctgca gggccagtca gagtgttagc agcaatgtag cctggtacca gcagaaacct
                                                                       120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
                                                                       180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct
                                                                       240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
                                                                       300
cctgggacca aagtggatat caaa
                                                                       324
<210> SEQ ID NO 538
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 538
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
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
                        55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
                                        75
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
                                105
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<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 539
cagagtgtta gcagcaat
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<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
1
               5
<210> SEQ ID NO 545
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 545
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
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tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca
                                                                      120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca
ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaactc cttctatctt
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata
agaacaccct atgattattg gggccaggga accctggtca ccgtctcctc a
                                                                      351
<210> SEQ ID NO 546
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 546
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                                    10
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 Thr Leu
            100
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
ctctcctqca qqqccaqtca qaqtqttaqc aqcaatqtaq cctqqtacca qcaqaaacct
                                                                      120
qqccaqqctc ccaqqctcct catctatqqt qcatccacca qqqccactqq tatcccaqcc
                                                                      180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct
                                                                      240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
                                                                      300
                                                                      324
cctgggacca aagtggatat caaa
<210> SEQ 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 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 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 549 <211> LENGTH: 351 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 549 gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc 60 tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagct acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactatcca 180 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240 caaatgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag agagggaata agaacaccct atgattattg gggccaagga accctggtca ccgtctcctc a 351 <210> SEQ ID NO 550 <211> LENGTH: 117 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 550 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 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 100 105 110 Val Thr Val Ser Ser

Val Thr Val Ser Se 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
ctctcctgca gggccagtca gagtgttagc agcaatttag cctggtacca gcagaaacct
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
cctgggacca aagtggatat caaa
                                                                      324
<210> SEQ ID NO 552
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 552
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
                        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
           100
<210> SEQ ID NO 553
<211> LENGTH: 351
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 553
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
teetgtgeag eetetggatt eaceetaagt agetaegaea tgeactgggt eegeeaagea
                                                                     120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca
                                                                      180
ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaactc cttctatctt
                                                                      240
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata
agaacaccct atgattattg gggccaggga gcccgggtca ccgtctcctc a
                                                                     351
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<210> SEQ ID NO 554 <211> LENGTH: 117

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 554
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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 Ala Arg
                               105
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
attggcagta ctggtgacac a
                                                                       21
<210> SEQ ID NO 558
<211> LENGTH: 7
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 558
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Ile Gly Ser Thr Gly Asp Thr

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1
<210> SEQ ID NO 559
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 559
gcaagagagg gaataagaac accctatgat tat
                                                                       33
<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
<210> SEQ ID NO 561
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 561
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc
                                                                       60
ctctcctgca gggccagtca gagtgttagc agcaatgtag cctggtacca gcagaaacct
                                                                      120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
                                                                      180
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct
                                                                      240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
cctgggacca aagtggatat caaa
                                                                      324
<210> SEQ ID NO 562
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 562
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
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
                    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 563
<211> LENGTH: 18
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 563
cagagtgtta gcagcaat
                                                                         18
<210> SEQ ID NO 564
<211> LENGTH: 6
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 564
Gln Ser Val Ser Ser Asn
1
<210> SEQ ID NO 565
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 565
                                                                          9
ggtgcatcc
<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
                                                                         30
cagcagtata ataattggcc tccattcact
<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
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<211> LENGTH: 351

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<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 569
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
tcctgtgcag cctctggatt caccctaagt agctacgaca tgcactgggt ccgccaagca
                                                                      120
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactataca
ggctccgtga tgggccgatt caccatctcc agagacgctg ccaaaaaactc cttctatctt
gaaatgaaca gcctgagagt cggggacacg gctgtatatt actgtgcaag agagggaata
agaacaccct atgattattg gggccaggga accctggtca ccgtctcctc a
<210> SEQ ID NO 570
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 570
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 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
            100
                                105
Val Thr Val Ser Ser
<210> SEQ ID NO 571
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 571
gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc
                                                                       60
ctctcctgca gggccagtca gagtgttagc agcaatgtag cctggtacca gcagaaacct
                                                                      120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc
aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagtct
                                                                      240
gaagattttg cagtttatta ctgtcagcag tataataatt ggcctccatt cactttcggc
                                                                      300
cctgggacca aagtggatat caaa
<210> SEQ ID NO 572
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<211> LENGTH: 108

<212> TYPE: PRT

	Artificial Sequence									
<220> FEATURE: <223> OTHER INFORMATION: Synthetic										
<400> SEQUENCE: 572										
Glu Ile Val Met	Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro 5									
Glu Arg Ala Thr	Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Se 25 30	er Asn								
Val Ala Trp Tyr 35	Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Le	eu Ile								
Tyr Gly Ala Ser	Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Se	er Gly								
Ser Gly Ser Gly	Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gl	In Ser 80								
Glu Asp Phe Ala	Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pr 85 90 95									
Phe Thr Phe Gly	Pro Gly Thr Lys Val Asp Ile Lys 105									
<210> SEQ ID NO 573 <211> LENGTH: 351 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic										
<400> SEQUENCE: 573										
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc 60										
tectgtgcag cetet	tggatt caccctaagt agctacgaca tgcactgggt ccc	gccaagct 120								
acaggaaaag gtctggagtg ggtctcagct attggcagta ctggtgacac atactatcca 180										
ggetcegtga agggeegatt caccatetee agagaaaatg ceaagaacte ettgtatett 240										
caaatgaaca gcctg	gagagc cggggacacg gctgtgtatt actgtgcaag aga	agggaata 300								
agaacaccct atgattattg gggccaagga accetggtca ccgtctcctc a 351										
<210> SEQ ID NO 574 <211> LENGTH: 117 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic										
<400> SEQUENCE: 574										
Glu Val Gln Leu 1	Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gl 5 10 15									
Ser Leu Arg Leu 20	Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Se 25 30	er Tyr								
Asp Met His Trp 35	Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Tr 40 45	p Val								
Ser Ala Ile Gly 50	Ser Thr Gly Asp Thr Tyr Tyr Pro Gly Ser Va	il Lys								
Gly Arg Phe Thr 65	Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Ty 70 75	yr Leu 80								
Gln Met Asn Ser	Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cy 85 90 90									
Arg Glu Gly Ile	Arg Thr Pro Tyr Asp Tyr Trp Gly Gln Gly Tr 105 110	ır Leu								

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Val Thr Val Ser Ser 115 <210> SEQ ID NO 575 <211> LENGTH: 324 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 575 gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc ctctcctgca gggccagtca gagtgttagc agcaatttag cctggtacca gcagaaacct ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc aggttcagtg gcagtgggtc tgggacagag ttcactctca ccatcagcag cctgcagtct 240 gaaqattttq caqtttatta ctqtcaqcaq tataataatt qqcctccatt cactttcqqc 324 cctgggacca aagtggatat 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 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> SEOUENCE: 577 gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 120 tectgtgcag cetetggatt cacetttgat gattatgcca tgcactgggt ceggcaaget ccagggaagg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat geggaetetg tgaagggeeg atteaceate teeagagaea aegeeaagea eteeetgtat 240 ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgt aaaagaggtg 300 actacgggat actactacgg tatggacgtc tggggccaag ggaccacggt caccgtctcc

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tca
                                                                      363
<210> SEQ ID NO 578
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 578
Glu Val Gl<br/>n Leu Val Glu Ser Gly Gly Gly Leu Val Gl<br/>n Pro Gly Arg 1 \phantom{000} 5 \phantom{000} 10 \phantom{000} 15
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 \\ 0 \\ 0
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys His Ser Leu Tyr 65 70 75 75 80
Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Leu Tyr Tyr Cys 85 \phantom{0} 90 \phantom{0} 95
Gln Gly Thr Thr Val Thr Val Ser Ser
       115
<210> SEQ ID NO 579
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 579
ggattcacct ttgatgatta tgcc
                                                                          24
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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
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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 582
Ile Asn Trp Asn Ser Gly Ser Ile
<210> SEQ ID NO 583
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 583
gtaaaagagg tgactacggg atactactac ggtatggacg tc
<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
atcacttgct gggccagtca gggcattagc agttatttag cctggtatca gaaaaaacca
gggaaagccc ctaacctcct gatctatgat gcatccactt tgcaaagtgg ggtcccatca
aggttcagcg gcagtggatc tgggacagaa ttcactctca cactcagcag cctgcagcct
gaagattttg caacttatta ctgtcaacag cttaatattt acccattcac tttcggccct
gggaccaaag tggatatcaa a
<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
                5
                                    1.0
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
                           40
Tyr Asp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
                       55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Leu Ser Ser Leu Gln Pro
```

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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 587
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 587
cagggcatta gcagttat
                                                                       18
<210> SEQ ID NO 588
<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
<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
caacagctta 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
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1 <210> SEQ ID NO 593 <211> LENGTH: 363 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 593 gaagtgcagc tggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct ccagggaagg gcctggagtg ggtctcaggt attaattgga acagtggtag cataggctat geggaetetg tgaagggeeg atteaceate teeagagaea aegeeaagea eteeetgtat ctgcaaatga acagtctgag acctgaggac acggccttgt attactgtgt aaaagaggtg actacqqqat actactacqq tatqqacqtc tqqqqccaaq qqaccacqqt caccqtctcc tca 363 <210> SEQ ID NO 594 <211> LENGTH: 121 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 594 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg 1.0 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr 20 25 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 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 115 <210> SEQ ID NO 595 <211> LENGTH: 321 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 595 gacatccagt tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc 60 atcacttgct gggccagtca gggcattagc agttatttag cctggtatca gaaaaaacca gggaaagccc ctaacctcct gatctatgat gcatccactt tgcaaagtgg ggtcccatca 180 aggttcagcg gcagtggatc tgggacagaa ttcactctca cactcagcag cctgcagcct 240

gaagattttg caacttatta ctgtcaacag cttaatattt acccattcac tttcggccct

300

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gggaccaaag tggatatcaa a
                                                                      321
<210> SEQ ID NO 596
<211> LENGTH: 107
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 596
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
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
               55
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Leu Ser Ser Leu Gln Pro
                                        75
                  70
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ile Tyr Pro Phe
                85
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
tcctgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct
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
                                  10
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
    50
                     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 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
       115
<210> SEQ ID NO 599
<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 599
gacatccagt tgacccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc
                                                                      60
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
gggaccaaag tggatatcaa a
                                                                      321
<210> SEQ ID NO 600
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 600
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
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> SEQUENCE: 601
gaggtgcagt tgttggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt cacgtttagt agctatgcca tgaactgggt ccgccaggct
```

120

```
ccagggaagg ggctggattg ggtctcaggt atcagtggta atggtggtag cacctactac
gcagactccg tgaagggccg gttcaccatc tccagagaca tttccaagaa cacgctgtat
gtgcaaatgc acagcctgag agtcgaggac acggccgttt actactgtgc gaaagcccgt
tattacgatt tttggggggg gaatttcgat ctctggggcc gtggcaccca ggtcactgtc
tcctca
                                                                       366
<210> SEQ ID NO 602
<211> LENGTH: 122
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 602
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 1 5 10 15
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
Ser Gly Ile Ser Gly Asn Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 50 \phantom{0}
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
                                105
Gly Arg Gly Thr Gln Val Thr Val Ser Ser
<210> SEQ ID NO 603
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 603
ggattcacgt ttagtagcta tgcc
<210> SEQ ID NO 604
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 604
Gly Phe Thr Phe Ser Ser Tyr Ala
             5
<210> SEQ ID NO 605
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 605
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atcagtggta atggtggtag cacc
                                                                      24
<210> SEQ ID NO 606
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 606
Ile Ser Gly Asn Gly Gly Ser Thr
<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
                                                                      45
<210> SEQ ID NO 608
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 608
Ala Lys Ala Arg Tyr Tyr Asp Phe Trp Gly Gly Asn Phe Asp Leu
<210> SEQ ID NO 609
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 609
gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc
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
                                                                     324
<210> SEQ ID NO 610
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 610
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
                        10
             5
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ile Arg
                               25
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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
<210> SEQ ID NO 611
<211> LENGTH: 21
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 611
cagagtgtta gcatcaggta c
                                                                       21
<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
<210> SEQ ID NO 614
<211> LENGTH: 3
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 614
Gly Ala Ser
<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
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<210> SEQ ID NO 616

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<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
                5
<210> SEQ ID NO 617
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 617
gaggtgcagt tgttggagtc tgggggaggc ttggtacagc ctggggggtc cctgagactc
                                                                      60
tcctgtgcag cctctggatt cacgtttagt agctatgcca tgaactgggt ccgccaggct
                                                                     120
ccagggaagg ggctggattg ggtctcaggt atcagtggta atggtggtag cacctactac
                                                                      180
gcagactccg tgaagggccg gttcaccatc tccagagaca tttccaagaa cacgctgtat
                                                                      240
qtqcaaatqc acaqcctqaq aqtcqaqqac acqqccqttt actactqtqc qaaaqcccqt
                                                                      300
tattacgatt tttgggggg 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
                                    10
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
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
       115
                           120
<210> SEQ ID NO 619
<211> LENGTH: 324
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 619
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gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc
ctctcctgca gggccagtca gagtgttagc atcaggtact tagcctggta tcagcagaaa
                                                                     120
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca
gacaggttca gtgtcagtgt gtctgggaca gacttcactc tcaccatcac tagactggag
cctgaagatt ttgcagtcta ttactgtcag caatatggta gttcaccgct cactttcggc
ggagggacca aggtggagat caaa
                                                                     324
<210> SEQ ID NO 620
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 620
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
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
                            40
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
                        55
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
teetgtgeag eetetggatt eacgtttagt agetatgeea tgagetgggt eegeeagget
ccagggaagg ggctggagtg ggtctcagct atcagtggta atggtggtag cacctactac
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagcccgt
                                                                     300
tattacgatt tttggggggg gaatttcgat ctctggggcc gtggcaccct ggtcactgtc
                                                                     360
tectea
                                                                     366
<210> SEQ ID NO 622
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 622
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Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 1 5 10 15

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 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 Leu Gln Met Asn Ser Leu Arg Ala 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 623 <211> LENGTH: 324 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 623 gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60 ctctcctgca gggccagtca gagtgttagc atcaggtact tagcctggta ccagcagaaa cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 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 Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu 40 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 90 Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys <210> SEQ ID NO 625 <211> LENGTH: 381

<212> TYPE: DNA

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 625
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc
                                                                      60
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 ttattattcc tactacgtta tggacgtctg gggccaaggg
accacggtca ccgtctcctc a
<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 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
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 627
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 627
                                                                      24
qqttacacct ttaccaccta tqqt
<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
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Gly Tyr Thr Phe Thr Thr Tyr Gl 1 5

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<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
<400> SEQUENCE: 630
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
togagagato gittagtagt accacotgoo cittattati cotactacgi tatggacgio
                                                                       60
<210> SEQ ID NO 632
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 632
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Ser Tyr Tyr
                 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
gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc
                                                                       60
atotootgoa ggtotagtoa aagootogta tacagtgatg gaaacacota ottgaattgg
                                                                      120
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 634
<211> LENGTH: 112
<212> TYPE: PRT
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<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
                                   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
                                105
<210> SEQ ID NO 635
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 635
                                                                       33
caaagcctcg tatacagtga tggaaacacc tac
<210> SEQ ID NO 636
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 636
Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr
<210> SEQ ID NO 637
<211> LENGTH: 9
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 637
aaqqtttct
                                                                        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
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<210> SEQ ID NO 639

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<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 639
atgcaaggta cacactggcc gtacact
                                                                      27
<210> SEQ ID NO 640
<211> LENGTH: 9
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 640
Met Gln Gly Thr His Trp Pro Tyr Thr
<210> SEQ ID NO 641
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 641
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc
                                                                      60
teetgeaagg ettetggtta cacetttaec acetatggta teagttgggt acgacaggee
                                                                     120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
                                                                     180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
                                                                     300
ttagtagtac cacctgccct ttattattcc tactacgtta tggacgtctg gggccaaggg
accaeggica eegieteete a
                                                                     381
<210> SEQ ID NO 642
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 642
Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Asn Pro Gly Ala
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
                       55
Gln Asp Arg Val Ala Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
                   7.0
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
                               105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
```

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115 120 125 <210> SEQ ID NO 643 <211> LENGTH: 336 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 643 gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac tetggggtee cagacagatt cageggeagt gggteaggea etgattteae aetgaaaate agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg tacacttttg gccaggggac caagctggag atcaaa 336 <210> SEQ ID NO 644 <211> LENGTH: 112 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 644 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 25 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 <210> SEQ ID NO 645 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 645 caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60 teetgeaagg ettetggtta eacetttace acetatggta teagetgggt gegacaggee 120 cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat 180 gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240 300 atggagetga ggageetgag atetgaegae aeggeegtgt attactgtte gagagategt ttagtagtac cacctgccct ttattattcc tactacgtta tggacgtctg ggggcaaggg 360 accacggtca ccgtctcctc a 381

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<210> SEQ ID NO 646
<211> LENGTH: 127
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 646
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
                                    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 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 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 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
atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
tacacttttg gccaggggac caagctggag atcaaa
<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
                                    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 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
```

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```
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
                85
                                    90
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
                              105
<210> SEQ ID NO 649
<211> LENGTH: 381
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 649
caggttcagc tggtgcagtc tggacctgag gtgaagaacc ctggggcctc agtgaaggtc
teetgeaagg ettetggtta cacetttace acetatggta teagttgggt acgacaggee
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
                                                                     240
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
                                                                     300
ttaqtaqtac cacctqccct taattattac tactacqtta tqqacqtctq qqqccaaqqq
                                                                    360
accacggtca ccgtctcctc a
                                                                     381
<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 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
                              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
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ggttacacct ttaccaccta tggt

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<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
<210> SEQ ID NO 654
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 654
Ile Ser Gly Tyr Asn Gly Lys Thr
                 5
<210> SEQ ID NO 655
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 655
tcgagagatc gtttagtagt accacctgcc cttaattatt actactacgt tatggacgtc
<210> SEQ ID NO 656
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 656
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Asn Tyr Tyr Tyr Tyr
Val Met Asp Val
            20
<210> SEQ ID NO 657
<211> LENGTH: 336
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 657
gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc
                                                                        60
atotoctgca ggtotagtca aagootogta tacagtgatg gaaacacota ottgaattgg
```

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tttcagcaga ggccaggtca atctccaagg cgcctaattt ataaggtttc taaccgggac
tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc
                                                                       240
agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg
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
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 35 40 45
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
                                    90
Thr His Trp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100
                                105
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<212> TYPE: DNA
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Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr Tyr
<210> SEQ ID NO 661
<211> LENGTH: 9
<212> TYPE: DNA
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<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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                                                                         9
<210> SEQ ID NO 662
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<211> LENGTH: 3

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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Lys Val Ser
<210> SEQ ID NO 663
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<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
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atgcaaggta cacactggcc gtacact
<210> SEQ ID NO 664
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 664
Met Gln Gly Thr His Trp Pro Tyr Thr
<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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cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg gggccaaggg
accacggtca ccgtctcctc a
<210> SEQ ID NO 666
<211> LENGTH: 127
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 666
Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Asn Pro Gly Ala
                                    1.0
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
        35
                            40
Gly Trp Ile Ser Gly Tyr Asn Gly Lys Thr Asn Asp Ala Gln Lys Phe
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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 Asn Tyr Tyr Tyr Tyr Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <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 ateteetgea ggtetagtea aageetegta tacagtgatg gaaacaeeta ettgaattgg 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 336 <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 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 105 100 110 <210> SEQ ID NO 669 <211> LENGTH: 381 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 669

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teetgeaagg ettetggtta eacetttace acetatggta teagetgggt gegacaggee
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat
                                                                     180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac
atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt
ttagtagtac cacctgccct taattattac tactacgtta tggacgtctg ggggcaaggg
accaeggica eegieteete a
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 670
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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
                           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
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
                               105
Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
       115
                           120
                                               125
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 671
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atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg
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
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<211> LENGTH: 112
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEOUENCE: 672
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Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly

												COII	C III.	aca		
1				5					10					15		
Gln	Pro	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25	Ser	Gln	Ser	Leu	Val 30	Tyr	Ser	
Asp	Gly	Asn 35	Thr	Tyr	Leu	Asn	Trp 40	Phe	Gln	Gln	Arg	Pro 45	Gly	Gln	Ser	
Pro	Arg 50	Arg	Leu	Ile	Tyr	Lys 55	Val	Ser	Asn	Arg	Asp 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	CÀa	Met	Gln 95	Gly	
Thr	His	Trp	Pro 100	Tyr	Thr	Phe	Gly	Gln 105	Gly	Thr	Lys	Leu	Glu 110	Ile	Lys	
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tcct	gcaa	agg o	ettet	ggtt	ta ca	acctt	taco	c acc	tato	ggta	tcaç	gttg	ggt a	acgao	caggcc	120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat 180																
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac 240										240						
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt 300																
ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg gggccaaggg 36									360							
accaeggtea ecgteteete a 381																
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1				5					10					15 Thr		
		-	20		-	-		25	_	-			30		_	
_		35	_				40		_		-	45		Trp		
Gly	Trp 50	Ile	Ser	Gly	Tyr	Asn 55	Gly	Lys	Thr	Asn	Asp 60	Ala	Gln	Lys	Phe	
Gln 65	Asp	Arg	Val	Ala	Met 70	Thr	Thr	Asp	Thr	Ser 75	Thr	Ser	Thr	Ala	Tyr 80	
Met	Glu	Leu	Arg	Ser 85	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Ile	Tyr	Tyr 95	CÀa	
Ser	Arg	Asp	Arg 100	Leu	Val	Val	Pro	Pro 105	Ala	Leu	Tyr	Tyr	Tyr 110	Tyr	Tyr	
Val	Met	Asp 115	Val	Trp	Gly	Gln	Gly 120	Thr	Thr	Val	Thr	Val 125	Ser	Ser		

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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 676
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<210> SEQ ID NO 677
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
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<223 > OTHER INFORMATION: Synthetic
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<210> SEQ ID NO 678
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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Ile Ser Gly Tyr Asn Gly Lys Thr
<210> SEQ ID NO 679
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223 > OTHER INFORMATION: Synthetic
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<210> SEQ ID NO 680
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 680
Ser Arg Asp Arg Leu Val Val Pro Pro Ala Leu Tyr Tyr Tyr Tyr Tyr
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Val Met Asp Val
<210> SEQ ID NO 681
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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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 682
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 682
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
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
<210> SEQ ID NO 683
<211> LENGTH: 33
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 683
                                                                       33
caaageeteg tatacagtga tggaaacace tac
<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
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<210> SEQ ID NO 685
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<211> LENGTH: 9

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<212> TYPE: DNA
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<223 > OTHER INFORMATION: Synthetic
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<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
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<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 687
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<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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                                                                         120
cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaacgat
                                                                         180
gcacagaagt tccaggacag agtcgccatg accacagaca catccacgag cacagcctac
                                                                         240
atggagetga ggageetgag atetgaegae aeggeeattt attaetgtte gagagategt
                                                                         300
ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg gggccaaggg
accacggtca ccgtctcctc a
                                                                         381
<210> SEQ ID NO 690
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<212> TYPE: PRT
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<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 690 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 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 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 <400> SEQUENCE: 691 gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 6.0 atctcctgca ggtctagtca aagcctcgta tacagtgatg gaaacaccta cttgaattgg 120 tttcagcaga ggccaggtca 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 692 <211> LENGTH: 112 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 692 Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly 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 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 70 75 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 105

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<210> SEQ ID NO 693 <211> LENGTH: 381 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 693 caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctgggggcctc agtgaaggtc tcctgcaagg cttctggtta cacctttacc acctatggta tcagctgggt gcgacaggcc cctggacaag ggcttgagtg gatgggatgg atcagcggtt acaatggtaa aacaaactat gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac atggagctga ggagcctgag atctgacgac acggccgtgt attactgttc gagagatcgt ttagtagtac cacctgccct ttattattac tactacgtta tggacgtctg ggggcaaggg accaeggica eegicteete a 381 <210> SEQ ID NO 694 <211> LENGTH: 127 <212> TYPE: PRT <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEOUENCE: 694 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 Tyr 25 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 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 Val Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser <210> SEQ ID NO 695 <211> LENGTH: 336 <212> TYPE: DNA <213 > ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEOUENCE: 695 gatgttgtga tgactcagtc tccactctcc ctgcccgtca cccttggaca gccggcctcc 60 atctcctqca qqtctaqtca aaqcctcqta tacaqtqatq qaaacaccta cttqaattqq 120 tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240 agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggccg 300 tacacttttg gccaggggac caagctggag atcaaa 336

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<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 696
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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 697
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 697
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ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat
gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat
ctacatatga acagceteag ageegaegae aeggeegtgt attactgtge gagagateag
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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
                                   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
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

```
65
Leu His Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85
                                    90
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 Ala Ser
                            120
<210> SEQ ID NO 699
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<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 699
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<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEOUENCE: 700
Gly Phe Thr Phe Ser Asp His Tyr
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<210> SEQ ID NO 701
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 701
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                                                                        24
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<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
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gcgagagatc agggatatat tggctacgac tcgtattatt actattccta cggtatggac
                                                                        60
gtc
<210> SEQ ID NO 704
<211> LENGTH: 21
<212> TYPE: PRT
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<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 704
Ala Arg Asp Gln Gly Tyr Ile Gly Tyr Asp Ser Tyr Tyr Tyr Tyr Ser
                                    10
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
aaaattqtqt tqacqcaqtc tccaqqcacc ctqcctttqt ttccaqqqqa aaqaqccacc
ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
totggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca
                                                                       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:
<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
                                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
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
           100
<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
                                                                        2.1
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<210> SEQ ID NO 708

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<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
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 711
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<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> SEQ ID NO 713
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 713
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teetgtgeag cetetggatt cacetteagt gaccactaca tgagetggat cegecagget
ccagggaagg ggctggagtg gatttcatac attagtaatg atggtggtac caaatactat
                                                                         180
gtggactctg tggagggccg attcatcatt tccagggaca acgccaagaa ctcattgtat
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ctacatatga acagceteag ageegaegae aeggeegtgt attactgtge gagagateag
ggatatattg gctacgactc gtattattac tattcctacg gtatggacgt ctggggccaa
                                                                     360
gggaccacgg tcaccgtctc ctca
                                                                     384
<210> SEQ ID NO 714
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 714
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
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
Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
       115
                           120
                                                125
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<211> LENGTH: 321
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 715
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ctctcctgta gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa
totggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca
gacaggttca gtggcagtgg gtctgggacc gacttcactc tcaccatcag cggactggag
cctgaagatt ttgaagtgta ttattgtcaa gtatatggta actcactcac tttcggcgga
                                                                     300
gggaccaagg tggagatcaa a
                                                                     321
<210> SEQ ID NO 716
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 716
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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Asn Lys
                                25
Phe Leu Ala Trp Tyr Gln Gln Lys Ser Gly Gln Ala Pro Arg Leu Leu
```

				COIICI	iraca	
35		40		45		
Ile Tyr Gly Ala 50	Ser Ser Arg 55	Ala Thr (Gly Ile	Pro Asp Ar 60	g Phe Se	er
Gly Ser Gly Ser 65	Gly Thr Asp	Phe Thr l	Leu Thr 75	Ile Ser Gl	y Leu G 80	
Pro Glu Asp Phe	Glu Val Tyr 85		Gln Val	Tyr Gly As	n Ser Le 95	eu
Thr Phe Gly Gly	Gly Thr Lys	Val Glu 1	Ile Lys			
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teetgtgeag eete	tggatt cacct	tcagt gac	cactaca	tgagctggat	ccgcca	ggct 120
ccagggaagg ggct	ggagtg ggttt	catac atta	agtaatg	atggtggtac	caaata	ctac 180
gcagactctg tgaa	gggccg attca	.ccatc tcca	agggaca	acgccaagaa	ctcact	gtat 240
ctgcaaatga acag	cctgag agccg	aggac acg	gccgtgt	attactgtgc	gagagat	cag 300
ggatatattg gcta	cgactc gtatt	attac tati	tcctacg	gtatggacgt	ctgggg	gcaa 360
gggaccacgg tcac	cgtctc ctca					384
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Gln Val Gln Leu 1	Val Glu Ser 5		Gly Leu 10	Val Lys Pr	o Gly G	ly
Ser Leu Arg Leu 20	Ser Cys Ala	. Ala Ser (Gly Phe	Thr Phe Se	r Asp H:	is
Tyr Met Ser Trp 35	Ile Arg Gln	Ala Pro (Gly Lys	Gly Leu Gl 45	u Trp Va	al
Ser Tyr Ile Ser 50	Asn Asp Gly	Gly Thr I	Lys Tyr	Tyr Ala As	p Ser Va	al
Lys Gly Arg Phe	Thr Ile Ser	Arg Asp A	Asn Ala 75	Lys Asn Se	r Leu Ty 80	
Leu Gln Met Asn	Ser Leu Arg 85		Asp Thr 90	Ala Val Ty	r Tyr Cy 95	\a
Ala Arg Asp Gln		Gly Tyr 1	Asp Ser	Tyr Tyr Ty		er
Tyr Gly Met Asp 115	Val Trp Gly	Gln Gly 1	Thr Thr	Val Thr Va 125	l Ser Se	∍r
<pre><210> SEQ ID NO <211> LENGTH: 3 <212> TYPE: DNA <213> ORGANISM: <220> FEATURE: <223> OTHER INF</pre>	21 Artificial					

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<400> SEQUENCE: 719 gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60 ctctcctgca gggccagtca gagtgttaac aacaaattct tagcctggta ccagcagaaa 120 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240 cctgaagatt ttgcagtgta ttactgtcaa gtatatggta actcactcac tttcggcgga 321 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 40 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 100 <210> SEQ ID NO 721 <211> LENGTH: 378 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic <400> SEQUENCE: 721 caaattctgc tggtgcaatc tggacctgag gtgaaggagc ctggggcctc agtgaaggtc teetgeaagg ettetggtta cacetttace aactaegeta teagetgggt gegacaggte 120 cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat 180 gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac 240 atggagetga ggageetgag atetgaegae aeggeeatgt attactgtge gagagggggt 300 gtagtegtge cagttgetee ceaettetae aaeggtatgg aegtetgggg ceaagggace 360 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

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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 85 \ 90 \ 95
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 723
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 723
ggttacacct ttaccaacta cgct
                                                                        24
<210> SEQ ID NO 724
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 724
Gly Tyr Thr Phe Thr Asn Tyr Ala
                5
<210> SEQ ID NO 725
<211> LENGTH: 24
<212> TYPE: DNA
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 725
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
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<212> TYPE: DNA

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<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 727
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<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
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                                                                       60
atotoctgca ggtotagtca gagootoctg 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 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 35 40 45
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
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<210> SEQ ID NO 731 <211> LENGTH: 33

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<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
<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
<210> SEQ ID NO 735
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 735
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atgcaagctc ttcaaactcc gtggacg
<210> SEQ ID NO 736
<211> LENGTH: 9
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 736
Met Gln Ala Leu Gln Thr Pro Trp Thr
1
<210> SEQ ID NO 737
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 737 caggttcagc tggtgcagtc tggacctgag gtgaaggagc ctgggggcctc agtgaaggtc 60 teetgeaagg ettetggtta cacetttace aactaegeta teagetgggt gegacaggte cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat gcacatgaag tccagggcag agtcaccatg accacagaca catccacgac cacagcctac atggagetga ggageetgag atetgaegae aeggeeatgt attactgtge gagagggggt gtagtegtge cagttgetee ceaettetae aaeggtatgg aegtetgggg ceaagggace 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 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 70 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 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 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:

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<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 Asn Glu Tyr Asn Tyr Leu Asp Trp Tyr Leu Lys Lys Pro Gly Gln Ser 40 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> SEQUENCE: 741 caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60 teetgeaagg ettetggtta eacetttace aactaegeta teagetgggt gegacaggee 120 cctggacaag ggcttgagtg gatgggatgg gtcagcgctt acaatggtca cacaaactat gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac atggagetga ggageetgag atetgaegae aeggeegtgt attactgtge gagagggggt gtagtcgtgc cagttgctcc ccacttctac aacggtatgg acgtctgggg gcaagggacc acggtcaccg tctcctca 378 <210> SEQ ID NO 742 <211> LENGTH: 126 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223 > OTHER INFORMATION: Synthetic <400> SEQUENCE: 742 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 55 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 100 105 110

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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
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atctcctgca ggtctagtca gagcctcctg catattaatg aatacaacta tttggattgg
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct tcaaactccg
tggacgttcg gccaagggac caaggtggaa atcaaa
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<210> SEQ ID NO 744
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<400> SEQUENCE: 744
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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
<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
<210> SEQ ID NO 746
<211> LENGTH: 8
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1) ... (8)
<223> OTHER INFORMATION: Xaa - Any amino acid
<400> SEQUENCE: 746
Xaa Xaa Xaa Xaa Xaa Xaa Xaa
<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
5
                                 10
Xaa Xaa Xaa Xaa
<210> SEQ ID NO 748
<211> LENGTH: 12
<212> TYPE: PRT
<213 > ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)...(12)
<223> OTHER INFORMATION: Xaa = Any amino acid
<400> SEQUENCE: 748
<210> SEQ ID NO 749
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1) ... (3)
<223> OTHER INFORMATION: Xaa = Any amino acid
<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
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 1 5
<210> SEQ ID NO 751 <211> LENGTH: 330 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 751
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Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr 20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser 35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser 50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr 65 70 75 80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys 85 90 95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys 100 105 110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro 115 120 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys 130 135 140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp 145 150 155 160
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu 165 170 175
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu 180 185 190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn 195 200 205
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly 210 215 220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu 225 230 240
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr 245 250 250
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn 260 265 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe 275 280 280
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn 290 295 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr 305 310 315 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 325 330

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<211> LENGTH: 327
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<400> SEQUENCE: 752
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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 Lys Thr
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
                              105
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                          120
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
                                    155
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                                 170
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                               185
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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Leu Ser Leu Ser Leu Gly Lys
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<210> SEQ ID NO 753
<211> LENGTH: 327
<212> TYPE: PRT
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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic

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ctqqtqctaq ccttqcqttc cqaqqaqqac qqcctqqccq aaqcacccqa qcacqqaacc

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gtgctgaagg	aggagaccca	cctctcgcag	tcagagcgca	ctgcccgccg	cctgcaggcc	300	
caggetgeee	gccggggata	cctcaccaag	atcctgcatg	tcttccatgg	ccttcttcct	360	
ggcttcctgg	tgaagatgag	tggcgacctg	ctggagctgg	ccttgaagtt	gccccatgtc	420	
gactacatcg	aggaggactc	ctctgtcttt	gcccagagca	tcccgtggaa	cctggagcgg	480	
attacccctc	cacggtaccg	ggcggatgaa	taccageeee	ccgacggagg	cagcctggtg	540	
gaggtgtatc	tcctagacac	cagcatacag	agtgaccacc	gggaaatcga	gggcagggtc	600	
atggtcaccg	acttcgagaa	tgtgcccgag	gaggacggga	cccgcttcca	cagacaggcc	660	
agcaagtgtg	acagtcatgg	cacccacctg	gcaggggtgg	tcagcggccg	ggatgccggc	720	
gtggccaagg	gtgccagcat	gcgcagcctg	cgcgtgctca	actgccaagg	gaagggcacg	780	
gttagcggca	ccctcatagg	cctggagttt	attcggaaaa	gccagctggt	ccagcctgtg	840	
gggccactgg	tggtgctgct	gcccctggcg	ggtgggtaca	gccgcgtcct	caacgccgcc	900	
tgccagcgcc	tggcgagggc	tggggtcgtg	ctggtcaccg	ctgccggcaa	cttccgggac	960	
gatgcctgcc	tctactcccc	agcctcagct	cccgaggtca	tcacagttgg	ggccaccaat	1020	
gcccaggacc	agccggtgac	cctggggact	ttggggacca	actttggccg	ctgtgtggac	1080	
ctctttgccc	caggggagga	catcattggt	gcctccagcg	actgcagcac	ctgctttgtg	1140	
tcacagagtg	ggacatcaca	ggctgctgcc	cacgtggctg	gcattgcagc	catgatgctg	1200	
tctgccgagc	cggagctcac	cctggccgag	ttgaggcaga	gactgatcca	cttctctgcc	1260	
aaagatgtca	tcaatgaggc	ctggttccct	gaggaccagc	gggtactgac	ccccaacctg	1320	
gtggccgccc	tgccccccag	cacccatggg	gcaggttggc	agctgttttg	caggactgtg	1380	
tggtcagcac	actcggggcc	tacacggatg	gccacagcca	tegecegetg	cgccccagat	1440	
gaggagctgc	tgagctgctc	cagtttctcc	aggagtggga	agcggcgggg	cgagcgcatg	1500	
gaggcccaag	ggggcaagct	ggtctgccgg	gcccacaacg	cttttggggg	tgagggtgtc	1560	
tacgccattg	ccaggtgctg	cctgctaccc	caggccaact	gcagcgtcca	cacageteca	1620	
ccagctgagg	ccagcatggg	gacccgtgtc	cactgccacc	aacagggcca	cgtcctcaca	1680	
ggctgcagct	cccactggga	ggtggaggac	cttggcaccc	acaagccgcc	tgtgctgagg	1740	
ccacgaggtc	agcccaacca	gtgcgtgggc	cacagggagg	ccagcatcca	cgcttcctgc	1800	
tgccatgccc	caggtctgga	atgcaaagtc	aaggagcatg	gaatcccggc	ccctcaggag	1860	
caggtgaccg	tggcctgcga	ggagggctgg	accctgactg	gctgcagtgc	cctccctggg	1920	
acctcccacg	teetggggge	ctacgccgta	gacaacacgt	gtgtagtcag	gagccgggac	1980	
gtcagcacta	caggcagcac	cagcgaagag	gccgtgacag	ccgttgccat	ctgctgccgg	2040	
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<210> SEQ ID NO 755
<211> LENGTH: 692
<212> TYPE: PRT
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n Glu 20

Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu

<213 > ORGANISM: Homo sapiens

<400> SEQUENCE: 755

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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	Leu	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	Gly	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	Pro	Arg 165	Tyr	Arg	Ala	Asp	Glu 170	Tyr	Gln	Pro	Pro	Asp 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	Asn	Val
Pro	Glu 210	Glu	Asp	Gly	Thr	Arg 215	Phe	His	Arg	Gln	Ala 220	Ser	ГÀа	Cys	Asp
Ser 225	His	Gly	Thr	His	Leu 230	Ala	Gly	Val	Val	Ser 235	Gly	Arg	Asp	Ala	Gly 240
Val	Ala	ГÀа	Gly	Ala 245	Ser	Met	Arg	Ser	Leu 250	Arg	Val	Leu	Asn	Сув 255	Gln
Gly	Lys	Gly	Thr 260	Val	Ser	Gly	Thr	Leu 265	Ile	Gly	Leu	Glu	Phe 270	Ile	Arg
ГÀа	Ser	Gln 275	Leu	Val	Gln	Pro	Val 280	Gly	Pro	Leu	Val	Val 285	Leu	Leu	Pro
Leu	Ala 290	Gly	Gly	Tyr	Ser	Arg 295	Val	Leu	Asn	Ala	Ala 300	CÀa	Gln	Arg	Leu
Ala 305	Arg	Ala	Gly	Val	Val 310	Leu	Val	Thr	Ala	Ala 315	Gly	Asn	Phe	Arg	Asp 320
Asp	Ala	Càa	Leu	Tyr 325	Ser	Pro	Ala	Ser	Ala 330	Pro	Glu	Val	Ile	Thr 335	Val
Gly	Ala	Thr	Asn 340	Ala	Gln	Asp	Gln	Pro 345	Val	Thr	Leu	Gly	Thr 350	Leu	Gly
Thr	Asn	Phe 355	Gly	Arg	Cys	Val	Asp 360	Leu	Phe	Ala	Pro	Gly 365	Glu	Asp	Ile
Ile	Gly 370	Ala	Ser	Ser	Asp	Cys 375	Ser	Thr	Cys	Phe	Val 380	Ser	Gln	Ser	Gly
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	Gly 450	Ala	Gly	Trp	Gln	Leu 455	Phe	Сла	Arg	Thr	Val 460	Trp	Ser	Ala	His

Ser Gly Pro Thr Arg Met Ala Thr Ala Ile Ala Arg Cys Ala Pro Asp

470

Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg Gly Glu Arg Met Glu Ala Gln Gly Gly Lys Leu Val Cys Arg Ala His Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu Leu Pro Gln Ala Asn Cys Ser Val His Thr Ala Pro Pro Ala Glu Ala 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 Thr Val 615 Ala Cys Glu Glu Gly Trp Thr Leu Thr Gly Cys Ser Ala Leu Pro Gly 630 635 Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val 650 Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Glu Glu Ala Val 665 Thr Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Ala Gln Ala Ser 680 Gln Glu Leu Gln 690 <210> SEQ ID NO 756 <211> LENGTH: 692 <212> TYPE: PRT <213> ORGANISM: Macaca mulata <400> SEQUENCE: 756 Met Gly Thr Val Ser Ser Arg Arg Ser Trp Trp Pro Leu Pro Leu Pro Leu Leu Leu Leu Leu Gly Pro Ala Gly Ala Arg Ala Gln Glu Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu Glu Asp Gly Leu Ala Asp Ala Pro Glu His Gly Ala Thr Ala Thr Phe His Arg Cys Ala Lys Asp Pro Trp Arg Leu Pro Gly Thr Tyr Val Val Val Leu Lys Glu Glu Thr His Arg Ser Gln Ser Glu Arg Thr Ala Arg 90 Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu His Val Phe His His Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val Asp Tyr Ile Glu

_	130					135					140				
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	Сув	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
Gly	Lys	Gly	Thr 260	Val	Ser	Gly	Thr	Leu 265	Ile	Gly	Leu	Glu	Phe 270	Ile	Arg
Lys	Ser	Gln 275	Leu	Val	Gln	Pro	Val 280	Gly	Pro	Leu	Val	Val 285	Leu	Leu	Pro
Leu	Ala 290	Gly	Gly	Tyr	Ser	Arg 295	Val	Phe	Asn	Ala	Ala 300	Càa	Gln	Arg	Leu
Ala 305	Arg	Ala	Gly	Val	Val 310	Leu	Val	Thr	Ala	Ala 315	Gly	Asn	Phe	Arg	Asp 320
Asp	Ala	Cys	Leu	Tyr 325	Ser	Pro	Ala	Ser	Ala 330	Pro	Glu	Val	Ile	Thr 335	Val
Gly	Ala	Thr	Asn 340	Ala	Gln	Asp	Gln	Pro 345	Val	Thr	Leu	Gly	Thr 350	Leu	Gly
Thr	Asn	Phe 355	Gly	Arg	CAa	Val	360 38p	Leu	Phe	Ala	Pro	Gly 365	Glu	Asp	Ile
Ile	Gly 370	Ala	Ser	Ser	Asp	Сув 375	Ser	Thr	Сув	Phe	Val 380	Ser	Arg	Ser	Gly
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 450	Ala	Gly	Trp	Gln	Leu 455	Phe	CAa	Arg	Thr	Val 460	Trp	Ser	Ala	His
Ser 465	Gly	Pro	Thr	Arg	Met 470	Ala	Thr	Ala	Val	Ala 475	Arg	CAa	Ala	Gln	Asp 480
Glu	Glu	Leu	Leu	Ser 485	Cys	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	СЛа	Arg 510	Ala	His
Asn	Ala	Phe 515	Gly	Gly	Glu	Gly	Val 520	Tyr	Ala	Ile	Ala	Arg 525	Cys	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	Сув	His	Gln	Gln 555	Gly	His	Val	Leu	Thr 560

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 Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys 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 Pro Leu Pro Gly 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 Lys Glu Ala Val Ala Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Val Gln Ala Ser Gln Glu Leu Gln 690 <210> SEO ID NO 757 <211> LENGTH: 694 <212> TYPE: PRT <213 > ORGANISM: Mus muscular <400> SEOUENCE: 757 Met Gly Thr His Cys Ser Ala Trp Leu Arg Trp Pro Leu Leu Pro Leu Leu Pro Pro Leu Leu Leu Leu Leu Leu Leu Cys Pro Thr Gly Ala 25 Gly Ala Gln Asp Glu Asp Gly Asp Tyr Glu Glu Leu Met Leu Ala Leu Pro Ser Gln Glu Asp Gly Leu Ala Asp Glu Ala Ala His Val Ala Thr Ala Thr Phe Arg Arg Cys Ser Lys Glu Ala Trp Arg Leu Pro Gly Thr Tyr Ile Val Val Leu Met Glu Glu Thr Gln Arg Leu Gln Ile Glu Gln Thr Ala His Arg Leu Gln Thr Arg Ala Ala Arg Arg Gly Tyr Val Ile Lys Val Leu His Ile Phe Tyr Asp Leu Phe Pro Gly Phe Leu Val Lys Met Ser Ser Asp Leu Leu Gly Leu Ala Leu Lys Leu Pro His Val Glu 135 Tyr Ile Glu Glu Asp Ser Phe Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg Ile Ile Pro Ala Trp His Gln Thr Glu Glu Asp Arg Ser Pro Asp Gly Ser Ser Gln Val Glu Val Tyr Leu Leu Asp Thr Ser Ile 185 Gln Gly Ala His Arg Glu Ile Glu Gly Arg Val Thr Ile Thr Asp Phe Asn Ser Val Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg

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22	5				230					235					240
As]	o Ala	Gly	Val	Ala 245	Lys	Gly	Thr	Ser	Leu 250	His	Ser	Leu	Arg	Val 255	Leu
Ası	n Cys	Gln	Gly 260	Lys	Gly	Thr	Val	Ser 265	Gly	Thr	Leu	Ile	Gly 270	Leu	Glu
Ph	e Ile	Arg 275	Lys	Ser	Gln	Leu	Ile 280	Gln	Pro	Ser	Gly	Pro 285	Leu	Val	Val
Le	ı Leu 290	Pro	Leu	Ala	Gly	Gly 295	Tyr	Ser	Arg	Ile	Leu 300	Asn	Ala	Ala	СЛа
Ar	g His 5	Leu	Ala	Arg	Thr 310	Gly	Val	Val	Leu	Val 315	Ala	Ala	Ala	Gly	Asn 320
Ph	e Arg	Asp	Asp	Ala 325	Cys	Leu	Tyr	Ser	Pro 330	Ala	Ser	Ala	Pro	Glu 335	Val
Il	e Thr	Val	Gly 340	Ala	Thr	Asn	Ala	Gln 345	Asp	Gln	Pro	Val	Thr 350	Leu	Gly
Th	r Leu	Gly 355	Thr	Asn	Phe	Gly	Arg 360	Cys	Val	Asp	Leu	Phe 365	Ala	Pro	Gly
Ly	370	Ile	Ile	Gly	Ala	Ser 375	Ser	Asp	Càa	Ser	Thr 380	Cys	Phe	Met	Ser
G1: 38:	n Ser	Gly	Thr	Ser	Gln 390	Ala	Ala	Ala	His	Val 395	Ala	Gly	Ile	Val	Ala 400
Ar	g Met	Leu	Ser	Arg 405	Glu	Pro	Thr	Leu	Thr 410	Leu	Ala	Glu	Leu	Arg 415	Gln
Ar	g Leu	Ile	His 420	Phe	Ser	Thr	Lys	Asp 425	Val	Ile	Asn	Met	Ala 430	Trp	Phe
Pr	o Glu	Asp 435	Gln	Gln	Val	Leu	Thr 440	Pro	Asn	Leu	Val	Ala 445	Thr	Leu	Pro
Pr	Ser 450	Thr	His	Glu	Thr	Gly 455	Gly	Gln	Leu	Leu	Cys 460	Arg	Thr	Val	Trp
Se:	r Ala 5	His	Ser	Gly	Pro 470	Thr	Arg	Thr	Ala	Thr 475	Ala	Thr	Ala	Arg	Cys 480
Al.	a Pro	Glu	Glu	Glu 485	Leu	Leu	Ser	Cys	Ser 490	Ser	Phe	Ser	Arg	Ser 495	Gly
Ar	g Arg	Arg	Gly 500	Asp	Trp	Ile	Glu	Ala 505	Ile	Gly	Gly	Gln	Gln 510	Val	Cys
Ly	s Ala	Leu 515	Asn	Ala	Phe	Gly	Gly 520	Glu	Gly	Val	Tyr	Ala 525	Val	Ala	Arg
СУ	в Сув 530	Leu	Val	Pro	Arg	Ala 535	Asn	Cha	Ser	Ile	His 540	Asn	Thr	Pro	Ala
A1.	a Arg	Ala	Gly	Leu	Glu 550	Thr	His	Val	His	Суя 555	His	Gln	Lys	Asp	His 560
Va	l Leu	Thr	Gly	Суз 565	Ser	Phe	His	Trp	Glu 570	Val	Glu	Asp	Leu	Ser 575	Val
Ar	g Arg	Gln	Pro 580	Ala	Leu	Arg	Ser	Arg 585	Arg	Gln	Pro	Gly	Gln 590	CÀa	Val
Gl	y His	Gln 595	Ala	Ala	Ser	Val	Tyr 600	Ala	Ser	CAa	CAa	His 605	Ala	Pro	Gly
Le	ı Glu 610	Cys	Lys	Ile	Lys	Glu 615	His	Gly	Ile	Ser	Gly 620	Pro	Ser	Glu	Gln
Va 62	l Thr	Val	Ala	Cys	Glu 630	Ala	Gly	Trp	Thr	Leu 635	Thr	Gly	СЛа	Asn	Val 640
Le	ı Pro	Gly	Ala	Ser 645	Leu	Thr	Leu	Gly	Ala 650	Tyr	Ser	Val	Asp	Asn 655	Leu

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				325					330					335	
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 365	Gly	Leu	Ala
Val	Asp 370	Trp	Ile	His	Ser	Asn 375	Ile	Tyr	Trp	Thr	Asp	Ser	Val	Leu	Gly
Thr 385	Val	Ser	Val	Ala	Asp 390	Thr	Lys	Gly	Val	Tys	Arg	Lys	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	ГЛа	Leu 470	His	Ser	Ile	Ser	Ser 475	Ile	Asp	Val	Asn	Gly 480
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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
Asn 545	Leu	Thr	Gln	Pro	Arg 550	Gly	Val	Asn	Trp	Сув 555	Glu	Arg	Thr	Thr	Leu 560
Ser	Asn	Gly	Gly	565 565	Gln	Tyr	Leu	CAa	Leu 570	Pro	Ala	Pro	Gln	Ile 575	Asn
Pro	His	Ser	Pro 580	Lys	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
Pro	Gly	Ala	Thr	Pro 645	Gly	Leu	Thr	Thr	Val 650	Glu	Ile	Val			
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					ر sa]	pien	o .								
			NCE:		т	C	т	41	C	mi	7A 7 -	D1	77-7	т	րե -
Met 1	GLU	Arg	arg	Ala 5	тrр	ser	ьeu	GIN	Cys 10	Tnr	Ala	Рne	Val	Leu 15	rne
Cys	Ala	Trp	Cys 20	Ala	Leu	Asn	Ser	Ala 25	Lys	Ala	Lys	Arg	Gln 30	Phe	Val

20 25 30

Asn Glu Trp Ala Ala Glu Ile Pro Gly Gly Pro Glu Ala Ala Ser Ala 35 40 45

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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
Asp	His	Asp 195	Pro	Phe	Pro	Arg	Tyr 200	Asp	Pro	Thr	Asn	Glu 205	Asn	Lys	His
Gly	Thr 210	Arg	Cys	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
Asp	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
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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
Asp	Leu 370	His	Asn	Asp	CÀa	Thr 375	Glu	Thr	His	Thr	Gly 380	Thr	Ser	Ala	Ser
Ala 385	Pro	Leu	Ala	Ala	Gly 390	Ile	Phe	Ala	Leu	Ala 395	Leu	Glu	Ala	Asn	Pro 400
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Tyr	Asp	Pro	Leu 420	Ala	Asn	Asn	Pro	Gly 425	Trp	ГЛа	ГЛа	Asn	Gly 430	Ala	Gly
Leu	Met	Val 435	Asn	Ser	Arg	Phe	Gly 440	Phe	Gly	Leu	Leu	Asn 445	Ala	Lys	Ala
Leu	Val 450	Asp	Leu	Ala	Asp	Pro 455	Arg	Thr	Trp	Arg	Ser 460	Val	Pro	Glu	Lys
Lys	Glu	Cys	Val	Val	Lys	Asp	Asn	Asp	Phe	Glu	Pro	Arg	Ala	Leu	Lys

465					470					475					480
Ala	Asn	Gly	Glu	Val 485	Ile	Ile	Glu	Ile	Pro 490	Thr	Arg	Ala	Сув	Glu 495	Gly
Gln	Glu	Asn	Ala 500	Ile	Lys	Ser	Leu	Glu 505	His	Val	Gln	Phe	Glu 510	Ala	Thr
Ile	Glu	Tyr 515	Ser	Arg	Arg	Gly	Asp 520	Leu	His	Val	Thr	Leu 525	Thr	Ser	Ala
Ala	Gly 530	Thr	Ser	Thr	Val	Leu 535	Leu	Ala	Glu	Arg	Glu 540	Arg	Asp	Thr	Ser
Pro 545	Asn	Gly	Phe	Lys	Asn 550	Trp	Asp	Phe	Met	Ser 555	Val	His	Thr	Trp	Gly 560
Glu	Asn	Pro	Ile	Gly 565	Thr	Trp	Thr	Leu	Arg 570	Ile	Thr	Asp	Met	Ser 575	Gly
Arg	Ile	Gln	Asn 580	Glu	Gly	Arg	Ile	Val 585	Asn	Trp	Lys	Leu	Ile 590	Leu	His
Gly	Thr	Ser 595	Ser	Gln	Pro	Glu	His 600	Met	Lys	Gln	Pro	Arg 605	Val	Tyr	Thr
Ser	Tyr 610	Asn	Thr	Val	Gln	Asn 615	Asp	Arg	Arg	Gly	Val 620	Glu	Lys	Met	Val
Asp 625	Pro	Gly	Glu	Glu	Gln 630	Pro	Thr	Gln	Glu	Asn 635	Pro	Lys	Glu	Asn	Thr 640
Leu	Val	Ser	Lys	Ser 645	Pro	Ser	Ser	Ser	Ser 650	Val	Gly	Gly	Arg	Arg 655	Asp
Glu	Leu	Glu	Glu 660	Gly	Ala	Pro	Ser	Gln 665	Ala	Met	Leu	Arg	Leu 670	Leu	Gln
Ser	Ala	Phe 675	Ser	Lys	Asn	Ser	Pro 680	Pro	Lys	Gln	Ser	Pro 685	Lys	ГÀа	Ser
Pro	Ser 690	Ala	Lys	Leu	Asn	Ile 695	Pro	Tyr	Glu	Asn	Phe 700	Tyr	Glu	Ala	Leu
Glu 705	Lys	Leu	Asn	Lys	Pro 710	Ser	Gln	Leu	Lys	Asp 715	Ser	Glu	Asp	Ser	Leu 720
Tyr	Asn	Asp	Tyr	Val 725	Asp	Val	Phe	Tyr	Asn 730	Thr	Lys	Pro	Tyr	Lys 735	His
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Asn															
-01/) - CI	EQ II	NIO	760											
		ENGTI													
		YPE : RGANI		Homo	sa <u>r</u>	piens	3								
< 400)> SI	EQUEI	ICE :	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	Thr	Leu 70		Gln	Gln	Ala	Asp 75		Leu	Ala	Gln	Ala 80

Ala Gly Leu Val Asn Ala Gly Arg Ile Gly Glu Leu Gln Gly His Tyr

			85					90					95	
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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 Asn 145	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 Asn 225	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	Cys	Ser	Trp
Gly Pro 290	Asp	Asp	Asp	Gly	Lys 295	Thr	Val	Asp	Gly	Pro 300	His	Gln	Leu	Gly
Lys Ala 305	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	335	Asn
Cys 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	CAa	Ala
Ser Met 370	Leu	Ala	Val	Thr	Phe 375	Ser	Gly	Gly	Asp	380 TÀa	Met	Leu	Arg	Ser
Ile Val 385	Thr	Thr	Asp	Trp 390	Asp	Leu	Gln	ГЛа	Gly 395	Thr	Gly	Сув	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	Cys 425	Leu	Thr	Trp	Arg	Asp 430	Val	Gln
His Ile	Ile 435	Val	Phe	Thr	Ala	Thr 440	Arg	Tyr	Glu	Asp	Arg 445	Arg	Ala	Glu
Trp Val 450	Thr	Asn	Glu	Ala	Gly 455	Phe	Ser	His	Ser	His 460	Gln	His	Gly	Phe
Gly Leu 465	Leu	Asn	Ala	Trp 470	Arg	Leu	Val	Asn	Ala 475	Ala	Lys	Ile	Trp	Thr 480
Ser Val	Pro	Tyr	Leu 485	Ala	Ser	Tyr	Val	Ser 490	Pro	Val	Leu	Lys	Glu 495	Asn
Lys Ala	Ile	Pro 500	Gln	Ser	Pro	Arg	Ser 505	Leu	Glu	Val	Leu	Trp 510	Asn	Val

Ser Arg Met Asp Leu Glu Met Ser Gly Leu Lys Thr Leu Glu His Val 520 Ala Val Thr Val Ser Ile Thr His Pro Arg Arg Gly Ser Leu Glu Leu 535 Lys Leu Phe Cys Pro Ser Gly Met Met Ser Leu Ile Gly Ala Pro Arg Ser Met Asp Ser Asp Pro Asn Gly Phe Asn Asp Trp Thr Phe Ser Thr 570 Val Arg Cys Trp Gly Glu Arg Ala Arg Gly Thr Tyr Arg Leu Val Ile Arg Asp Val Gly Asp Glu Ser Phe Gln Val Gly Ile Leu Arg Gln Trp Gln Leu Thr Leu Tyr Gly Ser Val Trp Ser Ala Val Asp Ile Arg Asp Arg Gln Arg Leu Leu Glu Ser Ala Met Ser Gly Lys Tyr Leu His Asp 630 635 Asp Phe Ala Leu Pro Cys Pro Pro Gly Leu Lys Ile Pro Glu Glu Asp 650 645 Gly Tyr Thr Ile Thr Pro Asn Thr Leu Lys Thr Leu Val Leu Val Gly 665 Cys Phe Thr Val Phe Trp Thr Val Tyr Tyr Met Leu Glu Val Tyr Leu 680 Ser Gln Arg Asn Val Ala Ser Asn Gln Val Cys Arg Ser Gly Pro Cys 695 His Trp Pro His Arg Ser Arg Lys Ala Lys Glu Glu Gly Thr Glu Leu 710 715 Glu Ser Val Pro Leu Cys Ser Ser Lys Asp Pro Asp Glu Val Glu Thr Glu Ser Arg Gly Pro Pro Thr Thr Ser Asp Leu Leu Ala Pro Asp Leu 745 Leu Glu Gln Gly Asp Trp Ser Leu Ser Gln Asn Lys Ser Ala Leu Asp 760 Cys Pro His Gln His Leu Asp Val Pro His Gly Lys Glu Glu Gln Ile Cys <210> SEQ ID NO 761 <211> LENGTH: 692 <212> TYPE: PRT <213> ORGANISM: Macaca fascicularis <400> SEQUENCE: 761 Met Gly Thr Val Ser Ser Arg Arg Ser Trp Trp Pro Leu Pro Leu Pro 10 Leu Leu Leu Leu Leu Gly Pro Ala Gly Ala Arg Ala Gln Glu 25 Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu 40 Glu Asp Gly Leu Ala Asp Ala Pro Glu His Gly Ala Thr Ala Thr Phe His Arg Cys Ala Lys Asp Pro Trp Arg Leu Pro Gly Thr Tyr Val Val Val Leu Lys Glu Glu Thr His Arg Ser Gln Ser Glu Arg Thr Ala Arg

				85					90					95	
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His	Val	Phe		His	Leu	Leu	Pro 120		Phe	Leu	Val	Lys 125		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
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Pro	Glu 210	Glu	Asp	Gly	Thr	Arg 215	Phe	His	Arg	Gln	Ala 220	Ser	Lys	Cys	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
Gly	Lys	Gly	Thr 260	Val	Ser	Gly	Thr	Leu 265	Ile	Gly	Leu	Glu	Phe 270	Ile	Arg
_	Ser	275					280	_				285			
Leu	Ala 290	Gly	Gly	Tyr	Ser	Arg 295	Val	Phe	Asn	Ala	Ala 300	CÀa	Gln	Arg	Leu
Ala 305	Arg	Ala	Gly	Val	Val 310	Leu	Val	Thr	Ala	Ala 315	Gly	Asn	Phe	Arg	Asp 320
	Ala			325					330					335	
	Ala		340					345					350		
	Asn	355		_	-		360					365		_	
	Gly 370					375			-		380		_		
385	Ser				390					395					400
	Ala			405					410		_		_	415	
	Phe		420	-	-			425			-		430		-
	Arg	435					440					445			
His	Arg 450	Ala	Gly	Trp	Gln	Leu 455	Phe	Сув	Arg	Thr	Val 460	Trp	Ser	Ala	His
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Asn	Ala	Phe 515	Gly	Gly	Glu	Gly	Val 520	Tyr	Ala	Ile	Ala	Arg 525	Cys	Cya	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	Сла	His	Gln	Gln 555	Gly	His	Val	Leu	Thr 560
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Glu	Ala	Ser 595	Ile	His	Ala	Ser	Cys	Сла	His	Ala	Pro	Gly 605	Leu	Glu	СЛа
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Ala	Ala	Val 675	Ala	Ile	Cys	Cys	Arg 680	Ser	Arg	His	Leu	Val 685	Gln	Ala	Ser
Gln	Glu 690	Leu	Gln												
)> SE		ои о												
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<211 <212 <213 <400 Met 1 Leu Glu Asp Ala 65 Ile Met Ile	1> LH 2> TY 3> OF Gly Leu Asp Gly 50 Phe Val	YPE: RGAN: CQUENT Thr Leu Ala 35 Leu His Met Arg	PRT ISM: ISM: Ser Leu 20 Glu Ala Arg Leu Leu 100 Ile	Meso 762 Cys 5 Leu Tyr Asp Cys Ala 85 Gln	Ser Leu Glu Glu Pro 70 Glu Thr	Ala Leu Glu Thr 55 Glu Glu	Arg Leu 40 Asp Glu Ala Ala Phe 120	Pro Tyr 25 Met Glu Ala Gln Ala 105 Leu	Arg 10 Met Leu Ala Trp Trp 90 Arg	Gly Thr Pro Arg 75 Val Arg	Ala Leu Gln 60 Val His Gly	Ser Gln 45 Gly Pro Ile Tyr Val	Ala 30 Ser Ala Gly Glu Val	15 Gln Gln Thr Thr Ile Lys	Asp Ala Tyr 80 Thr Lys Met
<211 <212 <213 <400 Met 1 Leu Glu Asp Ala 65 Ile Met Ile Ser	l> LH 2> TY 3> OF Gly Leu Asp Gly 50 Phe Val His Gln	YPE: RGAN: CQUENT Thr Leu Ala 35 Leu His Met Arg His 115	PRT ISM: ISM: Ser Leu 20 Glu Ala Arg Leu 100 Ile Leu	Meson Meson 762 Cys 5 Leu Tyr Asp Cys Ala 85 Gln Phe Leu	Ser Leu Glu Glu Pro 70 Glu Thr Tyr	Ala Leu Glu Thr 55 Glu Glu Gln Asp Leu 135	Arg Leu 40 Asp Glu Ala Ala Phe 120 Ala	Pro Tyr 25 Met Glu Ala Gln Ala 105 Leu Leu	Arg 10 Met Leu Ala Trp 90 Arg Pro	Gly Thr Pro Arg 75 Val Arg Ala	Ala Leu Gln 60 Val His Gly Phe	Ser Gln 45 Gly Pro Ile Tyr Val 125 His	Ala 30 Ser Ala Gly Glu Val 1100	15 Gln Gln Thr Thr Lys Lys	Asp Ala Tyr 80 Thr Lys Met
<211 <212 <213 <400 Met 1 Leu Glu Asp Ala 65 Ile Met Ile Ser Ile 145	l> LH 2> TY 3> OF Gly Leu Asp Gly 50 Phe Val His Gln Ser 130 Glu	YPE: CQUENT Thr Leu Ala 35 Leu His Met Arg His 115 Asp	PRT ISM: ISM: Ser Leu 20 Glu Ala Arg Leu 100 Ile Leu Asp	Mesor 762 Cys 5 Leu Tyr Asp Cys Gln Phe Leu Ser	Ser Leu Glu Glu Pro 70 Glu Thr Tyr Asp Leu 150	Ala Leu Glu Thr 55 Glu Glu Gln Asp Leu 135	Arg Leu 40 Asp Glu Ala Ala Phe 120 Ala	Pro Tyr 25 Met Glu Ala Gln Ala 105 Leu Leu Ala	Arg 10 Met Leu Ala Trp Trp 90 Arg Pro Lys Gln	Gly Thr Pro Arg 75 Val Arg Ala Leu Ser 155	Ala Leu Gln 60 Val His Gly Phe Pro 140 Ile	Ser Gln 45 Gly Pro Ile Tyr Val 125 His	Ala 30 Ser Ala Gly Glu Val 110 Val	15 Gln Gln Thr Thr Gln 95 Lys Lys Asn	Asp Asp Ala Tyr 80 Thr Lys Met Tyr Leu 160
<211 < 212 < 213 < 400 Met 1 Leu Glu Asp Ala 65 Ile Met Ile Ser Ile 145 Asp	l> LH 2> TY 3> OF Gly Leu Asp Gly 50 Phe Val His Gln Ser 130 Glu Arg	CYPE: CGAN: CQUENT Thr Leu Ala 35 Leu His Arg His 115 Asp Glu Ile	PRT [SM: ISM: ISM: ISM: ISM: ISM: ISM: ISM: I	Mesor 762 Cys 5 Leu Tyr Asp Cys Ala 85 Gln Phe Leu Ser Pro 165	Ser Leu Glu Glu Pro 70 Glu Thr Tyr Asp Leu 150 Ala	Ala Leu Glu Thr 55 Glu Glu Gln Asp Leu 135 Val	Arg Leu 40 Asp Glu Ala Phe 120 Ala Phe	Pro Tyr 25 Met Glu Ala Gln Ala 105 Leu Leu Ala Gln	Arg 10 Met Leu Ala Trp 90 Arg Pro Lys Gln Ala 170	Gly Thr Pro Arg 75 Val Arg Ala Leu Ser 155 Gln	Ala Leu Gln 60 Val His Gly Phe Ile Glu	Ser Gln 45 Gly Pro Ile Tyr Val 125 His Pro	Ala 30 Ser Ala Gly Glu Val 110 Val Trp	15 Gln Gln Thr Thr Gln 95 Ile Lys Asn Ser 175	Asp Asp Ala Tyr 80 Thr Lys Met Tyr Leu 160 Ser

Thr	Ser	Ile 195	Gln	Ser	Asp	His	Arg 200	Glu	Ile	Glu	Gly	Arg 205	Val	Thr	Val
Thr	Asp 210	Phe	Asn	Ser	Val	Pro 215	Glu	Glu	Asp	Gly	Thr 220	Arg	Phe	His	Arg
Gln 225	Ala	Ser	Lys	Cys	Asp 230	Ser	His	Gly	Thr	His 235	Leu	Ala	Gly	Val	Val 240
Ser	Gly	Arg	Asp	Ala 245	Gly	Val	Ala	Lys	Gly 250	Thr	Ile	Leu	His	Gly 255	Leu
Arg	Val	Leu	Asn 260	Сув	Gln	Gly	Lys	Gly 265	Ile	Val	Ser	Gly	Ile 270	Leu	Thr
Gly	Leu	Glu 275	Phe	Ile	Trp	Lys	Ser 280	Gln	Leu	Met	Gln	Pro 285	Ser	Gly	Pro
Gln	Val 290	Val	Leu	Leu	Pro	Leu 295	Ala	Gly	Arg	Tyr	Ser 300	Arg	Val	Leu	Asn
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	Cys	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	Cys	Val 365	Asp	Leu	Phe
Ala	Pro 370	Gly	Lys	Asp	Ile	Ile 375	Gly	Ala	Ser	Ser	380	CÀa	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	Gln	Arg 420	Leu	Ile	His	Phe	Ser 425	Thr	Lys	Asp	Ala	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	CAa	Arg
Thr 465	Val	Trp	Ser	Ala	His 470	Ser	Gly	Pro	Thr	Arg 475	Ala	Ala	Thr	Ala	Thr 480
Ala	Arg	Сув	Ala	Pro 485	Gly	Glu	Glu	Leu	Leu 490	Ser	Cys	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	Cys	Cys	Leu	Leu 535	Pro	Arg	Ala	Asn	Cys 540	Ser	Ile	His	Thr
Thr 545	Pro	Ala	Ala	Arg	Thr 550	Ser	Leu	Glu	Thr	His 555	Ala	His	Сув	His	Gln 560
Lys	Asp	His	Val	Leu 565	Thr	Gly	Сла	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	СЛв	СЛв	His

Ala Pro Gly Leu Glu Cys Lys Ile Lys Glu His Gly Ile Ser Gly Pro 615 Ala Glu Gln Val Thr Val Ala Cys Glu Ala Gly Trp Thr Leu Thr Gly Cys Asn Val Leu Pro Gly Ala Phe Ile Thr Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Ala Arg Ser Arg Val Thr Asp Thr Ala Gly Arg Thr Gly Glu Glu Ala Thr Val Ala Ala Ala Ile Cys Cys Arg Asn Arg Pro Ser Ala Lys Ala Ser Trp Val His Gln <210> SEQ ID NO 763 <211> LENGTH: 691 <212> TYPE: PRT <213> ORGANISM: Rattus norvegicus <400> SEQUENCE: 763 Met Gly Ile Arg Cys Ser Thr Trp Leu Arg Trp Pro Leu Ser Pro Gln 10 Leu Leu Leu Leu Leu Cys Pro Thr Gly Ser Arg Ala Gln Asp 25 Glu Asp Gly Asp Tyr Glu Glu Leu Met Leu Ala Leu Pro Ser Gln Glu Asp Ser Leu Val Asp Glu Ala Ser His Val Ala Thr Ala Thr Phe Arg Arg Cys Ser Lys Glu Ala Trp Arg Leu Pro Gly Thr Tyr Val Val Val 70 Leu Met Glu Glu Thr Gln Arg Leu Gln Val Glu Gln Thr Ala His Arg Leu Gln Thr Trp Ala Ala Arg Arg Gly Tyr Val Ile Lys Val Leu His Val Phe Tyr Asp Leu Phe Pro Gly Phe Leu Val Lys Met Ser Ser Asp 120 Leu Leu Gly Leu Ala Leu Lys Leu Pro His Val Glu Tyr Ile Glu Glu Asp Ser Leu Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg Ile Ile Pro Ala Trp Gln Gln Thr Glu Glu Asp Ser Ser Pro Asp Gly Ser Ser Gln Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Gly His 185 Arg Glu Ile Glu Gly Arg Val Thr Ile Thr Asp Phe Asn Ser Val Pro 200 Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly Val 230 235 Ala Lys Gly Thr Ser Leu His Ser Leu Arg Val Leu Asn Cys Gln Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg Lys 265 Ser Gln Leu Ile Gln Pro Ser Gly Pro Leu Val Val Leu Leu Pro Leu 280 285

												COII	CIII	ueu	
Ala	Gly 290	Gly	Tyr	Ser	Arg	Ile 295	Leu	Asn	Thr	Ala	300 Cys	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	CAa	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	CAa	Val	Asp	Leu 360	Phe	Ala	Pro	Gly	Lys 365	Asp	Ile	Ile
Gly	Ala 370	Ser	Ser	Asp	Cys	Ser 375	Thr	Сув	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		Thr	Arg	Thr	Ala 470	Thr	Ala	Thr	Ala	Arg 475	Сув	Ala	Pro	Glu	Glu 480
Glu	Leu	Leu	Ser	Cys 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	Cys	Lys	Ala 510	Leu	Asn
Ala	Phe	Gly 515	Gly	Glu	Gly	Val	Tyr 520	Ala	Val	Ala	Arg	Сув 525	Cys	Leu	Leu
Pro	Arg 530	Val	Asn	Сув	Ser	Ile 535	His	Asn	Thr	Pro	Ala 540	Ala	Arg	Ala	Gly
Pro 545	Gln	Thr	Pro	Val	His 550	Сув	His	Gln	Lys	Asp 555	His	Val	Leu	Thr	Gly 560
Cys	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	CAa	Val	Gly	His 590	Gln	Glu
Ala	Ser	Val 595	His	Ala	Ser	СЛв	Cys		Ala	Pro	Gly	Leu 605	Glu	Сув	Lys
Ile	Lys 610	Glu	His	Gly	Ile	Ala 615	Gly	Pro	Ala	Glu	Gln 620	Val	Thr	Val	Ala
Cys 625	Glu	Ala	Gly	Trp	Thr	Leu	Thr	Gly	CÀa	Asn 635	Val	Leu	Pro	Gly	Ala 640
Ser	Leu	Pro	Leu	Gly 645	Ala	Tyr	Ser	Val	Asp 650	Asn	Val	Cys	Val	Ala 655	Arg
Ile	Arg	Asp	Ala 660		Arg	Ala	Asp	Arg 665		Ser	Glu	Glu	Ala 670		Val
Ala	Ala			Сув	Cys	Arg			Pro	Ser	Ala	_	Ala	Ser	Trp
Val	His	675 Gln					680					685			
	690														

We claim:

- 1. A method for treating a subject selected from the group consisting of: a subject indicated for LDL apheresis, a subject with a PCSK9 gain of function mutation, and a subject with primary hypercholesterolemia who is statin intolerant or statin uncontrolled, the method comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising an antibody or antigen-binding fragment thereof which specifically binds hPCSK9, wherein the antibody or antigen-binding fragment comprises the heavy and light chain CDRs of a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs:90/92 and 218/226.
- 2. The method of claim 1, wherein the antibody or antigen-binding fragment comprises heavy and light chain CDR amino acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232.
- 3. The method of claim 2, wherein the antibody or antigen-binding fragment comprises an HCVR having the amino acid sequence of SEQ ID NO:218 and an LCVR having the amino acid sequence of SEQ ID NO:226.
- **4.** The method of claim **1**, wherein the antibody or antigen-binding fragment comprises heavy and light chain CDR amino acid sequences having SEQ ID NOs:76, 78, 80, 84, 86 and 88.

464

- **5**. The method of claim **4**, wherein the antibody or antigen-binding fragment comprises an HCVR having the amino acid sequence of SEQ ID NO:90 and an LCVR having the amino acid sequence of SEQ ID NO:92.
- 6. The method of claim 1, wherein the antibody or antigen-binding fragment binds to the same epitope on hPCSK9 as an antibody comprising heavy and light chain CDR amino acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232; or SEQ ID NOs: 76, 78, 80, 84, 86 and 88.
- 7. The method of claim 1, wherein the antibody or antigen-binding fragment competes for binding to hPCSK9 with an antibody comprising heavy and light chain CDR amino acid sequences having SEQ ID NOs:220, 222, 224, 228, 230 and 232; or SEQ ID NOs: 76, 78, 80, 84, 86 and 88
- **8**. The method of claim **1**, wherein the subject has familial hypercholesterolemia (FH).
- 9. The method of claim 8, wherein the familial hyperc-20 holesterolemia is heterozygous familial hypercholesterolemia (heFH).
 - 10. The method of claim 8, wherein the familial hypercholesterolemia is homozygous familial hypercholesterolemia (hoFH).

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